Table 2_JMDC Baseline Demographics VTE Cohorts, Matched [JMDC]

	Baricitinib			TNFi (N = 213)	Std. Diff. (Any vs TNFi)	Total (N = 426)
	Any (N = 213)	4 mg (N = 121)	2 mg (N = 92)			
Age [yrs]						
n	213	121	92	213		426
Mean (SD)	51.55 (10.20)	50.96 (9.97)	52.34 (10.50)	51.66 (10.48)	0.01	51.61 (10.33)
Median	53.00 [46.00, 58.50]	52.00 [44.50, 58.00]	53.00 [47.00, 59.00]	53.00 [46.00, 59.00]		53.00 [46.00, 59.00]
Min, Max	19.0, 74.0	23.0, 72.0	19.0, 74.0	21.0, 72.0		19.0, 74.0
≥65 years	15 (7.0%)	6 (5.0%)	9 (9.8%)	21 (9.9%)	0.10	36 (8.5%)
Sex						
Male	44 (20.7%)	20 (16.5%)	24 (26.1%)	51 (23.9%)	0.08	95 (22.3%)
Female	169 (79.3%)	101 (83.5%)	68 (73.9%)	162 (76.1%)	0.08	331 (77.7%)

Abbreviations: JMDC = JMDC, Inc's claims database; Max = maximum; Min = minimum; N = count of patients in the specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus; VTE = venous thromboembolism.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\jmdc_JMDC\3. Table 6.2. - Baseline Demographics VTE Cohorts, Matched [Japanese Medical Data Center Payer-Based].docx

Table 7_JMDC Clinical Characteristics Primary VTE Cohorts, Matched [JMDC]

Characteristic[a,b]	Baricitinib[c] Any (N = 213)	Baricitinib[c] 2 mg (N = 92)	Baricitinib[c] 4 mg (N = 121)	TNFi (N = 213)	Std. Diff.
Clinical Conditions during baseline					
Cancer	9 (4.2%)	4 (4.3%)	5 (4.1%)	8 (3.8%)	0.02
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Chronic lung disease	33 (15.5%)	9 (9.8%)	24 (19.8%)	20 (9.4%)	0.19
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	1 (0.5%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0.10
Cardiovascular revascularization	1 (0.5%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0.10
Congestive heart failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0.10
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Unstable angina	1 (0.5%)	0 (0.0%)	1 (0.8%)	2 (0.9%)	0.06
Ventricular arrhythmia	1 (0.5%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0.10
Diabetes Mellitus	6 (2.8%)	1 (1.1%)	5 (4.1%)	4 (1.9%)	0.06
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.9%)	0.14
Type II	6 (2.8%)	1 (1.1%)	5 (4.1%)	2 (0.9%)	0.14
Dyslipidaemia	16 (7.5%)	9 (9.8%)	7 (5.8%)	14 (6.6%)	0.04
Hypertension	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0.10
Immune disorders	14 (6.6%)	8 (8.7%)	6 (5.0%)	13 (6.1%)	0.02
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Antiphospholipid syndrome	NA	NA	NA	NA	NA
SLE	11 (5.2%)	6 (6.5%)	5 (4.1%)	4 (1.9%)	0.18
Primary Sjögren syndrome	7 (3.3%)	4 (4.3%)	3 (2.5%)	9 (4.2%)	0.05
Liver disorder	3 (1.4%)	3 (3.3%)	0 (0.0%)	1 (0.5%)	0.10
Obesity	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
RA severity (CIRAS Index), mean (SD)	6.59 (1.30)	6.42 (1.42)	6.72 (1.19)	6.57 (1.27)	0.02
Smoking[d]	9 (4.2%)	5 (5.4%)	4 (3.3%)	11 (5.2%)	0.04
Surgery, trauma & hospitalization, recent	19 (8.9%)	7 (7.6%)	12 (9.9%)	21 (9.9%)	0.03
TIA	1 (0.5%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0.10
DMARDs					
cDMARDs, during baseline					
n, total	180 (84.5%)	78 (84.8%)	102 (84.3%)	181 (85.0%)	0.01
Mean (SD)	1.01 (0.58)	1.02 (0.57)	1.01 (0.58)	1.03 (0.58)	0.02
Median	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	-
Min, Max	0.0, 3.0	0.00, 2.00	0.00, 2.00	0.0, 3.0	-

Characteristic[a,b]	Baricitinib[c] Any (N = 213)	Baricitinib[c] 2 mg (N = 92)	Baricitinib[c] 4 mg (N = 121)	TNFi (N = 213)	Std. Diff.
Clinical Conditions during baseline					
>1 cDMARD concomitantly	35 (16.4%)	16 (17.4%)	19 (15.7%)	37 (17.4%)	0.03
Hydroxychloroquine	2 (0.9%)	0 (0.0%)	2 (1.7%)	3 (1.4%)	0.04
Leflunomide	3 (1.4%)	3 (3.3%)	0 (0.0%)	1 (0.5%)	0.10
Methotrexate	160 (75.1%)	65 (70.7%)	95 (78.5%)	158 (74.2%)	0.02
Minocycline	2 (0.9%)	1 (1.1%)	1 (0.8%)	6 (2.8%)	0.14
Sulfasalazine	38 (17.8%)	19 (20.7%)	19 (15.7%)	46 (21.6%)	0.10
bDMARDs, during baseline[a]					
n, total	106 (49.8%)	40 (43.5%)	66 (54.5%)	108 (50.7%)	0.02
Mean (SD)	0.54 (0.59)	0.48 (0.58)	0.60 (0.59)	0.54 (0.57)	0.00
Median	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-
Min, Max	0.0, 2.0	0.00, 2.00	0.00, 2.00	0.0, 2.0	-
cDMARDs, concomitant	78 (36.6%)	31 (33.7%)	47 (38.8%)	84 (39.4%)	0.06
abatacept	18 (8.5%)	7 (7.6%)	11 (9.1%)	26 (12.2%)	0.12
adalimumab[e]	6 (2.8%)	2 (2.2%)	4 (3.3%)	9 (4.2%)	0.08
anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
certolizumab pegol[e]	6 (2.8%)	3 (3.3%)	3 (2.5%)	2 (0.9%)	0.14
etanercept[e]	22 (10.3%)	8 (8.7%)	14 (11.6%)	14 (6.6%)	0.14
golimumab[e]	13 (6.1%)	2 (2.2%)	11 (9.1%)	5 (2.3%)	0.19
infliximab[e]	1 (0.5%)	0 (0.0%)	1 (0.8%)	17 (8.0%)	0.38
rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
sarilumab	9 (4.2%)	2 (2.2%)	7 (5.8%)	4 (1.9%)	0.14
tocilizumab	41 (19.2%)	20 (21.7%)	21 (17.4%)	39 (18.3%)	0.02
Other Prescription Medications					
Antibiotics	70 (32.9%)	32 (34.8%)	38 (31.4%)	82 (38.5%)	0.12
Antidiabetic agents	13 (6.1%)	8 (8.7%)	5 (4.1%)	16 (7.5%)	0.06
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (2.8%)	0.24
Non-insulins	13 (6.1%)	8 (8.7%)	5 (4.1%)	11 (5.2%)	0.04
Aspirin	2 (0.9%)	0 (0.0%)	2 (1.7%)	3 (1.4%)	0.04
Cardiovascular					
Anticoagulant	5 (2.3%)	1 (1.1%)	4 (3.3%)	2 (0.9%)	0.11
Antihypertensives	49 (23.0%)	25 (27.2%)	24 (19.8%)	42 (19.7%)	0.08
Antiplatelet	14 (6.6%)	7 (7.6%)	7 (5.8%)	11 (5.2%)	0.06
Nitrates	2 (0.9%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0.14
Hormonal					
HRT	7 (3.3%)	3 (3.3%)	4 (3.3%)	4 (1.9%)	0.09
Oral Contraceptives	NA	NA	NA	NA	NA
SERMs	4 (1.9%)	3 (3.3%)	1 (0.8%)	5 (2.3%)	0.03

Characteristic[a,b]	Baricitinib[c] Any (N = 213)	Baricitinib[c] 2 mg (N = 92)	Baricitinib[c] 4 mg (N = 121)	TNFi (N = 213)	Std. Diff.
Clinical Conditions during baseline					
Lipid-lowering agents					
Bile acid binding	1 (0.5%)	0 (0.0%)	1 (0.8%)	1 (0.5%)	0.00
Cholesterol absorption inhibitor	4 (1.9%)	1 (1.1%)	3 (2.5%)	1 (0.5%)	0.13
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.9%)	0.14
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Omega-3 fatty acids	2 (0.9%)	1 (1.1%)	1 (0.8%)	1 (0.5%)	0.06
Statins	25 (11.7%)	16 (17.4%)	9 (7.4%)	28 (13.1%)	0.04
Rheumatoid arthritis-related					
Cox-2 Inhibitor	70 (32.9%)	24 (26.1%)	46 (38.0%)	61 (28.6%)	0.09
Glucocorticosteroid	131 (61.5%)	57 (62.0%)	74 (61.2%)	133 (62.4%)	0.02
Vaccinations	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	0.10

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARDs = biologic disease-modifying antirheumatic drugs; cDMARDs = conventional disease-modifying antirheumatic drugs; CIRAS = Claims-Based Index for RA Severity; DMARDs = disease-modifying antirheumatic drugs; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; JMDC = Japanese Medical Data Center, Inc's claims database; Max = maximum; Min = minimum; N = count of patients in the specified category; NA = not applicable; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SLE = systemic lupus erythematosus; Std. Diff = standardised difference; SERM = selective oestrogen receptor modifier; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] All conditions and characteristics, except for bDMARDs, are measured during the 6 months prior to initiation of study medication including the date at which the qualifying exposure of baricitinib or TNFi occurs (index date). bDMARDs are measured from the 6 months prior to the initiation of study medication until the day prior to baricitinib or the index TNFi exposure, excluding the index date.

[b] Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 (see Section 8.3.3, Annex 19) for each outcome (eg, hospitalized congestive heart failure) for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias (eg, Type I diabetes) for VTE.

[c] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose when numbers of patients are sufficient to warrant separate reporting.

[d] In JMDC data, smoking was defined based on information recorded in the variable "Annual health checkup – Smoking habit".

[e] TNFi.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\jmdc_JMDC\3. Table 6.7. - Clinical Characteristics Primary VTE Cohorts, Matched [Japanese Medical Data Center Payer-Based].docx

Table 12B_JMDC Baseline Healthcare Resource Utilisation Primary VTE Cohorts, Matched [JMDC], Count at Most 1 Visit per Day

Type of Resource Use	Baricitinib (N = 213)	TNFi (N = 213)	Std. Diff.
Physician Office Visits[a]			
n, patients	141 (66.2%)	143 (67.1%)	0.02
n, events	311	294	
Mean (SD)	1.46 (1.56)	1.38 (1.39)	0.05
Median	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	
Min, Max	0.0, 8.0	0.0, 6.0	
Rheumatologist Visits[a]			
n, patients	18 (8.5%)	18 (8.5%)	0.00
n, events	45	41	
Mean (SD)	0.21 (0.92)	0.19 (0.84)	0.02
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 7.0	0.0, 7.0	
Other Outpatient Visits[a]			
n, patients	213 (100.0%)	213 (100.0%)	0
n, events	2,967	2,895	
Mean (SD)	13.93 (11.21)	13.59 (10.09)	0.03
Median	11.00 [7.00, 17.50]	11.00 [7.00, 17.00]	
Min, Max	2.0, 113.0	2.0, 90.0	
Inpatient Visits[a]			
n, patients	27 (12.7%)	29 (13.6%)	0.03
n, events	268	330	
Mean (SD)	1.26 (4.66)	1.55 (5.72)	0.06
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 38.0	0.0, 48.0	
ED Visits[b]			
n, patients	-	-	-
n, events	-	-	-
Mean (SD)	- (-)	- (-)	
Median	- [-, -]	- [-, -]	
Min, Max	-, -	-, -	

Abbreviations: ED = emergency department; JMDC = Japanese Medical Data Center, Inc's claims database; Max = maximum; Min = minimum; n = number of patients within each specific category; PS = propensity score; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] In this table, results describe the utilisation of healthcare where a maximum of 1 event was allowed per day. In the PS-matching analyses, multiple claims on the same day were allowed to capture additional information on the amount of services received in a given visit. These results are presented in Table 12A_JMDC.

[b] Type(s) of healthcare encounter(s) not applicable to the JMDC.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\jmdc_JMDC\3. Table 6.12B (count at most 1 visit per day). Baseline Healthcare Resource Utilisation Primary VTE Cohorts, Matched [Japanese Medical Data Center Payer-Based].docx

10.2.2.5.2. MACE

After propensity score matching, there were a total of 448 patients (224 each in the any baricitinib and TNFi cohorts) included in the analysis of MACE (Table 3_JMDC). Within the baricitinib cohort, 131 patients recorded 4 mg and 93 recorded 2 mg. On average, patients analysed were aged 51.57 years at baseline (range 19 to 74 years) and were majority (81.9%) female. After propensity score matching, patients treated with any baricitinib were similar in terms of demographics and other characteristics compared to the TNFi cohort (standardised differences <0.10).

Clinical characteristics of patients at baseline are described in Table 8_JMDC. Patients within the JMDC had a much lower burden of comorbidity compared to other data sources (US and European). Noting the lower overall prevalence, the most commonly observed conditions with at least 10 total cases were chronic lung disease (any baricitinib 15.6%, TNFi 9.8%), dyslipidaemia (any baricitinib 8%, TNFi 7.1%), diabetes (any baricitinib 2.7%, TNFi 1.8%), and cancer (any baricitinib 3.6%, TNFi 5.8%). No smokers were identified with the definition used in other insurance claims databases (see Section 9.4.3), so smoking in the clinical characteristics table below is defined based on the variable “Annual health checkup – Smoking habit”. Regarding RA severity, the CIRAS score was similar across treatments (baricitinib 6.56, TNFi 6.43).

RA treatment received prior to the index medication is described in Table 8_JMDC. The vast majority of patients used cDMARDs (any baricitinib 82.6%, TNFi 79.9%), with methotrexate recorded most frequently (any baricitinib 72.8%, TNFi 71%). The same proportion of patients treated with baricitinib and TNFi (14.7%) recorded use of >1 concomitant cDMARD. Proportion of patients with prior use of bDMARDs was similar in the baricitinib and TNFi cohorts (any baricitinib 51.3%, TNFi 51.8%). Tocilizumab was the most frequently recorded prior bDMARD (18.8% in both the any baricitinib and TNFi cohorts).

Baseline healthcare resource utilisation was generally similar across the baricitinib and TNFi cohorts in the JMDC (Table 13B_JMDC); however, patients treated with baricitinib tended to have more rheumatologist visits. Note that the table reports visit days per patient (ie, at most 1 visit per day, but the propensity scores model controlled for the total number of visits during the period (ie, more than one visit; see Table 13A in Annex 15) could occur per day.

Table 3_JMDC Baseline Demographics MACE Cohorts, Matched [JMDC]

	Baricitinib			TNFi (N = 224)	Std. Diff. (Any vs TNFi)	Total (N = 448)
	Any (N = 224)	4 mg (N = 131)	2 mg (N = 93)			
Age [yrs]						
n	224	131	93	224		448
Mean (SD)	51.78 (9.92)	51.73 (9.63)	51.84 (10.37)	51.37 (10.12)	0.04	51.57 (10.01)
Median	53.00 [46.00, 59.00]	53.00 [45.00, 59.00]	52.00 [47.00, 58.50]	52.00 [46.00, 58.00]		52.00 [46.00, 59.00]
Min, Max	19.0, 74.0	23.0, 72.0	19.0, 74.0	23.0, 72.0		19.0, 74.0
≥65 years	16 (7.1%)	7 (5.3%)	9 (9.7%)	19 (8.5%)	0.05	35 (7.8%)
Sex						
Male	44 (19.6%)	22 (16.8%)	22 (23.7%)	37 (16.5%)	0.08	81 (18.1%)
Female	180 (80.4%)	109 (83.2%)	71 (76.3%)	187 (83.5%)	0.08	367 (81.9%)

Abbreviations: JMDC = JMDC, Inc's claims database; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; Max = maximum; Min = minimum; N = count of patients in the specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\jmdc_JMDC\3. Table 6.3. - Baseline Demographics MACE Cohorts, Matched [Japanese Medical Data Center Payer-Based].docx

Table 8_JMDC Clinical Characteristics MACE Cohorts, Matched [JMDC]

	Baricitinib[c]			TNFi	
Characteristic[a,b]	Any (N = 224)	2 mg (N = 93)	4 mg (N = 131)	(N = 224)	Std. Diff.
Clinical conditions during baseline					
Cancer	8 (3.6%)	3 (3.2%)	5 (3.8%)	13 (5.8%)	0.11
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Chronic lung disease	35 (15.6%)	10 (10.8%)	25 (19.1%)	22 (9.8%)	0.18
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	1 (0.4%)	0 (0.0%)	1 (0.8%)	2 (0.9%)	0.10
Cardiovascular revascularization	1 (0.4%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0.10
Congestive heart failure, hospitalised	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.4%)	0.10
Coronary artery disease	1 (0.4%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0.10
Ischemic heart disease	1 (0.4%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0.10
Unstable angina	1 (0.4%)	0 (0.0%)	1 (0.8%)	1 (0.4%)	0.00
Ventricular arrhythmia	1 (0.4%)	0 (0.0%)	1 (0.8%)	1 (0.4%)	0.00
Diabetes Mellitus	6 (2.7%)	0 (0.0%)	6 (4.6%)	4 (1.8%)	0.06
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.4%)	0.10
Type II	6 (2.7%)	0 (0.0%)	6 (4.6%)	3 (1.3%)	0.10

Characteristic[a,b]	Baricitinib[c] Any (N = 224)	Baricitinib[c] 2 mg (N = 93)	Baricitinib[c] 4 mg (N = 131)	TNFi (N = 224)	Std. Diff.
Dyslipidaemia	18 (8.0%)	8 (8.6%)	10 (7.6%)	16 (7.1%)	0.03
Hypertension	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Immune disorders	14 (6.2%)	7 (7.5%)	7 (5.3%)	8 (3.6%)	0.12
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Antiphospholipid syndrome	NA	NA	NA	NA	NA
SLE	11 (4.9%)	6 (6.5%)	5 (3.8%)	5 (2.2%)	0.15
Primary Sjögren syndrome	7 (3.1%)	3 (3.2%)	4 (3.1%)	3 (1.3%)	0.12
Liver disorder	2 (0.9%)	2 (2.2%)	0 (0.0%)	2 (0.9%)	0.00
Obesity	1 (0.4%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0.10
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
RA severity (CIRAS Index), mean (SD)	6.56 (1.27)	6.42 (1.38)	6.66 (1.18)	6.43 (1.31)	0.10
Smoking[e]	10 (4.5%)	5 (5.4%)	5 (3.8%)	10 (4.5%)	0.00
Surgery, trauma & hospitalization, recent	24 (10.7%)	7 (7.5%)	17 (13.0%)	17 (7.6%)	0.11
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.02
DMARDs					
cDMARDs, during baseline					
n, total	185 (82.6%)	77 (82.8%)	108 (82.4%)	179 (79.9%)	0.07
Mean (SD)	0.98 (0.58)	0.99 (0.58)	0.97 (0.58)	0.96 (0.64)	0.02
Median	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	-
Min, Max	0.0, 3.0	0.00, 2.00	0.00, 3.00	0.0, 4.0	-
>1 cDMARD concomitantly	33 (14.7%)	15 (16.1%)	18 (13.7%)	33 (14.7%)	0.00
Hydroxychloroquine	2 (0.9%)	0 (0.0%)	2 (1.5%)	2 (0.9%)	0.00
Leflunomide	3 (1.3%)	3 (3.2%)	0 (0.0%)	1 (0.4%)	0.10
Methotrexate	163 (72.8%)	64 (68.8%)	99 (75.6%)	159 (71.0%)	0.04
Minocycline	2 (0.9%)	1 (1.1%)	1 (0.8%)	7 (3.1%)	0.16
Sulfasalazine	37 (16.5%)	18 (19.4%)	19 (14.5%)	40 (17.9%)	0.04
bDMARDs, during baseline[a]					
n, total	115 (51.3%)	41 (44.1%)	74 (56.5%)	116 (51.8%)	0.01
Mean (SD)	0.56 (0.59)	0.49 (0.62)	0.60 (0.56)	0.57 (0.60)	0.02
Median	1.00 [0.00, 1.00]	0.00 [0.00, 1.00]	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-
Min, Max	0.0, 3.0	0.00, 3.00	0.00, 2.00	0.0, 3.0	-
cDMARDs, concomitant	79 (35.3%)	29 (31.2%)	50 (38.2%)	82 (36.6%)	0.03
abatacept	23 (10.3%)	8 (8.6%)	15 (11.5%)	27 (12.1%)	0.06
adalimumab[d]	5 (2.2%)	1 (1.1%)	4 (3.1%)	7 (3.1%)	0.06

Characteristic[a,b]	Baricitinib[c] Any (N = 224)	Baricitinib[c] 2 mg (N = 93)	Baricitinib[c] 4 mg (N = 131)	TNFi (N = 224)	Std. Diff.
anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
certolizumab pegol[d]	9 (4.0%)	4 (4.3%)	5 (3.8%)	2 (0.9%)	0.20
etanercept[d]	24 (10.7%)	9 (9.7%)	15 (11.5%)	19 (8.5%)	0.08
golimumab[d]	13 (5.8%)	3 (3.2%)	10 (7.6%)	4 (1.8%)	0.21
infliximab[d]	1 (0.4%)	0 (0.0%)	1 (0.8%)	21 (9.4%)	0.42
rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
sarilumab	8 (3.6%)	2 (2.2%)	6 (4.6%)	5 (2.2%)	0.08
tocilizumab	42 (18.8%)	19 (20.4%)	23 (17.6%)	42 (18.8%)	0.00
Other Prescription Medications					
Antibiotics	77 (34.4%)	31 (33.3%)	46 (35.1%)	94 (42.0%)	0.16
Antidiabetic agents	13 (5.8%)	8 (8.6%)	5 (3.8%)	12 (5.4%)	0.02
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (2.7%)	0.24
Non-insulins	13 (5.8%)	8 (8.6%)	5 (3.8%)	8 (3.6%)	0.11
Aspirin	2 (0.9%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	0.13
Cardiovascular					
Anticoagulant	6 (2.7%)	2 (2.2%)	4 (3.1%)	7 (3.1%)	0.03
Antihypertensives	53 (23.7%)	26 (28.0%)	27 (20.6%)	55 (24.6%)	0.02
Antiplatelet	12 (5.4%)	6 (6.5%)	6 (4.6%)	10 (4.5%)	0.04
Nitrates	3 (1.3%)	0 (0.0%)	3 (2.3%)	0 (0.0%)	0.17
Hormonal					
HRT	6 (2.7%)	3 (3.2%)	3 (2.3%)	5 (2.2%)	0.03
Oral contraceptives	NA	NA	NA	NA	NA
SERMs	5 (2.2%)	3 (3.2%)	2 (1.5%)	6 (2.7%)	0.03
Lipid-lowering agents					
Bile acid binding	1 (0.4%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0.10
Cholesterol absorption inhibitor	4 (1.8%)	1 (1.1%)	3 (2.3%)	2 (0.9%)	0.08
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.4%)	0.10
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Omega-3 fatty acids	1 (0.4%)	0 (0.0%)	1 (0.8%)	1 (0.4%)	0.00
Statins	26 (11.6%)	15 (16.1%)	11 (8.4%)	28 (12.5%)	0.03
Rheumatoid arthritis-related					
Cox-2 Inhibitor	73 (32.6%)	23 (24.7%)	50 (38.2%)	55 (24.6%)	0.18
Glucocorticosteroid	140 (62.5%)	59 (63.4%)	81 (61.8%)	140 (62.5%)	0.00
Vaccinations	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARDs = biologic disease-modifying antirheumatic drugs; cDMARDs = conventional disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; DMARDs = disease-modifying antirheumatic drugs; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; Max = maximum; Min = minimum; N = count of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective oestrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] All conditions and characteristics, except for bDMARDs, are measured during the 6 months prior to initiation of study medication including the date at which the qualifying exposure of baricitinib or TNFi occurs (index date). bDMARDs are measured from the 6 months prior to the initiation of study medication until the day prior to baricitinib or the index TNFi exposure, excluding the index date.

[b] Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 (see Section 8.3.3, Annex 19) for each outcome (eg, hospitalised congestive heart failure) for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias (eg, Type I diabetes) for VTE.

[c] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose when numbers of patients are sufficient to warrant separate reporting.

[d] TNF inhibitors.

[e] In JMDC, smoking is defined based on information recorded in the variable “Annual health checkup – Smoking habit”.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\jmdc_JMDC\3. Table 6.8. - Clinical Characteristics MACE Cohorts, Matched [Japanese Medical Data Center Payer-Based].docx

Table 13B_JMDC Baseline Healthcare Resource Utilisation MACE Cohorts, Matched [JMDC], Count at Most 1 Visit Per Day

Type of Resource Use	Baricitinib (N = 224)	TNFi (N = 224)	Std. Diff.
Physician Office Visits[a]			
n, patients	146 (65.2%)	161 (71.9%)	0.15
n, events	325	334	
Mean (SD)	1.45 (1.57)	1.49 (1.52)	0.03
Median	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	
Min, Max	0.0, 8.0	0.0, 10.0	
Rheumatologist Visits[a]			
n, patients	18 (8.0%)	11 (4.9%)	0.13
n, events	40	29	
Mean (SD)	0.18 (0.84)	0.13 (0.80)	0.06
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 6.0	0.0, 7.0	
Other Outpatient Visits[a]			
n, patients	224 (100.0%)	223 (99.6%)	0.10
n, events	3,174	2,820	
Mean (SD)	14.17 (11.13)	12.59 (7.46)	0.17
Median	11.00 [7.00, 17.00]	11.00 [7.25, 16.00]	
Min, Max	2.0, 113.0	0.0, 53.0	
Inpatient Visits[a]			
n, patients	32 (14.3%)	28 (12.5%)	0.05
n, events	435	417	
Mean (SD)	1.94 (7.03)	1.86 (9.35)	0.01
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 51.0	0.0, 94.0	
ED Visits[b]			
n, patients	-	-	-
n, events	-	-	
Mean (SD)	- (-)	- (-)	
Median	- [-, -]	- [-, -]	
Min, Max	-, -	-, -	

Abbreviations: ED = emergency department; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; Max = maximum; Min = minimum; N = count of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

[a] In this table, results describe utilisation of healthcare where a maximum of 1 event was allowed per day. In the propensity-score-matching analyses, multiple claims on the same day were allowed to capture additional information on the amount of services received in a given visit. These results are presented in Table 13A_JMDC in Annex 15.

[b] Type(s) of healthcare encounter not applicable to the Japanese Medical Data Center Payer-Based database.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\jmdc_JMDC\3. Table 6.13B (count at most 1 visit per day). Baseline Healthcare Resource Utilisation MACE Cohorts, Matched [Japanese Medical Data Center Payer-Based].docx

10.2.2.5.3. Serious infections

After propensity score matching, there were a total of 440 patients (220 each in the baricitinib and TNFi cohorts) included in the analysis of serious infection (Annex 15, Table 4). Within the baricitinib cohort, 130 patients recorded 4 mg and 90 recorded 2 mg. On average, patients analysed were aged 52.35 years (range 19 to 74 years) and the great majority (81.8%) were female. After propensity score matching, patients treated with any baricitinib were less often aged ≥65 years compared to the patients treated with TNFi (any baricitinib 6.8%, TNFi 13.2%). This age difference is driven by the difference in proportion of patients ≥65 years old receiving baricitinib 4 mg (3.8%) vs 2 mg (11.1%).

Clinical characteristics of patients at baseline are described in Annex 15, Table 9. Patients within the JMDC had a much lower burden of comorbidity compared to other data sources (US and European). Noting the lower overall prevalence, the most commonly observed conditions with at least 10 total cases were chronic lung disease (any baricitinib 14.5%, TNFi 15%), dyslipidaemia (any baricitinib 7.7%, TNFi 9.5%), diabetes (any baricitinib 2.7%, TNFi 3.2%), and cancer (any baricitinib 3.6%, TNFi 5%). Smoking data was not available; hence all data appears as 0%. With regard to RA severity, the CIRAS score was similar in the two cohorts (any baricitinib 6.56, TNFi 6.52).

RA treatment received prior to the index medication is described in Annex 15, Table 9. Most patients used cDMARDs (baricitinib 84.1%, TNFi 82.7%) and methotrexate was the most frequently recorded cDMARD (baricitinib 75%, TNFi 73.2%). A similar proportion of patients in the baricitinib and TNFi cohorts recorded >1 cDMARD concomitantly (baricitinib 16.4%, TNFi 14.5%). All patients in the TNFi cohort received a bDMARD in baseline (most frequently golimumab 34.5% or etanercept 32.7%) whereas 50% of baricitinib cohort received a bDMARD in baseline.

10.2.2.6. SNDS

There were 3,242 eligible patients treated with baricitinib (2,616 with 4 mg and 622 with 2 mg) and 10,202 eligible TNFi patients in the SNDS data. Demographic and clinical characteristics for these unmatched cohorts are in Annex 16. From these unmatched cohorts, the number of patients included in analyses of VTE, MACE, or serious infection after 1:1 matching varies. Details of these analysis-specific cohorts follow.

10.2.2.6.1. VTE

After propensity score matching, there were a total of 5,718 patients (2,859 each in the any baricitinib and TNFi cohorts) included in the analysis of VTE (Table 2_SNDS). Within the matched baricitinib cohort, 81% of patients were treated with the 4 mg dose (n = 2306) and the rest with 2 mg (n = 551). On average, patients analysed were aged 58.4 years at baseline (range 18 to 94 years) and were majority (79.9%) female. After propensity score matching, patients treated with baricitinib were not dissimilar from patients treated with TNFi in terms of age and gender.

Clinical characteristics of patients at baseline are described in Table 7_SNDS. After matching, the distribution of clinical conditions was balanced between the two cohorts, as determined by

standardised differences <0.1. The most commonly observed condition prevalent in at least 10% of patients was chronic lung disease, excluding cystic fibrosis (any baricitinib 13.3%, TNFi 11.4%). Diabetes was also prevalent (any baricitinib 9.9%, TNFi 9.5%). SNDS did not have available data for dyslipidaemia or hypertension and all other clinical characteristics had low prevalence. However, medicines used in baseline can inform clinical conditions. In the baricitinib and TNFi cohort, 12.2% and 11.3% used anti-platelets, respectively, and antihypertensives were used in 34% and 34.1% of baricitinib and TNFi cohorts, respectively. Patients in the any baricitinib cohort and TNFi cohort reported similar use of lipid-lowering agents (16.8% and 16.1%, respectively). Some patients with SLE were included in both cohorts; 0.9% (n = 27) and 0.6% (n = 17) in the baricitinib and TNFi cohorts, respectively. Based on the small standardised difference of 0.04, there was no important difference between cohorts that could lead to confounding by SLE in the analysis of VTE and bias results. RA severity did not differ between the two cohorts (any baricitinib 6.5, TNFi 6.4).

RA treatment received prior to the index medication is described in Table 7_SNDS. The majority of patients used cDMARDs (any baricitinib 68%, TNFi 65.8%), with methotrexate recorded most frequently (any baricitinib 53.3%, TNFi 52%). Proportion of patients with prior use of bDMARDs was similar in the baricitinib and TNFi cohorts (any baricitinib 55.9%, TNFi 56.3%). Abatacept was the most frequently recorded prior bDMARD in both cohorts (baricitinib 15.1%, TNFi 14.7%).

Baseline healthcare resource utilisation was similar across the baricitinib and TNFi cohorts in the SNDS (Table 12_SNDS).

Table 2_SNDS Baseline Demographics VTE Cohorts, Matched [SNDS]

	Baricitinib Any[a] N = 2859	Baricitinib 4 mg N = 2306	Baricitinib 2 mg N = 551	TNFi[b] N = 2859	Std. Diff. (Any vs TNFi)	Total N = 5718
Age at index date [in years]					0.000	
n (missing)	2859 (0)	2306 (0)	551 (0)	2859 (0)		5718 (0)
Mean (SD)	58.4 (13.2)	55.9 (12.0)	68.7 (12.9)	58.4 (13.3)		58.4 (10.6)
Median	59.0	57.0	71.0	59.0		59.0
Min, Max	18.0, 92.0	18.0, 90.0	20.0, 92.0	18.0, 94.0		18.0, 94.0
Age (in years), in categories, n (%)						
[18-30[	65 (2.3)	58 (2.5)	≤10	72 (2.5)		137 (2.4)
[30-40[	196 (6.9)	184 (8.0)	12 (2.2)	193 (6.8)		389 (6.8)
[40-50[	424 (14.8)	389 (16.9)	35 (6.4)	391 (13.7)		815 (14.3)
[50-60[	810 (28.3)	748 (32.4)	61 (11.1)	804 (28.1)		1614 (28.2)
[60-65[	394 (13.8)	343 (14.9)	51 (9.3)	411 (14.4)		805 (14.1)
≥65	970 (33.9)	584 (25.3)	385 (69.9)	988 (34.6)		1958 (34.2)
Sex, n (%)					0.031	
Male	591 (20.7)	487 (21.1)	104 (18.9)	556 (19.4)		1147 (20.1)
Female	2268 (79.3)	1819 (78.9)	447 (81.1)	2303 (80.6)		4571 (79.9)

Abbreviations: N = count of patients in the specified category; SD = standard deviation; SNDS = Système National des Données de Santé; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus; VTE = venous thromboembolism.

[a] n = 2 subjects were dispensed both baricitinib 4 mg and 2 mg at index date and are included in the overall (Baricitinib Any) group but not in the strata according to the dosage.

[b] Matching ratio 1:1 is applied.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\french snds_SNDS\BARICITINIB_RAS_SNDS_2019_Match_1_1_Point VII_V1.0 20220228.docx - page 25

Table 7_SNDS Clinical Characteristics Primary VTE Cohorts, Matched [SNDS]

Characteristics[a]	Baricitinib, Any[b] N = 2859	Baricitinib, 4 mg N = 2306	Baricitinib, 2 mg N = 551	TNFi[c] N = 2859	Std. Diff. (Any vs TNFi)
Clinical conditions during baseline period, n (%)					
Cancer, excluding NMSC	88 (3.1)	63 (2.7)	25 (4.5)	94 (3.3)	-0.012
NMSC	≤10	≤10	≤10	≤10	-0.009
Chronic lung disease, excl. cystic fibrosis[e]	381 (13.3)	278 (12.1)	103 (18.7)	325 (11.4)	0.060
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	29 (1.0)	13 (0.6)	16 (2.9)	27 (0.9)	0.007
Cardiovascular revascularization procedure	≤10	≤10	≤10	≤10	-0.013
Congestive heart failure, hospitalised	12 (0.4)	≤10	≤10	13 (0.5)	-0.005
Coronary artery disease	127 (4.4)	83 (3.6)	44 (8.0)	121 (4.2)	0.010
Unstable angina	≤10	0 (0.0)	≤10	≤10	-0.043
Ventricular arrhythmia	17 (0.6)	≤10	≤10	24 (0.8)	-0.029
Stroke	25 (0.9)	17 (0.7)	≤10	22 (0.8)	0.012
Haemorrhagic	≤10	≤10	0 (0.0)	≤10	-0.027
Ischemic	≤10	≤10	≤10	≤10	0.024
Unknown	21 (0.7)	15 (0.7)	≤10	17 (0.6)	0.017
TIA	≤10	0 (0.0)	≤10	≤10	0.000
Diabetes Mellitus[e]	283 (9.9)	205 (8.9)	77 (14.0)	271 (9.5)	0.014
Treated insulin dependent	NA	NA	NA	NA	
Treated non-insulin dependent	NA	NA	NA	NA	
Dyslipidaemia (not available in SNDS)	NA	NA	NA	NA	
Hypertension (not available in SNDS)					
History of hypertension	NA	NA	NA	NA	
Current hypertension	NA	NA	NA	NA	
Immune disorders	104 (3.6)	74 (3.2)	30 (5.4)	108 (3.8)	-0.007
AIDS/HIV	0 (0.0)	0 (0.0)	0 (0.0)	≤10	-0.053
Antiphospholipid syndrome	NA	NA	NA	NA	
SLE	27 (0.9)	24 (1.0)	≤10	17 (0.6)	0.040
Primary Sjogren Syndrome	83 (2.9)	55 (2.4)	28 (5.1)	92 (3.2)	-0.018

Characteristics[a]	Baricitinib, Any[b] N = 2859	Baricitinib, 4 mg N = 2306	Baricitinib, 2 mg N = 551	TNFi[c] N = 2859	Std. Diff. (Any vs TNFi)
Liver or pancreatic disorder[e]	89 (3.1)	68 (2.9)	20 (3.6)	85 (3.0)	0.008
Obesity (not available in SNDS)	NA	NA	NA	NA	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date)	≤10	≤10	0 (0.0)	12 (0.4)	-0.024
RA Severity (CIRAS Index)					0.029
Mean (± SD)	6.5 (1.4)	6.6 (1.3)	5.8 (1.4)	6.4 (1.4)	
Smoking (not available in SNDS)	NA	NA	NA	NA	
DMARDs, n (%)					
cDMARDs, during baseline period					
n, total (%)	1945 (68.0)	1606 (69.6)	337 (61.2)	1882 (65.8)	0.047
Mean (SD)	0.8 (0.6)	0.8 (0.6)	0.7 (0.7)	0.7 (0.6)	0.064
Median	1.0	1.0	1.0	1.0	
Min, Max	0.0, 4.0	0.0, 4.0	0.0, 3.0	0.0, 3.0	
>1 cDMARD concomitantly	163 (5.7)	132 (5.7)	31 (5.6)	125 (4.4)	0.061
Hydroxychloroquine	165 (5.8)	128 (5.6)	37 (6.7)	138 (4.8)	0.042
Chloroquine	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Azathioprine	≤10	≤10	≤10	≤10	-0.006
Leflunomide	361 (12.6)	299 (13.0)	62 (11.3)	310 (10.8)	0.055
Methotrexate	1523 (53.3)	1266 (54.9)	256 (46.5)	1486 (52.0)	0.026
Mycophenolate mofetil	≤10	≤10	0 (0.0)	≤10	-0.015
Sulfasalazine	101 (3.5)	76 (3.3)	25 (4.5)	105 (3.7)	-0.008
Cyclosporin	≤10	≤10	≤10	≤10	0.015
Penicillamine	0 (0.0)	0 (0.0)	0 (0.0)	≤10	-0.037
bDMARDs, during baseline period					
n, total (%)	1599 (55.9)	1351 (58.6)	246 (44.6)	1611 (56.3)	-0.009
Mean (SD)	0.6 (0.6)	0.6 (0.6)	0.5 (0.5)	0.6 (0.6)	-0.011
Median	1.0	1.0	0.0	1.0	
Min, Max	0.0, 3.0	0.0, 3.0	0.0, 3.0	0.0, 3.0	
cDMARDs, concomitant	910 (31.8)	784 (34.0)	124 (22.5)	847 (29.6)	0.048
Adalimumab[d]	212 (7.4)	182 (7.9)	30 (5.4)	228 (8.0)	-0.021
Certolizumab pegol[d]	119 (4.2)	106 (4.6)	13 (2.4)	122 (4.3)	-0.005
Etanercept[d]	329 (11.5)	279 (12.1)	50 (9.1)	353 (12.3)	-0.026
Golimumab[d]	101 (3.5)	93 (4.0)	≤10	109 (3.8)	-0.015
Infliximab[d]	81 (2.8)	72 (3.1)	≤10	87 (3.0)	-0.012
Rituximab	59 (2.1)	44 (1.9)	15 (2.7)	37 (1.3)	0.06
Sarilumab	23 (0.8)	17 (0.7)	≤10	25 (0.9)	-0.008
Abatacept	433 (15.1)	361 (15.7)	71 (12.9)	420 (14.7)	0.013
Tocilizumab	357 (12.5)	304 (13.2)	53 (9.6)	351 (12.3)	0.006
Anakinra	14 (0.5)	≤10	≤10	14 (0.5)	0
TNFi naïve at baseline	2054 (71.8)	1609 (69.8)	445 (80.8)	1979 (69.2)	0.058
Other prescription medications during baseline period, n (%)					
Antibiotics	1183 (41.4)	925 (40.1)	256 (46.5)	1147 (40.1)	0.026
Antidiabetic agents	276 (9.7)	203 (8.8)	72 (13.1)	253 (8.8)	0.028
Insulins	102 (3.6)	75 (3.3)	27 (4.9)	81 (2.8)	0.042
Non-insulins	224 (7.8)	168 (7.3)	55 (10.0)	210 (7.3)	0.019

Characteristics[a]	Baricitinib, Any[b] N = 2859	Baricitinib, 4 mg N = 2306	Baricitinib, 2 mg N = 551	TNFi[c] N = 2859	Std. Diff. (Any vs TNFi)
Cardiovascular					
Antithrombotic agents	449 (15.7)	300 (13.0)	148 (26.9)	428 (15.0)	0.02
Anticoagulant	130 (4.5)	75 (3.3)	55 (10.0)	125(4.4)	0.009
Antiplatelet	349 (12.2)	240 (10.4)	108 (19.6)	322 (11.3)	0.029
Antihypertensives	973 (34.0)	662 (28.7)	310 (56.3)	976 (34.1)	-0.002
Angiotensin converting enzyme inhibitors (ACE)	254 (8.9)	171 (7.4)	83 (15.1)	260 (9.1)	-0.007
Angiotensin receptor blockers (ARB)	362 (12.7)	245 (10.6)	117 (21.2)	420 (14.7)	-0.059
Beta blocker	427 (14.9)	284 (12.3)	142 (25.8)	413 (14.4)	0.014
Calcium channel blocker	286 (10.0)	180 (7.8)	105 (19.1)	282 (9.9)	0.005
Nitrates	25 (0.9)	11 (0.5)	14 (2.5)	32 (1.1)	-0.025
Acyclovir	14 (0.5)	≤10	≤10	20 (0.7)	-0.027
Valacyclovir	104 (3.6)	77 (3.3)	27 (4.9)	102 (3.6)	0.004
Hormonal	365 (12.8)	321 (13.9)	44 (8.0)	380 (13.3)	-0.016
HRT	213 (7.5)	183 (7.9)	30 (5.4)	218 (7.6)	-0.007
Oral contraceptives	147 (5.1)	134 (5.8)	13 (2.4)	153 (5.4)	-0.009
SERMs	≤10	≤10	≤10	≤10	-0.006
Topic with progestogens and/or oestrogens	≤10	≤10	0 (0.0)	≤10	-0.013
Lipid-lowering agents	481 (16.8)	337 (14.6)	143 (26.0)	459 (16.1)	0.021
HMG CoA reductase inhibitors	394 (13.8)	273 (11.8)	120 (21.8)	372 (13.0)	0.023
Fibrates	37 (1.3)	24 (1.0)	13 (2.4)	43 (1.5)	-0.018
Bile acid sequestrants	11 (0.4)	≤10	≤10	≤10	0.032
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Other lipid-modifying agents	23 (0.8)	16 (0.7)	≤10	27 (0.9)	-0.015
Lipid-modifying agents, combinations	38 (1.3)	31 (1.3)	≤10	30 (1.0)	0.026
Rheumatoid arthritis-related					
Aspirin	37 (1.3)	25 (1.1)	11 (2.0)	35 (1.2)	0.006
Cox-2 Inhibitor	156 (5.5)	138 (6.0)	18 (3.3)	175 (6.1)	-0.029
NSAIDs	1041 (36.4)	885 (38.4)	156 (28.3)	1104 (38.6)	-0.046
Glucocorticosteroid	2026 (70.9)	1616 (70.1)	408 (74.0)	2002 (70.0)	0.018
Vaccines	855 (29.9)	649 (28.1)	206 (37.4)	830 (29.0)	0.019
Antineoplastic agents	11 (0.4)	≤10	≤10	12 (0.4)	-0.006

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARDs = biologic disease-modifying antirheumatic drugs; cDMARDs = conventional disease-modifying antirheumatic drugs; CIRAS = Claims-Based Index for RA Severity; HIV = human immunodeficiency virus; HMG CoA reductase inhibitors = statins; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = count of patients in the specified category; NMSC = non-melanoma skin cancer; NSAID = nonsteroidal anti-inflammatory drug; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective oestrogen receptor modulators; SLE = systemic lupus erythematosus; SNDS = Système National des Données de Santé; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; TIA = transient ischemic attack;
vs = versus; VTE = venous thromboembolism.

[a] All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort, index date excluded.
[b] n = 2 subjects were dispensed both baricitinib 4 mg and 2 mg at index date and are included in the overall (Baricitinib Any) group but not in the strata according to the dosage.
[c] Matching ratio 1:1 is applied.
[d] TNF inhibitors
[e] CNAM algorithm based on the year preceding the year of inclusion.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\french snds_SNDS\BARICITINIB_RAS_SNDS_2019_Match_1_1_Point VII_V1.0 20220228.docx - pages 35-39

Table 12_SNDS Baseline Healthcare Resource Utilisation Primary VTE Cohorts, Matched [SNDS]

Type of resource use during baseline period[a]	Baricitinib Any[b] N = 2859	Baricitinib 4 mg N = 2306	Baricitinib 2 mg N = 551	TNFi[c] N = 2859	Std. Diff. (Any vs TNFi)
Physician Office Visits (rheumatologist visits excluded)					
n, patients (%)	1765 (61.7)	1382 (59.9)	383 (69.5)	1756 (61.4)	0.007
n, events	5041	3827	1214	5267	
Mean (SD)	1.8 (2.6)	1.7 (2.6)	2.2 (2.7)	1.8 (3.2)	-0.027
Median	1.0	1.0	1.0	1.0	
Min, Max	0.0, 41.0	0.0, 41.0	0.0, 19.0	0.0, 85.0	
Rheumatologist Visits					
n, patients (%)	1815 (63.5)	1478 (64.1)	336 (61.0)	1786 (62.5)	0.021
n, events	4047	3273	768	4033	
Mean (SD)	1.4 (1.5)	1.4 (1.5)	1.4 (1.6)	1.4 (1.5)	0.003
Median	1.0	1.0	1.0	1.0	
Min, Max	0.0, 11.0	0.0, 9.0	0.0, 11.0	0.0, 13.0	
Other Outpatient Visits					
n, patients (%)	2657 (92.9)	2122 (92.0)	533 (96.7)	2652 (92.8)	0.007
n, events	55331	37534	17682	49689	
Mean (SD)	19.4 (32.3)	16.3 (26.7)	32.1 (47.0)	17.4 (29.6)	0.064
Median	8.0	7.0	15.0	7.0	
Min, Max	0.0, 322.0	0.0, 322.0	0.0, 266.0	0.0, 280.0	
Inpatient Visits[d]					
n, patients (%)	1347 (47.1)	1030 (44.7)	316 (57.4)	1287 (45.0)	0.042
n, events	3110	2393	710	3051	
Mean (SD)	1.1 (1.7)	1.0 (1.7)	1.3 (1.8)	1.1 (2.4)	0.010
Median	0.0	0.0	1.0	0.0	
Min, Max	0.0, 14.0	0.0, 14.0	0.0, 12.0	0.0, 76.0	
ED Visits	NA	NA	NA	NA	
n, patients (%)					
n, events					
Mean (SD)					
Median					
Min, Max					

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = count of patients in the specified category; SD = standard deviation; SNDS = Système National des Données de Santé; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

[a] Index date excluded.

[b] n = 2 subjects were dispensed both baricitinib 4 mg and 2 mg at index date and are included in the overall (Baricitinib Any) group but not in the strata according to the dosage.

[c] Matching ratio 1:1 is applied.

[d] Inpatient visits include number of hospitalisations.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\french snds_SNDS\BARICITINIB_RAS_SNDS_2019_Match_1_1_Point VII_V1.0 20220228.docx - pages 57-58

10.2.2.6.2. MACE

After propensity score matching, there were a total of 5,728 patients (2,864 each in the any baricitinib and TNFi cohorts) included in the analysis of MACE (Table 3_SNDS). Within the matched baricitinib cohort, 81% of patients were treated with the 4-mg dose (n = 2314) with the rest treated with 2 mg (n = 548). On average, patients analysed were aged 58.4 years at baseline (range 18 to 92 years) and the majority (79.9%) were female. After propensity score matching, patients treated with baricitinib were similar to patients treated with TNFi in terms of age and gender, and other characteristics.

Clinical characteristics of patients at baseline are described in Table 8_SNDS. After matching, the distribution of clinical conditions was balanced between the two cohorts, as determined by standardised differences <0.1. The most commonly observed conditions prevalent in at least 10% of patients were chronic lung disease, excluding cystic fibrosis (any baricitinib 13.7%, TNFi 11.7%) and diabetes (any baricitinib 10.0%, TNFi 10.1%). SNDS did not have available data for dyslipidaemia or hypertension and all other clinical characteristics had low prevalence. However, non-RA prescription medicines used in baseline can inform clinical conditions. In the baricitinib and TNFi cohort, 12.0% and 12.8% used anti-platelets, respectively whereas antihypertensives were used in 33.7% and 35.7% of any baricitinib and TNFi cohorts. Patients in the any baricitinib cohort and TNFi cohort reported similar use of lipid-lowering agents (16.7% and 17.4%, respectively). Some patients with SLE were included in both cohorts; 0.9% (n = 25) and 0.4% (n = 11) in the baricitinib and TNFi cohorts, respectively. Based on the small standardised difference of 0.06, there was no important difference between cohorts that could lead to confounding by SLE in the analysis of MACE and bias results. RA severity using the CIRAS index was the same between the two cohorts (any baricitinib 6.5, TNFi 6.5).

RA treatment received prior to the index medication is described in Table 8_SNDS. The majority of patients used cDMARDs (any baricitinib 67.6%, TNFi 67.1%), with methotrexate recorded most frequently (any baricitinib 53.2%, TNFi 52.7%). Proportion of patients with prior use of bDMARDs was similar in the baricitinib and TNFi cohorts (any baricitinib 56.0%, TNFi 56.6%). Abatacept was the most frequently recorded prior bDMARD in both cohorts (any baricitinib 14.9%, TNFi 14.5%).

Baseline healthcare resource utilisation was similar across the baricitinib and TNFi cohorts in the SNDS (Table 13_SNDS).

Table 3_SNDS Baseline Demographics MACE Cohorts, Matched [SNDS]

	Baricitinib Any[a] N = 2864	Baricitinib 4 mg N = 2314	Baricitinib 2 mg N = 548	TNFi[b] N = 2864	Std. Diff. (Any vs TNFi)	Total N = 5728
Age at index date [in years]					0.013	
n (missing)	2864 (0)	2314 (0)	548 (0)	2864 (0)		5728 (0)
Mean (SD)	58.5 (13.3)	56.0 (12.1)	69.0 (12.9)	58.4 (13.2)		58.4 (13.2)
Median	59.0	57.0	72.0	59.0		59.0
Min, Max	18.0, 90.0	18.0, 90.0	20.0, 89.0	18.0, 92.0		18.0, 92.0
Age (in years), in categories, n (%)						
[18-30[	68 (2.4)	61 (2.6)	≤10	78 (2.7)		146 (2.5)
[30-40[	195 (6.8)	183 (7.9)	12 (2.2)	176 (6.1)		371 (6.5)
[40-50[	411 (14.4)	379 (16.4)	32 (5.8)	402 (14.0)		813 (14.2)
[50-60[	810 (28.3)	749 (32.4)	60 (10.9)	813 (28.4)		1623 (28.3)
[60-65[	390 (13.6)	344 (14.9)	46 (8.4)	413 (14.4)		803 (14.0)
≥65	990 (34.6)	598 (25.8)	391 (71.4)	982 (34.3)		1972 (34.4)
Sex, n (%)					0.017	
Male	585 (20.4)	487 (21.0)	98 (17.9)	566 (19.8)		1151 (20.1)
Female	2279 (79.6)	1827 (79.0)	450 (82.1)	2298 (80.2)		4577 (79.9)

Abbreviations: MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; Max = maximum; Min = minimum; N = count of patients in the specified category; SD = standard deviation; SNDS = Système National des Données de Santé; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

[a] n = 2 subjects were dispensed both baricitinib 4 mg and 2 mg at index date and are included in the overall (Baricitinib Any) group but not in the strata according to the dosage.

[b] Matching ratio 1:1 is applied.

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Table 8_SNDS Clinical Characteristics MACE Cohorts, Matched (SNDS)

Characteristics[a]	Baricitinib Any[b] N = 2864	Baricitinib 4 mg N = 2314	Baricitinib 2 mg N = 548	TNFi[c] N = 2864	Std. Diff. (Any vs TNFi)
Clinical conditions during baseline period, n (%)					
Cancer, excluding NMSC	88 (3.1)	62 (2.7)	26 (4.7)	99 (3.5)	-0.022
NMSC	≤10	≤10	≤10	≤10	-0.014
Chronic lung disease, excluding cystic fibrosis[e]	392 (13.7)	288 (12.4)	104 (19.0)	334 (11.7)	0.061
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	30 (1.0)	14 (0.6)	16 (2.9)	11 (0.4)	0.079
Cardiovascular revascularization procedure	≤10	≤10	≤10	≤10	-0.034
Congestive heart failure, hospitalised	≤10	≤10	≤10	11 (0.4)	-0.006
Coronary artery disease	118 (4.1)	76 (3.3)	42 (7.7)	135 (4.7)	-0.029
Unstable angina	0 (0.0)	0 (0.0)	0 (0.0)	≤10	-0.037
Ventricular arrhythmia	13 (0.5)	≤10	≤10	19 (0.7)	-0.028
Stroke (LTD or associated diagnosis)	23 (0.8)	17 (0.7)	≤10	16 (0.6)	0.030
Haemorrhagic	≤10	≤10	0 (0.0)	≤10	0.000
Ischemic	≤10	≤10	≤10	≤10	0.043
Unknown	18 (0.6)	14 (0.6)	≤10	14 (0.5)	0.019
TIA	≤10	0 (0.0)	≤10	0 (0.0)	0.026
Diabetes Mellitus[e]	285 (10.0)	211 (9.1)	73 (13.3)	288 (10.1)	-0.004
Treated insulin dependent	NA	NA	NA	NA	
Treated non-insulin dependent	NA	NA	NA	NA	
Dyslipidaemia (not available in SNDS)	NA	NA	NA	NA	

Characteristics[a]	Baricitinib Any[b] N = 2864	Baricitinib 4 mg N = 2314	Baricitinib 2 mg N = 548	TNFi[c] N = 2864	Std. Diff. (Any vs TNFi)
Hypertension (not available in SNDS)					
History of hypertension	NA	NA	NA	NA	
Current hypertension	NA	NA	NA	NA	
Immune disorders	100 (3.5)	70 (3.0)	30 (5.5)	112 (3.9)	-0.022
AIDS/HIV	0 (0.0)	0 (0.0)	0 (0.0)	≤10	-0.037
Antiphospholipid syndrome	NA	NA	NA	NA	
SLE	25 (0.9)	22 (1.0)	≤10	11 (0.4)	0.062
Primary Sjogren Syndrome	80 (2.8)	52 (2.2)	28 (5.1)	101 (3.5)	-0.042
Liver or pancreatic disorder[e]	83 (2.9)	66 (2.9)	17 (3.1)	77 (2.7)	0.013
Obesity (not available in SNDS)	NA	NA	NA	NA	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date)	≤10	≤10	0 (0.0)	24 (0.8)	-0.075
RA Severity (CIRAS Index)					0.014
Mean (± SD)	6.5 (1.4)	6.6 (1.3)	5.8 (1.4)	6.5 (1.4)	
Smoking (not available in SNDS)	NA	NA	NA	NA	
DMARDs, n (%)					
cDMARDs, during baseline period					
n, total (%)	1937 (67.6)	1600 (69.1)	335 (61.1)	1921 (67.1)	0.012
Mean (SD)	0.7 (0.6)	0.8 (0.6)	0.7 (0.6)	0.7 (0.6)	0.031
Median	1.0	1.0	1.0	1.0	
Min, Max	0.0, 4.0	0.0, 4.0	0.0, 3.0	0.0, 4.0	
>1 cDMARD concomitantly	160 (5.6)	128 (5.5)	32 (5.8)	126 (4.4)	0.055
Hydroxychloroquine	159 (5.6)	125 (5.4)	34 (6.2)	138 (4.8)	0.033
Chloroquine	≤10	0 (0.0)	≤10	≤10	0.000
Azathioprine	≤10	≤10	≤10	≤10	0.000
Leflunomide	351 (12.3)	297 (12.8)	54 (9.9)	342 (11.9)	0.010
Methotrexate	1523 (53.2)	1262 (54.5)	259 (47.3)	1509 (52.7)	0.010
Mycophenolate mofetil	≤10	≤10	0 (0.0)	≤10	-0.015
Sulfasalazine	100 (3.5)	76 (3.3)	24 (4.4)	92 (3.2)	0.016
Cyclosporin	≤10	≤10	≤10	≤10	0.015
Penicillamine	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000

Characteristics[a]	Baricitinib Any[b] N = 2864	Baricitinib 4 mg N = 2314	Baricitinib 2 mg N = 548	TNFi[c] N = 2864	Std. Diff. (Any vs TNFi)
bDMARDs, during baseline period					
n, total (%)	1605 (56.0)	1360 (58.8)	243 (44.3)	1620 (56.6)	-0.011
Mean (SD)	0.6 (0.6)	0.6 (0.6)	0.5 (0.6)	0.6 (0.6)	-0.020
Median	1.0	1.0	0.0	1.0	
Min, Max	0.0, 3.0	0.0, 3.0	0.0, 3.0	0.0, 3.0	
cDMARDs, concomitant	898 (31.4)	775 (33.5)	121 (22.1)	878 (30.7)	0.015
Adalimumab[d]	213 (7.4)	184 (8.0)	29 (5.3)	234 (8.2)	-0.027
Certolizumab pegol[d]	117 (4.1)	105 (4.5)	12 (2.2)	122 (4.3)	-0.009
Etanercept[d]	321 (11.2)	272 (11.8)	49 (8.9)	362 (12.6)	-0.044
Golimumab[d]	100 (3.5)	93 (4.0)	≤10	110 (3.8)	-0.019
Infliximab[d]	77 (2.7)	69 (3.0)	≤10	78 (2.7)	-0.002
Rituximab	63 (2.2)	48 (2.1)	15 (2.7)	36 (1.3)	0.072
Sarilumab	30 (1.0)	23 (1.0)	≤10	25 (0.9)	0.018
Abatacept	427 (14.9)	347 (15.0)	79 (14.4)	416 (14.5)	0.011
Tocilizumab	364 (12.7)	316 (13.7)	48 (8.8)	360 (12.6)	0.004
Anakinra	12 (0.4)	≤10	≤10	14 (0.5)	-0.01
TNFi naïve at baseline	2070 (72.3)	1622 (70.1)	447 (81.6)	1978 (69.1)	0.071
Other prescription medications during baseline period, n (%)					
Antibiotics	1193 (41.7)	931 (40.2)	261 (47.6)	1161 (40.5)	0.023
Antidiabetic agents	275 (9.6)	206 (8.9)	68 (12.4)	275 (9.6)	0.000
Insulins	107 (3.7)	78 (3.4)	29 (5.3)	91 (3.2)	0.031
Non-insulins	220 (7.7)	169 (7.3)	50 (9.1)	230 (8.0)	-0.013
Cardiovascular					
Antithrombotic agents	444 (15.5)	299 (12.9)	144 (26.3)	456 (15.9)	-0.012
Anticoagulant	128 (4.5)	74 (3.2)	54 (9.9)	109 (3.8)	0.033
Antiplatelet	345 (12.0)	238 (10.3)	106 (19.3)	367 (12.8)	-0.023
Antihypertensives	965 (33.7)	660 (28.5)	304 (55.5)	1022 (35.7)	-0.042
Angiotensin converting enzyme inhibitors (ACE)	249 (8.7)	172 (7.4)	77 (14.1)	264 (9.2)	-0.018
Angiotensin receptor blockers (ARB)	375 (13.1)	253 (10.9)	122 (22.3)	448 (15.6)	-0.073
Beta blocker	420 (14.7)	280 (12.1)	139 (25.4)	420 (14.7)	0.000
Calcium channel blocker	283 (9.9)	174 (7.5)	108 (19.7)	297 (10.4)	-0.016
Nitrates	23 (0.8)	11 (0.5)	12 (2.2)	36 (1.3)	-0.045
Acyclovir	13 (0.5)	≤10	≤10	25 (0.9)	-0.052
Valacyclovir	105 (3.7)	78 (3.4)	27 (4.9)	109 (3.8)	-0.007
Hormonal	349 (12.2)	305 (13.2)	44 (8.0)	399 (13.9)	-0.052
HRT	203 (7.1)	173 (7.5)	30 (5.5)	231 (8.1)	-0.037
Oral contraceptives	142 (5.0)	129 (5.6)	13 (2.4)	157 (5.5)	-0.024
SERMs	≤10	≤10	≤10	≤10	-0.006

Characteristics[a]	Baricitinib Any[b] N = 2864	Baricitinib 4 mg N = 2314	Baricitinib 2 mg N = 548	TNFi[c] N = 2864	Std. Diff. (Any vs TNFi)
Topic with progestogens and/or oestrogens	≤10	≤10	0 (0.0)	≤10	-0.014
Lipid-lowering agents	478 (16.7)	336 (14.5)	141 (25.7)	498 (17.4)	-0.019
HMG CoA reductase inhibitors	394 (13.8)	275 (11.9)	118 (21.5)	410 (14.3)	-0.016
Fibrates	32 (1.1)	20 (0.9)	12 (2.2)	41 (1.4)	-0.028
Bile acid sequestrants	≤10	≤10	≤10	≤10	0.000
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Other lipid modifying agents	22 (0.8)	15 (0.6)	≤10	33 (1.2)	-0.039
Lipid modifying agents, combinations	41 (1.4)	33 (1.4)	≤10	37 (1.3)	0.012
Rheumatoid arthritis-related					
Aspirin	34 (1.2)	22 (1.0)	11 (2.0)	37 (1.3)	-0.01
Cox-2 Inhibitor	156 (5.4)	138 (6.0)	17 (3.1)	168 (5.9)	-0.018
NSAIDs	1047 (36.6)	894 (38.6)	153 (27.9)	1096 (38.3)	-0.035
Glucocorticosteroid	2034 (71.0)	1627 (70.3)	406 (74.1)	2033 (71.0)	0.001
Vaccines	864 (30.2)	658 (28.4)	206 (37.6)	857 (29.9)	0.005
Antineoplastic agents	12 (0.4)	≤10	≤10	12 (0.4)	0.000

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARDs = biologic disease-modifying antirheumatic drugs; cDMARDs = conventional disease-modifying antirheumatic drugs; CIRAS = Claims-Based Index for RA Severity;; HIV = human immunodeficiency virus; HMG CoA reductase inhibitors = statins; HRT = hormone replacement therapy; LTD = long-term disease; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specific category; n = number of patients within each specific category; NMSC = non-melanoma skin cancer; NSAID = nonsteroidal anti-inflammatory drug; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective oestrogen receptor modulators; SLE = systemic lupus erythematosus; SNDS = Système National des Données de Santé; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

[a] All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort, index date excluded.

[b] n = 2 subjects were dispensed both baricitinib 4 mg and 2 mg at index date and are included in the overall (Baricitinib Any) group but not in the strata according to the dosage.

[c] Matching ratio 1:1 is applied

[d] TNF inhibitors.

[e] CNAM algorithm based on the year preceding the year of inclusion.

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Table 13_SNDS Baseline Healthcare Resource Utilisation MACE Cohorts, Matched [SNDS]

Type of Resource Use During Baseline Period[a]	Baricitinib Any[b] N = 2864	Baricitinib 4 mg N = 2314	Baricitinib 2 mg N = 548	TNFi[c] N = 2864	Std. Diff. (Any vs TNFi)
Physician Office Visits (rheumatologist visits excluded)					
n, patients (%)	1763 (61.6)	1385 (59.9)	378 (69.0)	1772 (61.9)	-0.007
n, events	5050	3844	1206	5191	
Mean (SD)	1.8 (2.6)	1.7 (2.6)	2.2 (2.7)	1.8 (2.8)	-0.018
Median	1.0	1.0	1.0	1.0	
Min, Max	0.0, 41.0	0.0, 41.0	0.0, 19.0	0.0, 49.0	
Rheumatologist Visits					
n, patients (%)	1819 (63.5)	1479 (63.9)	339 (61.9)	1795 (62.7)	0.017
n, events	4027	3253	768	4082	
Mean (SD)	1.4 (1.5)	1.4 (1.5)	1.4 (1.6)	1.4 (1.5)	-0.013
Median	1.0	1.0	1.0	1.0	
Min, Max	0.0, 9.0	0.0, 9.0	0.0, 9.0	0.0, 13.0	
Other Outpatient Visits					
n, patients (%)	2662 (92.9)	2131 (92.1)	530 (96.7)	2636 (92.0)	0.035
n, events	56411	38487	17885	50031	
Mean (SD)	19.7 (32.7)	16.6 (27.3)	32.6 (47.2)	17.5 (29.8)	0.071
Median	8.0	7.0	15.0	8.0	
Min, Max	0.0, 283.0	0.0, 283.0	0.0, 266.0	0.0, 283.0	
Inpatient Visits[d]					
n, patients (%)	1346 (47.0)	1037 (44.8)	308 (56.2)	1343 (46.9)	0.002
n, events	3186	2473	710	2993	
Mean (SD)	1.1 (1.8)	1.1 (1.7)	1.3 (1.8)	1.0 (2.0)	0.036
Median	0.0	0.0	1.0	0.0	
Min, Max	0.0, 14.0	0.0, 14.0	0.0, 12.	0.0, 56.0	
ED Visits	NA	NA	NA	NA	
n, patients (%)					
n, events					
Mean (SD)					
Median					
Min, Max					

Abbreviations: ED = emergency department; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; Max = maximum; Min = minimum; N = count of patients in the specified category; SD = standard deviation; SNDS = Système National des Données de Santé; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

Note: Physician office visits do not include rheumatologist visits.

[a] Index date excluded.

[b] n = 3 subjects were dispensed both baricitinib 4 mg and 2 mg at index date and are included in the overall (Baricitinib Any) group but not in the strata according to the dosage.

[c] Matching ratio 1:1 is applied.

[d] Inpatient visits include number of hospitalisations.

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10.2.2.6.3. Serious infections

After propensity score matching, there were a total of 5,958 patients (2,979 each in the baricitinib and TNFi cohorts) included in the analysis of serious infections (SNDS Table 4 Annex 16). Within the matched baricitinib cohort, almost all patients recorded 4 mg (n = 2385) with n = 591 on 2 mg. On average, patients analysed were aged 58.9 years at baseline (range 18 to 92 years) and were majority (79.6%) female. After propensity score matching, patients treated with baricitinib were not dissimilar from patients treated with TNFi in terms of age and gender.

Clinical characteristics of patients at baseline are described in SNDS Table 9 Annex 16. After matching, the distribution of clinical conditions was balanced between the two cohorts, as determined by standardised differences <0.1. The most commonly observed conditions prevalent in at least 10% of patients were chronic lung disease, excluding cystic fibrosis (any baricitinib 13.7%, TNFi 12.5%) and diabetes (any baricitinib 10.0%, TNFi 9.9%). SNDS did not have available data for dyslipidaemia or hypertension and all other clinical characteristics had low prevalence. However, medicines used in baseline can inform clinical conditions. In the baricitinib and TNFi cohort, 12.3% and 11.0% used anti-platelets, respectively and antihypertensives were used by 35.7% and 35.0% of baricitinib and TNFi cohorts. Patients in the baricitinib and TNFi cohorts reported slightly higher use of lipid-lowering agents compared with the TNFi cohort (17.6% and 16.2%, respectively). RA severity using the CIRAS index was the same between the two cohorts (any baricitinib 6.4, TNFi 6.4).

RA treatment received prior to the index medication is described in SNDS Table 9 Annex 16. The majority of patients used cDMARDs (any baricitinib 67.6%, TNFi 67.3%), with methotrexate recorded most frequently (any baricitinib 52.9%, TNFi 53.2%). Proportion of patients with prior use of bDMARDs was similar in the baricitinib and TNFi cohorts (any baricitinib 55.6%, TNFi 56.1%). Abatacept was the most frequently recorded prior bDMARD in both cohorts (any baricitinib 15.1%, TNFi 15.0%).

Baseline healthcare resource utilisation was similar across the baricitinib and TNFi cohorts in the SNDS (SNDS Table 14 Annex 16).

10.3. Results by data source

10.3.1. US data sources

10.3.1.1. Aetna

10.3.1.1.1. VTE

Within the unmatched eligible Aetna population, 0 of 69 patients in the baricitinib cohort had a VTE and 2 of 289 patients in the TNFi cohort had a VTE (Table 45_Aetna). In the matched cohorts, there were no patients with a VTE in either cohort. In addition to low sample size (37 in each of the matched cohorts), follow-up time was also low (baricitinib 12.78 PY, TNFi 22.18 PY). The IR of

VTE in the baricitinib cohort was 0.00 (95% CI 0.00, 28.88) per 100 PY and 0.00 (95% CI 0.00, 16.64) per 100 PY in the TNFi cohort. In the absence of any VTE events, the hazard ratio was not estimated.

Table 45_Aetna Incidence Rate of VTE, Primary Definition [Aetna]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 69)	TNFi (N = 289)	Baricitinib[a] (N = 37)	TNFi (N = 37)	Total (N = 74)
Overall					
Person-Years	29.61	173.51	12.78	22.18	34.95
VTE Events	0	2	0	0	0
VTE Events/100 PY	0.00	1.15	0.00	0.00	0.00
95% CI	0.00, 12.46	0.14, 4.16	0.00, 28.88	0.00, 16.64	0.00, 10.56
Concomitant MTX Use[b]					
Total, n	13 (18.8%)	81 (28.0%)	7 (18.9%)	14 (37.8%)	21 (28.4%)
Person-Years	8.04	67.58	4.53	10.74	15.27
VTE Events	0	0	0	0	0
VTE Events/100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 45.89	0.00, 5.46	0.00, 81.45	0.00, 34.34	0.00, 24.16
No Concomitant MTX Use[b]					
Total, n	56 (81.2%)	208 (72.0%)	30 (81.1%)	23 (62.2%)	53 (71.6%)
Person-Years	21.57	105.93	8.25	11.43	19.68
VTE Events	0	2	0	0	0
VTE Events/100 PY	0.00	1.89	0.00	0.00	0.00
95% CI	0.00, 17.10	0.23, 6.82	0.00, 44.73	0.00, 32.27	0.00, 18.75

Abbreviations: CI = confidence intervals; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

[b] Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.45. Incidence Rate of Event - VTE, Primary Definition [Healthagen (RA)].docx

10.3.1.1.2. MACE

Within the unmatched eligible Aetna population, 0 of 70 patients in the baricitinib cohort experienced a MACE and in the TNFi cohort, 1 of 289 patients had a MACE (Table 54_Aetna). In the matched cohorts, there were 0 patients with a MACE in both cohorts. In addition to low sample size (43 in each of the matched cohorts), follow-up time was also low (baricitinib 15.12 PY, TNFi 28.15 PY). The IR of MACE in the baricitinib cohort was 0.00 (95% CI 0.00, 24.40) per 100 PY and 0.00 (95% CI 0.00, 13.10) per 100 PY in the TNFi cohort. In the absence of any MACE events, the hazard ratio was not estimated.

Table 54_Aetna Incidence Rate of MACE [Aetna]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 70)	TNFi (N = 289)	Baricitinib[a] (N = 43)	TNFi (N = 43)	Total (N = 86)
Overall					
Person-Years	29.77	173.27	15.12	28.15	43.27
MACE	0	1	0	0	0
MACE/100 PY	0.00	0.58	0.00	0.00	0.00
95% CI	0.00, 12.39	0.02, 3.22	0.00, 24.40	0.00, 13.10	0.00, 8.53
MI					
MI	0	0	0	0	0
Person-Years	29.77	173.75	15.12	28.15	43.27
IR per 100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 12.39	0.00, 2.12	0.00, 24.40	0.00, 13.10	0.00, 8.53
Stroke, any					
Stroke	0	1	0	0	0
Person-Years	29.77	173.27	15.12	28.15	43.27
IR per 100 PY	0.00	0.58	0.00	0.00	0.00
95% CI	0.00, 12.39	0.02, 3.22	0.00, 24.40	0.00, 13.10	0.00, 8.53
Concomitant MTX Use[b]					
MACE	0	0	0	0	0
Person-Years	8.04	67.58	4.94	10.08	15.02
IR per 100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 45.89	0.00, 5.46	0.00, 74.68	0.00, 36.58	0.00, 24.55
No Concomitant MTX Use[b]					
MACE	0	1	0	0	0
Person-Years	21.73	105.68	10.18	18.07	28.24
IR per 100 PY	0.00	0.95	0.00	0.00	0.00
95% CI	0.00, 16.98	0.02, 5.27	0.00, 36.24	0.00, 20.42	0.00, 13.06

Abbreviations: CI = confidence interval; IR = incidence rate; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; MI = myocardial infarction; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

[b] Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.54. Incidence Rate of Event - MACE [Healthagen].docx

10.3.1.1.3. Serious infection

Within the unmatched eligible Aetna population, 1 of 73 patients in the baricitinib cohort had a first serious infection and 4 of 301 patients in the TNFi cohort had a serious infection (Table 59_Aetna). In the matched cohorts, there was one patient in each cohort with a serious infection. In addition to low sample size (44 in each of the matched cohorts), follow-up time was also low (baricitinib 16.71 PY, TNFi 23.99 PY). The rate of serious infection in the baricitinib cohort was 5.98 (95% CI 0.15, 33.34) per 100 PY and 4.17 (95% CI 0.11, 23.23) per 100 PY in the TNFi cohort. Patients treated with baricitinib had an approximately 70% greater risk of serious infection relative to those treated with TNFi (HR=1.71, 95% CI 0.10, 30.54) (Table 61_Aetna). Due to the small number of events and short follow-up time, the CIs are wide and limit interpretation from this single data source.

Table 59_Aetna Incidence Rate of First Serious Infection [Aetna]

Model	Unmatched		Matched		
	Baricitinib (N = 73)	TNFi (N = 301)	Baricitinib (N = 44)	TNFi (N = 44)	Total (N = 88)
SI Events	1	4	1	1	2
Person-years	31.32	177.83	16.71	23.99	40.70
IR per 100 PY	3.19	2.25	5.98	4.17	4.91
95% CI	0.08, 17.79	0.61, 5.76	0.15, 33.34	0.11, 23.23	0.60, 17.75

Abbreviations: CI = confidence interval; IR = incidence rate; N = number of patients in the specified category; PY = person-years; SI = serious infection; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. [Updated 2022.03.15] Table 6.59. Incidence Rate of Event - First Serious Infection [Healthagen RA].docx

Table 61_Aetna Comparative Risk of First Serious Infection Event [Aetna]

	TNFi	Baricitinib		P-Value
		HR	95% CI	
Base Model[a]	**Ref**	**1.71**	**0.10, 30.54**	**0.71**

Abbreviations: CI = confidence interval; HR = Cox proportional hazard ratio; Ref = referent group; TNFi = tumour necrosis factor inhibitor.

[a] Base model = propensity score-matched model.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\[2022.03.11] Table 6.61. Comparative Risk of First Serious Infection Event [Healthagen].docx

10.3.1.2. Anthem (HIRD)

10.3.1.2.1. VTE

Within the unmatched eligible HIRD cohorts, ≤10 of 255 patients in the baricitinib cohort had a VTE and ≤10 of the 1,304 patients in the TNFi cohort had a VTE (Table 45_HIRD). Anthem protects members' privacy by reporting "≤10" where patient counts are between 1 and 10. In the

matched cohorts, there were 0 patients with VTE in both cohorts. In addition to low sample size (123 in each of the matched cohorts), total follow-up time was also low (baricitinib 69.43 PY, TNFi 98.99 PY). The rate of VTE in the baricitinib cohort was 0.00 (95% CI 0.00, 5.31) per 100 PY and 0.00 (95% CI 0.00, 3.73) per 100 PY in the TNFi cohort. In the absence of any VTE events, the hazard ratio was not estimated.

Table 45_HIRD. Incidence rate of VTE, Primary Definition [HIRD]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 255)	TNFi (N = 1304)	Baricitinib[a] (N = 123)	TNFi (N = 123)	Total (N = 246)
Overall					
Person-Years[b]	NA	NA	69.43	98.99	168.42
VTE Events	≤ 10	≤ 10	0	0	0
VTE Events/100 PY	0.76	0.68	0.00	0.00	0.00
95% CI	0.02, 4.25	0.27, 1.40	0.00, 5.31	0.00, 3.73	0.00, 2.19
Concomitant MTX Use					
Total, n	28	283	16	24	40
Person-Years	26.77	NA	16.51	25.02	41.53
VTE Events	0	≤ 10	0	0	0
VTE Events/100 PY	0.00	0.64	0.00	0.00	0.00
95% CI	0.00, 13.78	0.08, 2.31	0.00, 22.35	0.00, 14.74	0.00, 8.88
No Concomitant MTX Use					
Total, n	227	1021	107	99	206
Person-Years	NA	NA	52.92	73.97	126.89
VTE Events	≤ 10	≤ 10	0	0	0
VTE Events/100 PY	0.96	0.70	0.00	0.00	0.00
95% CI	0.02, 5.34	0.23, 1.62	0.00, 6.97	0.00, 4.99	0.00, 2.91

Abbreviations: CI = confidence intervals; HIRD = HealthCore Integrated Research Database; MTX = methotrexate; N = number of patients in the specified category; NA = not applicable; PY = person-years; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

[b] Person-years are not reported when patient counts are between 1 and 10, to maintain privacy for this data source. Similarly, counts of events are reported as '≤10' when there are between 1 and 10 events. When no events have occurred, '0' is recorded.

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10.3.1.2.2. MACE

Within the unmatched eligible HIRD cohorts, none of the 255 patients in the baricitinib cohort had a MACE and ≤10 patients in the TNFi cohort had a MACE (Table 54_HIRD). In the matched cohorts, there were 0 patients with a MACE in both cohorts. In addition to low sample size (123 in each of the matched cohorts), total follow-up time was also low (baricitinib 69.43 PY, TNFi 97.05 PY). The rate of MACE in the baricitinib cohort was 0.00 (95% CI 0.00, 5.31) per 100 PY and 0.00 (95% CI

0.00, 3.80) per 100 PY in the TNFi cohort. In the absence of any MACE events, the hazard ratio was not estimated.

Table 54_HIRD Incidence Rate of MACE [HIRD]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 255)	TNFi (N = 1308)	Baricitinib[a] (N = 123)	TNFi (N = 123)	Total (N = 246)
Overall					
Person-Years[b]	131.16	NA	69.43	97.05	166.47
MACE	0	≤ 10	0	0	0
MACE/100 PY	0.00	0.67	0.00	0.00	0.00
95% CI	0.00, 2.81	0.27, 1.39	0.00, 5.31	0.00, 3.80	0.00, 2.22
MI					
MI	0	≤ 10	0	0	0
Person-Years[b]	131.16	NA	69.43	97.05	166.47
IR per 100 PY	0.00	0.19	0.00	0.00	0.00
95% CI	0.00, 2.81	0.02, 0.70	0.00, 5.31	0.00, 3.80	0.00, 2.22
Stroke, any					
Stroke	0	≤ 10	0	0	0
Person-Years[b]	131.16	NA	69.43	97.05	166.47
IR per 100 PY	0.00	0.48	0.00	0.00	0.00
95% CI	0.00, 2.81	0.16, 1.13	0.00, 5.31	0.01, 3.80	0.00, 2.22
Concomitant MTX Use					
n	28	285	16	18	34
MACE	0	0	0	0	0
Person-Years[b]	26.77	315.14	16.51	21.44	37.94
IR per 100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 13.78	0.00, 1.17	0.00, 22.35	0.00, 17.21	0.00, 9.72
No Concomitant MTX Use					
n	227	1023	107	105	212
MACE	0	≤ 10	0	0	0
Person-Years[b]	104.39	NA	52.92	75.61	128.53
IR per 100 PY	0.00	0.97	0.00	0.00	0.00
95% CI	0.00, 3.53	0.39, 2.00	0.00, 6.97	0.00, 4.89	0.00, 2.87

Abbreviations: CI = confidence interval; HIRD = HealthCore Integrated Research Database; IR = Incidence Rate; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; MI = myocardial infarction; MTX = methotrexate; N = number of patients in the specified category; NA = not applicable; PY = person-years; TNFi = tumour necrosis factor inhibitor.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

[b] Person-years are not reported when patient counts are between 1 and 10, to maintain privacy for this data source. Similarly, counts of events are reported as '≤10' when there are between 1 and 10 events. When no events have occurred, '0' is recorded.

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10.3.1.2.3. Serious infection

Within the unmatched eligible HIRD cohorts, ≤10 of 263 patients in the baricitinib cohort had a first serious infection and 19 of 1,342 patients in the TNFi cohort had a serious infection (Table 59_HIRD). In the matched cohorts, there were ≤10 patients with serious infection in each cohort.

The rate of serious infection in the baricitinib cohort was 1.36 (95% CI 0.03, 7.60) per 100 PY and 1.00 (95% CI 0.03, 5.57) per 100 PY in the TNFi cohort (Table 61_HIRD). The HR for serious infection was 1.12 (95% CI: 0.07, 18.07). Due to the small number of events, the CIs are wide and limit interpretation from this single data source.

Table 59_HIRD Incidence Rate of First Serious Infection [HIRD]

Model	Unmatched		Matched		
	Baricitinib (N = 263)	TNFi (N = 1342)	Baricitinib (N = 130)	TNFi (N = 130)	Total (N = 260)
SI Events	≤10	19	≤10	≤10	≤10
Person-years[a]	NA	1052.66	NA	NA	NA
IR per 100 PY	2.23	1.80	1.36	1.00	1.15
95% CI	0.46, 6.51	1.09, 2.82	0.03, 7.60	0.03, 5.57	0.14, 4.17

Abbreviations: CI = confidence interval; HIRD = HealthCore Integrated Research Database; IR = Incidence Rate; N = number of patients in the specified category; NA = not applicable; PY = person-years; SI = serious infection; TNFi = tumour necrosis factor inhibitor.

[a] Person-years are not reported when patient counts are between 1 and 10, to maintain privacy for this data source. Similarly, counts of events are reported as '≤10' when there are between 1 and 10 events. When no events have occurred, '0' is recorded.

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Table 61_HIRD Comparative Risk of First Serious Infection Event [HIRD]

Model	TNFi	Baricitinib		
		HR	95% CI	P-value
Base Model[a]	Ref	1.12	0.07, 18.07	0.94
Adjusted – Model [1][b]	Ref	1.22	0.08, 19.77	0.89

Abbreviations: CI = confidence interval; HIRD = HealthCore Integrated Research Database; HR = hazard ratio; Ref = reference group; TNFi = tumour necrosis factor inhibitor.

[a] Base model = propensity score-matched model.

[b] Model [1] = propensity score-matched model with outcome and baricitinib exposure, adjusted for variables that remain unbalanced after propensity score matching. Specifically, this model is adjusted for the number of rheumatologist visits during baseline. Other covariates that remained unbalanced after PS matching included antibiotic use during baseline, glucocorticoid use during baseline, number of emergency department visits during baseline, number of inpatient visits during baseline, and obesity during baseline; however, these covariates were not able to be included in the model due to non-convergence. The extent of the imbalance remaining is shown in the standardised differences presented in Table 9_HIRD, Annex 3.

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10.3.1.3. CorEvitas (US)

10.3.1.3.1. VTE

Within the unmatched (ie., 'pre-matched') eligible CorEvitas US population, 0 of 115 patients in the baricitinib cohort had a VTE and 7 of 1,864 patients in the TNFi cohort had a VTE

(Table 45_COR_US). In the matched cohorts (n = 112 in each cohort), there were 0 patients with VTE in baricitinib cohort and 1 in the TNFi cohort. In addition to low sample size (112 in each of the matched cohorts), total follow-up time was also low (baricitinib 76.2 PY, TNFi 84.6 PY). The rate of VTE in the baricitinib cohort was 0.00 (95% CI 0.00, 4.8) per 100 PY and 1.2 (95% CI 0.00, 6.6) per 100 PY in the TNFi cohort. In the absence of VTE events within the baricitinib cohort, the hazard ratio was not estimated.

The small size of the analysis cohort limits the ability to evaluate the IRs based on relevant stratifying factors. Table 45_COR_US presents counts and IRs of VTE among patients that were bDMARD naïve and experienced, as well as by concomitant use of methotrexate at index date and no use of methotrexate at index.

Table 45_COR_US Incidence rate of VTE, Primary Definition [COR_US]

Model	Pre-matched		Matched		
	Baricitinib (N = 115)	TNFi (N = 1864)	Baricitinib (N = 112)	TNFi (N = 112)	Total (N = 224)
Overall					
N	115	1864	112	112	224
VTE Events	0	7	0	1	1
Person-Years	78.9	1428.5	76.2	84.6	160.8
VTE Events/100 PY	0.0	0.5	0.0	1.2	0.6
95% CI	0.0, 4.7	0.2, 1.0	0.0, 4.8	0.0, 6.6	0.0, 3.5
Incidence rate difference: baricitinib-TNFi (95% CI)					-1.18 (-3.50, 1.13)
Incidence rate ratio: baricitinib-TNFi (95% CI)					0.00 (0.00, 43.31)
bDMARD-naïve					
N	15	895	15	17	32
VTE Events	0	4	0	1	1
Person-Years	12.2	699.0	12.2	12.2	24.3
VTE Events/100 PY	0.0	0.6	0.0	8.2	4.1
95% CI	0.0, 30.2	0.2, 1.5	0.0, 30.2	0.2, 45.7	0.1, 22.9
Incidence rate difference: baricitinib-TNFi (95% CI)					-8.22 (-24.33, 7.89)
Incidence rate ratio: baricitinib-TNFi (95% CI)					0.00 (0.00, 39.00)
bDMARD-experienced					
N	100	969	97	95	192
VTE Events	0	3	0	0	0
Person-Years	66.7	729.4	64.0	72.5	136.5
VTE Events/100 PY	0.0	0.4	0.0	0.0	0.0
95% CI	0.0, 5.5	0.1, 1.2	0.0, 5.8	0.0, 5.1	0.0, 2.7
Incidence rate difference: baricitinib-TNFi (95% CI)					0.0 (0.0, 0.0)
Incidence rate ratio: baricitinib-TNFi (95% CI)					-(-, -)
Concomitant MTX Use at Index Date					
N	51	964	50	54	104
VTE Events	0	3	0	1	1
Person-Years	37.5	752.9	37.2	43.5	80.7

Model	Pre-matched		Matched		
	Baricitinib (N = 115)	TNFi (N = 1864)	Baricitinib (N = 112)	TNFi (N = 112)	Total (N = 224)
VTE Events/100 PY	0.0	0.4	0.0	2.3	1.2
95% CI	0.0, 9.8	0.1, 1.2	0.0, 9.9	0.1, 12.8	0.0, 6.9
Incidence rate difference: baricitinib-TNFi (95% CI)					-2.30 (-6.80, 2.21)
Incidence rate ratio: baricitinib-TNFi (95% CI)					0.00 (0.00, 45.65)
No concomitant MTX Use at Index Date					
N	64	900	62	58	120
VTE Events	0	4	0	0	0
Person-Years	41.4	675.6	39.0	41.1	80.2
VTE Events/100 PY	0.0	0.6	0.0	0.0	0.0
95% CI	0.0, 8.9	0.2, 1.5	0.0, 9.5	0.0, 9.0	0.0, 4.6
Incidence rate difference: baricitinib-TNFi (95% CI)					0.0 (0.0, 0.0)
Incidence rate ratio: baricitinib-TNFi (95% CI)					-(-, -)

Abbreviations: bDMARD = biologic disease-modifying anti-rheumatic drug; CI = confidence interval; MTX = methotrexate; N = count of patients in specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

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10.3.1.3.2. MACE

Within the unmatched (ie., 'pre-matched') eligible CorEvitas US population, 2 of 114 patients in the baricitinib cohort had a MACE and 4 of the 1,864 patients in the TNFi cohort had a MACE (Table 54_COR_US). In the matched cohorts (n = 114 in each), there were 2 patients with a MACE in baricitinib cohort and 1 in the TNFi cohort. All 3 of these MACE events were MI, there were no stroke events. In addition to low sample size (114 in each of the matched cohorts), total follow-up time was also low (baricitinib 76.0 PY, TNFi 78.9 PY). The rate of MACE in the baricitinib cohort was 2.6 (95% CI 0.3, 9.5) per 100 PY and 1.3 (95% CI 0.0, 7.1) per 100 PY in the TNFi cohort. In Model[1], adjusted for variables remaining imbalanced after propensity score matching, confidence intervals are wide although the point estimate is consistent with an increase in risk of MACE among patients treated with baricitinib compared to TNFi ($HR_{Model\ [1]}$ = 1.6; 95% CI 0.11, 23.61) (Table 55_COR_US). However, the wide CIs limit interpretation of this result.

Counts and IRs of MACE among patients with and without concomitant methotrexate at index date are presented in Table 54_COR_US. The small size of the analysis cohort limits the ability to evaluate IRs based on these relevant stratifying factors. It is important to note that such stratification disrupts the propensity score matched cohorts; therefore, direct comparisons between strata and with other cohorts should be avoided.

Table 54_COR_US Incidence Rate of MACE [COR_US]

Model	Pre-matched		Matched		
	Baricitinib (N = 114)	TNFi (N = 1864)	Baricitinib (N = 114)	TNFi (N = 114)	Total (N = 228)
Overall					
N	114	1864	114	114	228
MACE Events	2	4	2	1	3
Person-Years	76.0	1426.3	76.0	78.9	154.9
MACE Events/100 PY	2.6	0.3	2.6	1.3	1.9
95% CI	0.3, 9.5	0.1, 0.7	0.3, 9.5	0.0, 7.1	0.4, 5.7
Incidence rate difference: baricitinib-TNFi (95% CI)					1.36 (-3.05, 5.77)
Incidence rate ratio: baricitinib-TNFi (95% CI)					2.07 (0.11, 122.39)
MI					
N	114	1864	114	114	228
MI Events	2	2	2	1	3
Person-Years	76.0	1428.7	76.0	78.9	154.9
MI Events/100 PY	2.6	0.1	2.6	1.3	1.9
95% CI	0.3, 9.5	0.0, 0.5	0.3, 9.5	0.0, 7.1	0.4, 5.7
Incidence rate difference: baricitinib-TNFi (95% CI)					1.36 (-3.05, 5.77)
Incidence rate ratio: baricitinib-TNFi (95% CI)					2.07 (0.11, 122.39)
Stroke					
N	114	1864	114	114	228
Stroke Events	0	2	0	0	0
Person-Years	77.1	1427.2	77.1	79.5	156.7
Stroke Events/100 PY	0.0	0.1	0.0	0.0	0.0
95% CI	0.0, 4.8	0.0, 0.5	0.0, 4.8	0.0, 4.6	0.0, 2.4
Incidence rate difference: baricitinib-TNFi (95% CI)					0.00 (0.00, 0.00)
Incidence rate ratio: baricitinib-TNFi (95% CI)					- (-, -)
Concomitant MTX Use at Index Date					
N	51	966	51	40	91
MACE Events	1	2	1	1	2
Person-Years	36.4	753.8	36.4	31.4	67.8
MACE Events/100 PY	2.7	0.3	2.7	3.2	2.9
95% CI	0.1, 15.3	0.0, 1.0	0.1, 15.3	0.1, 17.7	0.4, 10.7
Incidence rate difference: baricitinib-TNFi (95% CI)					-0.44 (-8.69, 7.80)
Incidence rate ratio: baricitinib-TNFi (95% CI)					0.86 (0.01, 67.63)
No concomitant MTX Use at Index Date					
N	63	898	63	74	137
MACE Events	1	2	1	0	1

Model	Pre-matched		Matched		
	Baricitinib (N = 114)	TNFi (N = 1864)	Baricitinib (N = 114)	TNFi (N = 114)	Total (N = 228)
Person-Years	39.6	672.5	39.6	47.5	87.1
MACE Events/100 PY	2.5	0.3	2.5	0.0	1.1
95% CI	0.1, 14.1	0.0, 1.1	0.1, 14.1	0.0, 7.8	0.0, 6.4
Incidence rate difference: baricitinib-TNFi (95% CI)					2.52 (-2.42, 7.47)
Incidence rate ratio: baricitinib-TNFi (95% CI)					-(-, -)

Abbreviations: CI = confidence interval; MI = myocardial infarction; MACE = major adverse cardiovascular event; MTX = methotrexate; N = count of patients in specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor.

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Table 55_COR_US Comparative Risk of MACE [Cor_US]

Model	TNFi	Baricitinib HR (95% CI)	P-value
Base model	Ref	2.21 (0.20, 24.46)	0.52
Adjusted- Model [1]	Ref	1.60 (0.11, 23.61)	0.73
Adjusted- Model [2]	Ref	1.68 (0.11, 24.74)	0.71
non-mtx cDMARD use	Ref	--	--
mtx cDMARD use	Ref	1.68 (0.12, 23.60)	0.70
prednisone use	Ref	--	--
Adjusted- Model [3]	Ref	--	--
prednisone use	Ref	--	--
Adjusted- Model [4]	Ref	1.90 (0.11, 33.71)	0.66
RA severity (CDAI)	Ref	0.95 (0.82, 1.09)	0.47
Adjusted- Model [5]	Ref	2.89 (0.11, 78.95)	0.53
Adjusted- Model [6]	Ref	2.22 (0.14, 34.64)	0.57

Abbreviations: BMI = body mass index; CDAI = clinical disease activity index; cDMARD = conventional disease-modifying anti-rheumatic drug; CI = confidence interval; HR = hazard ratio; mtx = methotrexate; MACE = major adverse cardiovascular event; RA = rheumatoid arthritis; Ref = reference group; TNFi = tumour necrosis factor inhibitor.
Base model: no adjusting covariates.
Model [1]: adjusted with covariates remained imbalanced after matching (education, history of chronic lung disease, history of CVD, history of VTE, history of ischaemic heart disease, prior serious infection). .
Model [2]: Model [1] + time-varying concomitant methotrexate use (time varying concomitant non-methotrexate cDMARD use and time varying prednisone use could not be included because there are no events among patients taking these medications).
Model [3]: Model [1] + time-varying prednisone use (model could not be estimated due to no events in patients taking prednisone).
Model [4]: Model [1] + RA severity (CDAI).
Model [5]: Model [4] + BMI + smoking status.
Model [6]: Model [1] + aspirin use.
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10.3.1.3.3. Serious infection

Within the unmatched (ie., 'pre-matched') eligible CorEvitas US cohorts, 3 of the 115 patients in the baricitinib cohort had a first serious infection and 44 of 1,881 patients in the TNFi cohort had a serious infection (Table 59_COR_US). In the matched cohorts (n = 114 in each), there were 3 patients with serious infection in baricitinib cohort and 0 in the TNFi cohort. The rate of serious infection in the baricitinib cohort was 4.0 (95% CI 0.8, 11.7) per 100 PY and 0.0 (95% CI 0.0, 4.5) per 100 PY in the TNFi cohort. In the absence of events within the TNFi cohort, the hazard ratio was not estimated.

Table 59_COR_US Incidence Rate of First Serious Infection [Cor_US]

Model	Pre-matched		Matched		
	baricitinib (N = 115)	TNFi (N = 1881)	baricitinib (N = 114)	TNFi (N = 114)	Total (N = 228)
Overall					
N	115	1881	114	114	228
SI Events	3	44	3	0	3
Person-Years	75.0	1423.6	74.9	81.7	156.6
SI Events/100 PY	4.0	3.1	4.0	0.0	1.9
95% CI	0.8, 11.7	2.2, 4.1	0.8, 11.7	0.0, 4.5	0.4, 5.6
Incidence rate difference: baricitinib-TNFi (95% CI)					4.01 (-0.53, 8.54)
Incidence rate difference: baricitinib-TNFi (95% CI)					- (-, -)

Abbreviations: CI = confidence interval; PY = person-years; SI = serious infection; TNFi = tumour necrosis factor inhibitor.

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10.3.1.4. Humana

10.3.1.4.1. VTE

Within the unmatched eligible Humana population, 1 of 89 patients in the baricitinib and 1 of 154 patients in the TNFi cohort had a VTE (Table 45_HUM). In the matched cohorts, there were 0 patients with a VTE in both cohorts. In addition to low sample size (49 in each of the matched cohorts), follow-up time was also low (baricitinib 19.83 PY, TNFi 20.57 PY). The rate of VTE in the baricitinib cohort was 0.00 (95% CI 0.00, 18.60) per 100 PY and 0.00 (95% CI 0.00, 17.94) per 100 PY in the TNFi cohort. In the absence of any VTE events, the hazard ratio was not estimated.

Table 45_HUM Incidence Rate of VTE, Primary Definition [HUM]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 89)	TNFi (N = 154)	Baricitinib[a] (N = 49)	TNFi (N = 49)	Total (N = 98)
Overall					
Person-Years	CCI	CCI	19.83	20.57	40.40
VTE Events	CCI	CCI	0	0	0
VTE Events/100 PY	2.46	1.43	0.00	0.00	0.00
95% CI	0.06, 13.69	0.04, 7.95	0.00, 18.60	0.00, 17.94	0.00, 9.13
Concomitant MTX Use[b]					
Total, n	13 (14.6%)	29 (18.8%)	CCI (CCI%)	CCI (CCI%)	13 (13.3%)
Person-Years	9.30	23.64	CCI	CCI	9.63
VTE Events	0	1	0	0	0

Model	Unmatched		Matched		
	Baricitinib[a] (N = 89)	TNFi (N = 154)	Baricitinib[a] (N = 49)	TNFi (N = 49)	Total (N = 98)
VTE Events/100 PY	0.00	4.23	0.00	0.00	0.00
95% CI	0.00, 39.67	0.11, 23.57	0.00, 78.97	0.00, 74.43	0.00, 38.32
No Concomitant MTX Use[b]					
Total, n	76 (85.4%)	125 (81.2%)	42 (85.7%)	43 (87.8%)	85 (86.7%)
Person-Years	CCI	46.41	15.16	15.61	30.77
VTE Events	CCI	0	0	0	0
VTE Events/100 PY	3.19	0.00	0.00	0.00	0.00
95% CI	0.08, 17.75	0.00, 7.95	0.00, 24.33	0.00, 23.63	0.00, 11.99

Abbreviations: CI = confidence intervals; HUM = Humana; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

[b] Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.45. Incidence Rate of Event - VTE, Primary Definition [Humana 1179 Curated (RA) - Rheumatoid Arthritis].docx

10.3.1.4.2. MACE

Within the unmatched eligible Humana population, 0 of 89 patients in the baricitinib cohort had a MACE and 2 of 153 patients in the TNFi cohort had a MACE (Table 54_HUM). In the matched cohorts, there were 0 patients with a MACE in the baricitinib cohort and 2 in the TNFi cohort. In addition to low sample size (51 in each of the matched cohorts), follow-up time was also low (baricitinib 21.39 PY, TNFi 25.47 PY). The rate of MACE in the baricitinib cohort was 0.00 (95% CI 0.00, 17.25) per 100 PY and 7.85 (95% CI 0.95, 28.36) per 100 PY in the TNFi cohort. In the absence of any MACE events in the baricitinib group, the hazard ratio was not estimated.

Table 54_HUM Incidence Rate of MACE [HUM]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 89)	TNFi (N = 153)	Baricitinib[a] (N = 51)	TNFi (N = 51)	Total (N = 102)
Overall					
Person-Years	41.29	CCI	21.39	CCI	CCI
MACE	0	CCI	0	CCI	CCI
MACE/100 PY	0.00	2.84	0.00	7.85	4.27
95% CI	0.00, 8.93	0.34, 10.24	0.00, 17.25	0.95, 28.36	0.52, 15.42
MI					
MI	0	CCI	0	CCI	CCI
Person-Years	41.29	CCI	21.39	CCI	CCI

Model	Unmatched		Matched		
	Baricitinib[a] (N = 89)	TNFi (N = 153)	Baricitinib[a] (N = 51)	TNFi (N = 51)	Total (N = 102)
IR per 100 PY	0.00	1.42	0.00	3.92	2.13
95% CI	0.00, 8.93	0.04, 7.90	0.00, 17.25	0.10, 21.87	0.05, 11.89
Stroke, any					
Stroke	0	[redacted]	0	[redacted]	[redacted]
Person-Years	41.29	[redacted]	21.39	[redacted]	[redacted]
IR per 100 PY	0.00	1.41	0.00	3.86	2.11
95% CI	0.00, 8.93	0.04, 7.85	0.00, 17.25	0.10, 21.51	0.05, 11.78
Concomitant MTX Use[b]					
MACE	0	0	0	0	0
Person-Years	9.30	24.67	4.91	11.65	16.56
IR per 100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 39.67	0.00, 14.95	0.00, 75.14	0.00, 31.66	0.00, 22.27
No Concomitant MTX Use[b]					
MACE	0	[redacted]	0	[redacted]	[redacted]
Person-Years	31.99	[redacted]	16.48	[redacted]	[redacted]
IR per 100 PY	0.00	4.36	0.00	14.47	6.60
95% CI	0.00, 11.53	0.53, 15.76	0.00, 22.39	1.75, 52.27	0.80, 23.84

Abbreviations: CI = confidence interval; IR = incidence rate; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

[b] Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.54. Incidence Rate of Event - MACE [Humana 1179 Curated (RA) - Rheumatoid Arthritis].docx

10.3.1.4.3. Serious infection

Within the unmatched eligible Humana population, [redacted] of 95 patients in the baricitinib cohort had a first serious infection and [redacted] of 162 patients in the TNFi cohort had a serious infection (Table 59_HUM). In the matched cohorts, there were [redacted] patients in the baricitinib cohort with a serious infection and [redacted] in the TNFi cohort. In addition to low sample size (53 in each of the matched cohorts), follow-up time was also low (baricitinib [redacted] PY, TNFi [redacted] PY). The rate of serious infection in the baricitinib cohort was 10.12 (95% CI 1.23, 36.54) per 100 PY and 3.66 (95% CI 0.09, 20.41) per 100 PY in the TNFi cohort. Patients treated with baricitinib had more than a 2-fold increased risk of serious infections relative to patients treated with TNFi, although the CI is wide resulting in an imprecise estimate (HR=2.41; 95% CI 0.21, 27.25) (Table 61_HUM).

Table 59_HUM Incidence Rate of First Serious Infection [HUM]

Model	Unmatched		Matched		
	Baricitinib (N = 95)	TNFi (N = 162)	Baricitinib (N = 53)	TNFi (N = 53)	Total (N = 106)
SI Events	CCI	CCI	CCI	CCI	CCI
Person-years	CCI	CCI	CCI	CCI	CCI
IR per 100 PY	4.52	3.98	10.12	3.66	6.37
95% CI	0.55, 16.32	0.82, 11.64	1.23, 36.54	0.09, 20.41	1.31, 18.62

Abbreviations: CI = confidence interval; HUM = Humana; IR = incidence rate; N = number of patients in the specified category; PY = person-years; SI = serious infection; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.59. Incidence Rate of Event - First Serious Infection [Humana 1179 Curated RA].docx

Table 61_HUM Comparative Risk of First Serious Infection Event [HUM]

		Baricitinib		
	TNFi	HR	95% CI	P-value
Base Model[a]	Ref	2.41	0.21, 27.25	0.48

Abbreviations: CI = confidence interval; HR = Cox proportional hazard ratio; HUM = Humana; Ref = referent group; TNFi = tumour necrosis factor inhibitor.

[a] Base model = propensity score-matched model.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\Table 6.61. Comparative Risk of First Serious Infection Event [Humana 1179 Curated (RA) - Rheumatoid Arthritis].docx

10.3.1.5. MarketScan

10.3.1.5.1. VTE

Within the unmatched eligible MarketScan population, 1 of 257 patients in the baricitinib cohort had a VTE and 6 of 1,599 patients in the TNFi cohort had a VTE (Table 45_MTSCN). In the matched cohorts, there was 1 patient with a VTE in each cohort. In addition to low sample size (185 in each of the matched cohorts), follow-up time was also low (baricitinib 84.42 PY, TNFi 77.60 PY). The rate of VTE in the baricitinib cohort was 1.19 (95% CI 0.03, 6.60) per 100 PY and 1.29 per 100 PY (95% CI 0.03, 7.18) per 100 PY in the TNFi cohort. While the point estimate for the HR was <1.0, with the wide CI no difference in risk should be noted (HR=0.79; 95% CI 0.05, 12.62) (Table 48_MTSCN).

Table 45_MTSCN Incidence Rate VTE, Primary Definition [MTSCN]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 257)	TNFi (N = 1599)	Baricitinib[a] (N = 185)	TNFi (N = 185)	Total (N = 370)
Overall					
Person-Years	120.62	763.53	84.42	77.60	162.02
VTE Events	1	6	1	1	2
VTE Events/100 PY	0.83	0.79	1.19	1.29	1.23
95% CI	0.02, 4.62	0.29, 1.71	0.03, 6.60	0.03, 7.18	0.15, 4.46
Concomitant MTX Use[b]					
Total, n	44 (17.1%)	338 (21.1%)	31 (16.8%)	31 (16.8%)	62 (16.8%)
Person-Years	29.50	232.96	19.50	17.99	37.49
VTE Events	0	0	0	0	0
VTE Events/100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 12.51	0.00, 1.58	0.00, 18.92	0.00, 20.50	0.00, 9.84
No Concomitant MTX Use[b]					
Total, n	213 (82.9%)	1261 (78.9%)	154 (83.2%)	154 (83.2%)	308 (83.2%)
Person-Years	91.12	530.56	64.92	59.61	124.53
VTE Events	1	6	1	1	2
VTE Events/100 PY	1.10	1.13	1.54	1.68	1.61
95% CI	0.03, 6.12	0.42, 2.46	0.04, 8.58	0.04, 9.35	0.20, 5.80

Abbreviations: CI = confidence intervals; MKTSCN = Marketscan; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

[b] Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.45. Incidence Rate of Event - VTE, Primary Definition [IBM MarketScan RA].docx

Table 48_MTSCN Comparative Risk of Incident VTE, Primary Definition [MTSCN]

		Baricitinib		
	TNFi	HR	95% CI	P-value
Base Model[a]	Ref	0.79	0.05, 12.62	0.87

Abbreviations: CI = confidence interval; HR = Cox proportional hazard ratio; MTSCN = Marketscan; Ref = referent group; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Base model = propensity score-matched model with confounders, outcome and baricitinib exposure.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.48. Comparative Risk of Incident VTE, Primary Definition [IBM MarketScan RA], updated base model = PS matched.docx

10.3.1.5.2. MACE

Within the unmatched eligible MarketScan population, 2 of 259 patients in the baricitinib cohort had a MACE and 1 of 1,604 patients in the TNFi cohort had a MACE (Table 54_MTSCN). In the matched cohorts, there was 1 patient with a MACE in the baricitinib cohort and 0 in the TNFi cohort. In addition to low sample size (192 in each of the matched cohorts), follow-up time was also low (baricitinib 86.61 PY, TNFi 78.33 PY). The rate of MACE in the baricitinib cohort was 1.15 (95% CI 0.03, 6.43) per 100 PY and 0.00 (95% CI 0.00, 4.71) per 100 PY in the TNFi cohort. In the absence of any MACE events in the TNFi cohort, the hazard ratio was not estimated.

Table 54_MTSCN Incidence Rate of MACE [MTSCN]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 259)	TNFi (N = 1604)	Baricitinib[a] (N = 192)	TNFi (N = 192)	Total (N = 384)
Overall					
Person-Years	120.69	767.21	86.61	78.33	164.94
MACE	2	1	1	0	1
MACE/100 PY	1.66	0.13	1.15	0.00	0.61
95% CI	0.20, 5.99	0.00, 0.73	0.03, 6.43	0.00, 4.71	0.02, 3.38
MI					
MI	1	1	1	0	1
Person-Years	121.11	767.21	86.61	78.33	164.94
IR per 100 PY	0.83	0.13	1.15	0.00	0.61
95% CI	0.02, 4.60	0.00, 0.73	0.03, 6.43	0.00, 4.71	0.02, 3.38
Stroke, any					
Stroke	1	0	0	0	0
Person-Years	120.86	767.45	86.78	78.33	165.11
IR per 100 PY	0.83	0.00	0.00	0.00	0.00
95% CI	0.02, 4.61	0.00, 0.48	0.00, 4.25	0.00, 4.71	0.00, 2.23
Concomitant MTX Use[b]					
MACE	0	0	0	0	0
Person-Years	28.87	232.96	19.39	14.68	34.07
IR per 100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 12.78	0.00, 1.58	0.00, 19.02	0.00, 25.13	0.00, 10.83
No Concomitant MTX Use[b]					
MACE	2	1	1	0	1
Person-Years	91.81	534.24	67.22	63.65	130.87
IR per 100 PY	2.18	0.19	1.49	0.00	0.76
95% CI	0.26, 7.87	0.01, 1.04	0.04, 8.29	0.00, 5.80	0.02, 4.26

Abbreviations: CI = confidence interval; IR = incidence rate; MACE = major adverse cardiovascular event, defined based on primary hospital discharge codes for acute myocardial infarction, ischemic or haemorrhagic stroke; MTSCN = Marketscan; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose when numbers of patients are sufficient to warrant separate reporting.

[b] Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.54. Incidence Rate of Event - MACE [IBM MarketScan RA].docx

10.3.1.5.3. Serious infection

Within the unmatched eligible MarketScan population, 2 of 263 patients in the baricitinib cohort had a first serious infection and 8 of 1,627 patients in the TNFi cohort had a serious infection (Table 59_MTSCN). In the matched cohorts, there was 1 patient in the baricitinib cohort with a serious infection and 0 in the TNFi cohort. In addition to low sample size (194 in each of the matched cohorts), follow-up time was also low (baricitinib 87.23 PY, TNFi 83.53 PY). The IR of serious infection in the baricitinib cohort was 1.15 (95% CI 0.03, 6.39) per 100 PY and 0.0 (95% CI 0.00, 4.42) per 100 PY in the TNFi cohort. In the absence of any serious infection events in the TNFi cohort, the hazard ratio was not estimated.

Table 59_MTSCN Incidence Rate of First Serious Infection [MTSCN]

Model	Unmatched		Matched		
	Baricitinib (N = 263)	TNFi (N = 1627)	Baricitinib (N = 194)	TNFi (N = 194)	Total (N = 388)
SI Events	2	8	1	0	1
Person-Years	122.96	773.31	87.23	83.53	170.76
IR per 100 PY	1.63	1.03	1.15	0.00	0.59
95% CI	0.20, 5.88	0.45, 2.04	0.03, 6.39	0.00, 4.42	0.02, 3.26

Abbreviations: CI = confidence interval; IR = incidence rate; N = number of patients in the specified category; PY = person-years; SI = serious infection; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.59. Incidence Rate of Event - First Serious Infection [IBM MarketScan RA].docx

10.3.1.6. MDR

10.3.1.6.1. VTE

Within the unmatched MDR data, 2 of 188 patients in the baricitinib cohort had a VTE and 3 of 1,686 patients in the TNFi cohort had a VTE (Table 45_MDR). In the matched cohorts, there was 1 patient with a VTE in each cohort. In addition to low sample size (114 in each of the matched cohorts), follow-up time was also low (baricitinib 61 PY, TNFi 70 PY). The IR of VTE in the baricitinib cohort was 1.6 (95% CI 0.2, 11.7) per 100 PY and 1.4 (95% CI 0.2, 10.1) per 100 PY in

the TNFi cohort. While the point estimate for the HR was slightly above the null, with wide CI, no difference should be noted in risk of VTE between cohorts (HR=1.23; 95% CI 0.1, 20.7) (Table 48_MDR).

Table 45_MDR Incidence Rate of VTE Primary Definition [MDR]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 188)	TNFi (N = 1686)	Baricitinib[a] (N = 114)	TNFi (N = 114)	Total (N = 228)
Overall					
Person-Years	95	959	61	70	131
VTE Events	2.0	3.0	1.0	1.0	2.0
VTE Events/100 PY	2.1	0.3	1.6	1.4	1.5
95% CI	(0.5, 8.4)	(0.1, 1.0)	(0.2, 11.7)	(0.2, 10.1)	(0.4, 6.1)
Rate difference events/100 PY	NA	NA	NA	NA	0.2
95% CI	NA	NA	NA	NA	(-4.1, 4.5)
Concomitant MTX Use					
Total, n	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Person-Years	0	0	0	0	0
VTE Events	0.0	0.0	0.0	0.0	0.0
VTE Events/100 PY	0.0	0.0	0.0	0.0	0.0
95% CI	NA	NA	NA	NA	NA
No Concomitant MTX Use					
Total, n	188 (100%)	1686 (100%)	114 (100%)	114 (100%)	228 (100%)
Person-Years	95	959	61	70	131
VTE Events	2.0	3.0	1.0	1.0	2.0
VTE Events/100 PY	2.1	0.3	1.6	1.4	1.5
95% CI	(0.5, 8.4)	(0.1, 1.0)	(0.2, 11.7)	(0.2, 10.1)	(0.4, 6.1)

Abbreviations: CI = confidence intervals; MDR = Military Data Health Repository; MTX = methotrexate; N = number of patients in the specified category; NA = not applicable; PY = person-years; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose when numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\military health_MDR\Lilly Baricitinib Results_Top-Line_Military Health_v2.0.docx -page 13

Table 48_MDR Comparative Risk of Incident VTE, Primary Definition [MDR]

Model	TNFi	Baricitinib		P-value
		HR	95% CI	
Base Model	Ref	1.23	0.1, 20.7	0.88

Abbreviations: CI = confidence interval; HR = hazard ratio; MDR = Military Data Health Repository; Ref = referent group; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.
Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\military health_MDR\Lilly Baricitinib Results_Top-Line_Military Health_v2.0.docx -page 14

10.3.1.6.2. MACE

Within the unmatched eligible MDR population, 0 of 188 patients in the baricitinib cohort had a MACE and 4 of 1,685 patients in the TNFi cohort had a MACE (Table 54_MDR). In the matched cohorts, no patients had a MACE event. In addition to low sample size (114 in each of the matched cohorts), follow-up time was also low (baricitinib 61 PY, TNFi 70 PY). In the absence of any MACE events in either cohort, the hazard ratio was not estimated.

Table 54_MDR Incidence Rate of MACE [MDR]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 188)	TNFi (N = 1685)	Baricitinib[a] (N = 114)	TNFi (N = 114)	Total (N = 228)
Overall					
Person-Years	96	956	61	70	130
MACE	0.0	4.0	0.0	0.0	0.0
MACE/100 PY	0.0	0.4	0.0	0.0	0.0
95% CI	NA	(0.2, 1.1)	(0, 6.05)	(0, 5.27)	NA
Rate difference events/100 PY	NA	NA	NA	NA	0.0
95% CI	NA	NA	NA	NA	(0.0, 0.0)
MI					
MI	0	2	0	0	0
Person-Years	95.6	955.9	60.8	69.7	130.5
IR /100 PY	0.0	0.2	0.0	0.0	0.0
95% CI	NA	(0.1, 0.8)	NA	NA	NA
Stroke, any					
Stroke	0	2	0	0	0
Person-Years	95.6	955.9	60.8	69.7	130.5
IR/100 PY	0.0	0.2	0.0	0.0	0.0
95% CI	NA	(0.1, 0.8)	NA	NA	NA
Concomitant MTX Use					
MACE	0	0	0	0	0
Person-Years	0.0	0.0	0.0	0.0	0.0
IR/100 PY	0.0	0.0	0.0	0.0	0.0
95% CI	NA	NA	NA	NA	NA
No Concomitant MTX Use					
MACE	0	4	0	0	0
Person-Years	95.6	955.9	60.8	69.7	130.5

Model	Unmatched		Matched		
	Baricitinib[a] (N = 188)	TNFi (N = 1685)	Baricitinib[a] (N = 114)	TNFi (N = 114)	Total (N = 228)
IR/100 PY	0.0	0.4	0.0	0.0	0.0
95% CI	NA	(0.2, 1.1)	NA	NA	NA

Abbreviations: CI = confidence interval; IR = incidence rate; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; MDR = Military Data Health Repository; MI = myocardial infarction; MTX = methotrexate; N = number of patients in the specified category; NA = not applicable; PY = person-years; TNFi = tumour necrosis factor inhibitor.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\military health_MDR\Lilly Baricitinib Results_Top-Line_Military Health_v2.0.docx -page 15

10.3.1.6.3. Serious infection

Within the unmatched eligible MDR cohorts, 0 of 191 patients in the baricitinib cohort and 16 of 1,743 patients in the TNFi cohort had a serious infection (Table 59_MDR). In the matched cohorts, there were 0 patients with serious infection in the baricitinib cohort and 2 in the TNFi cohort. The rate of serious infection in the baricitinib cohort was 0.00 per 100 PY and 3.0 (95% CI 0.8, 12.1) per 100 PY in the TNFi cohort. In the absence of any serious infection events in the baricitinib cohort, the hazard ratio was not estimated.

Table 59_MDR Incidence Rate of First Serious Infection [MDR]

Model	Unmatched		Matched		
	Baricitinib (N = 191)	TNFi (N = 1743)	Baricitinib (N = 115)	TNFi (N = 115)	Total (N = 230)
SI Events	0	16	0	2	2
Person-Years	95.8	992.7	60.0	66.2	126.2
IR per 100 PY	0.0	1.6	0.0	3.0	1.6
95% CI	NA	(1.0, 2.6)	0, 6.15	(0.8, 12.1)	(0.4, 6.3)
Rate difference events/ 100 PY	NA	NA	NA	NA	-3.0
95% CI	NA	NA	NA	NA	(-7.2, 1.2)

Abbreviations: CI = confidence interval; IR = incidence rate; MDR = Military Data Health Repository; N = number of patients in the specified category; NA = not applicable; PY = person-years; SI = serious infection; TNFi = tumour necrosis factor inhibitor.

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10.3.1.7. Optum

10.3.1.7.1. VTE

Within the unmatched eligible Optum population, [redacted] of 348 patients in the baricitinib cohort had a VTE and [redacted] of 1,441 patients in the TNFi cohort had a VTE (Table 45_Optum). In the matched cohorts (n = 284 in each), there were [redacted] patients with a VTE in the baricitinib cohort and none in the TNFi cohort. The rate of VTE in the baricitinib cohort and TNFi cohorts was 1.69 (95% CI 0.21, 6.12) per 100 PY and 0.0 (95% CI 0.00, 2.26) per 100 PY, respectively. In the absence of events within the TNFi cohort, the HR could not be estimated.

Table 45_Optum Incidence Rate of VTE, Primary Definition [Optum]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 348)	TNFi (N = 1441)	Baricitinib[a] (N = 284)	TNFi (N = 284)	Total (N = 568)
Overall					
Person-Years	CCI	CCI	CCI	163.06	CCI
VTE Events	CCI	CCI	CCI	0	CCI
VTE Events/100 PY	1.32	1.14	1.69	0.00	0.71
95% CI	0.16, 4.77	0.52, 2.16	0.21, 6.12	0.00, 2.26	0.09, 2.57
Concomitant MTX Use[b]					
Total, n	60 (17.2%)	289 (20.1%)	47 (16.5%)	59 (20.8%)	106 (18.7%)
Person-Years	CCI	CCI	CCI	40.93	CCI
VTE Events	CCI	CCI	CCI	0	CCI
VTE Events/100 PY	2.80	0.91	3.56	0.00	1.45
95% CI	0.07, 15.61	0.11, 3.29	0.09, 19.83	0.00, 9.01	0.04, 8.07
No Concomitant MTX Use[b]					
Total, n	288 (82.8%)	1,152 (79.9%)	237 (83.5%)	225 (79.2%)	462 (81.3%)
Person-Years	CCI	CCI	CCI	122.13	CCI
VTE Events	CCI	CCI	CCI	0	CCI
VTE Events/100 PY	0.86	1.22	1.11	0.00	0.47
95% CI	0.02, 4.81	0.49, 2.52	0.03, 6.20	0.00, 3.02	0.01, 2.63

Abbreviations: CI = confidence intervals; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

[b] Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.45. Incidence Rate of Event - VTE, Primary Definition [Optum CDM RA].docx

10.3.1.7.2. MACE

Within the unmatched eligible Optum population, CCI of 351 patients in the baricitinib cohort had a MACE and CCI of 1,440 patients in the TNFi cohort had a MACE (Table 54_Optum). In the matched cohorts (n = 287 in each cohort), there were CCI patients with a MACE in the baricitinib cohort and CCI in the TNFi cohort. The rate of MACE in the baricitinib cohort and TNFi cohorts was 1.65 (95% CI 0.20, 5.95) per 100 PY and 0.62 (95% CI 0.02, 3.45) per 100 PY, respectively. Patients treated with baricitinib had more than a 2.5-fold increased risk of MACE relative to patients treated with TNFi, although the CI is very wide resulting in an imprecise estimate (HR=2.63; 95% CI 0.24, 29.38) (Table 55_Optum).

Table 54_Optum Incidence Rate of MACE [Optum]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 351)	TNFi (N = 1440)	Baricitinib[a] (N = 287)	TNFi (N = 287)	Total (N = 574)
Overall					
Person-Years	CCI	CCI	CCI	CCI	CCI
MACE	CCI	CCI	CCI	CCI	CCI
MACE/100 PY	1.30	0.25	1.65	0.62	1.06
95% CI	0.16, 4.71	0.03, 0.91	0.20, 5.95	0.02, 3.45	0.22, 3.10
MI					
MI	0	CCI	0	CCI	CCI
Person-Years	153.38	CCI	121.61	CCI	CCI
IR per 100 PY	0.00	0.13	0.00	0.62	0.35
95% CI	0.00, 2.41	0.00, 0.70	0.00, 3.03	0.02, 3.45	0.01, 1.97
Stroke, any					
Stroke	CCI	CCI	CCI	0	CCI
Person-Years	CCI	CCI	CCI	161.58	CCI
IR per 100 PY	1.30	0.13	1.65	0.00	0.71
95% CI	0.16, 4.71	0.00, 0.70	0.20, 5.95	0.00, 2.28	0.09, 2.55
Concomitant MTX Use[b]					
MACE	0	CCI	0	CCI	CCI
Person-Years	37.09	CCI	32.21	CCI	CCI
IR per 100 PY	0.00	0.91	0.00	2.77	1.47
95% CI	0.00, 9.95	0.11, 3.28	0.00, 11.45	0.07, 15.46	0.04, 8.16
No Concomitant MTX Use[b]					
MACE	CCI	0	CCI	0	CCI
Person-Years	CCI	575.11	CCI	125.53	CCI
IR per 100 PY	1.72	0.00	2.24	0.00	0.93
95% CI	0.21, 6.22	0.00, 0.64	0.27, 8.09	0.00, 2.94	0.11, 3.36

Abbreviations: CI = confidence interval; IR = incidence rate; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; MI = myocardial infarction; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

[b] Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.54. Incidence Rate of Event - MACE [Optum CDM RA].docx

Table 55_Optum Comparative Risk of MACE [Optum]

Model	Baricitinib			
	TNFi	HR	95% CI	P-value
Base Model[a]	Ref	2.63	0.24, 29.38	0.43

Abbreviations: CI = confidence interval; HR = Cox proportional hazard ratio; MACE = major adverse cardiovascular event; Ref = referent group; TNFi = tumour necrosis factor inhibitor.

[a] Base model = propensity score-matched model with confounders, outcome and baricitinib exposure.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.55. - Comparative Risk of MACE [Optum CDM RA].docx

10.3.1.7.3. Serious infection

Within the unmatched eligible Optum cohorts, 4 of 366 patients in the baricitinib cohort had a first serious infection and 28 of 1,478 patients in the TNFi cohort had a serious infection (). In the matched cohorts, there were 3 patients with serious infection in the baricitinib cohort and 6 in the TNFi cohort. The rate of serious infections in the baricitinib cohort and TNFi cohorts were 2.39 (95% CI 0.49, 7.00) per 100 PY and 3.44 (95% CI 1.26, 7.49) per 100 PY, respectively. In the base adjustment model, the comparative model suggested possible lower risk of serious infection in patients treated with baricitinib relative to those treated with TNFi due to point estimate <1.0 (HR=0.69; 95% CI 0.17, 2.80) (Table 61_Optum). However, due to the small number of events, the CI is wide and interpretation from this single data source is limited.

Table 59_Optum Incidence Rate of First Serious Infection [Optum]

Model	Unmatched		Matched		
	Baricitinib (N = 366)	TNFi (N = 1478)	Baricitinib (N = 300)	TNFi (N = 300)	Total (N = 600)
SI Events	CCI	28	CCI	CCI	CCI
Person-years	CCI	806.12	CCI	CCI	CCI
IR per 100 PY	2.44	3.47	2.39	3.44	3.00
95% CI	0.67, 6.26	2.19, 4.76	0.49, 7.00	1.26, 7.49	1.37, 5.70

Abbreviations: CI = confidence interval; IR = incidence rate; N = number of patients in the specified category; PY = person-years; SI = serious infection; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.59. Incidence Rate of Event - First Serious Infection [Optum CDM RA].docx

Table 61_Optum Comparative Risk of First Serious Infection Event [Optum]

Model	Baricitinib			
	TNFi	HR	95% CI	P-value
Base Model[a]	Ref	0.69	0.17, 2.80	0.60

Abbreviations: CI = confidence interval; HR = Cox proportional hazard ratio; Ref = referent group; TNFi = tumour necrosis factor inhibitor.

[a] Base model = propensity score-matched model.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\ Table 6.61. - Comparative Risk of First Serious Infection Event [Optum CDM RA].docx

10.3.1.8. PharMetrics Plus

10.3.1.8.1. VTE

Within the eligible unmatched PharMetrics Plus population, 0 of 473 and 15 of 6,576 patients in the baricitinib and TNFi cohorts, respectively, had a VTE event (Table 45_PP). In the matched cohorts (n = 261 in each treatment group), no patient had a VTE. Due to the lack of events in either cohort, HR were not estimated.

Table 45_PP Incidence Rate of VTE Primary Definition [PP]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 473)	TNFi (N = 6576)	Baricitinib[a] (N = 261)	TNFi (N = 261)	Total (N = 522)
Overall					
Person-Years	248	3849	141	159	300
VTE Events	0.0	15.0	0.0	0.0	0.0
VTE Events/100 PY	0.0	0.4	0.0	0.0	0.0
95% CI	NA	(0.2, 0.6)	(0, 2.6)	(0, 2.3)	NA
Rate difference events/100 PY	NA	NA	NA	NA	0.0
95% CI	NA	NA	NA	NA	(0, 0)
Concomitant MTX Use					
Total, n	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Person-Years	0	0	0	0	0
VTE Events	0.0	0.0	0.0	0.0	0.0
VTE Events/100 PY	0.0	0.0	0.0	0.0	0.0
95% CI	NA	NA	NA	NA	NA
No Concomitant MTX Use					
Total, n	473 (100%)	6576 (100%)	261 (100%)	261 (100%)	522 (100%)
Person-Years	248	3849	141	159	300
VTE Events	0.0	15.0	0.0	0.0	0.0
VTE Events/100 PY	0.0	0.4	0.0	0.0	0.0
95% CI	NA	(0.2, 0.6)	NA	NA	NA

Abbreviations: CI = confidence intervals; MTX = methotrexate; N = number of patients in the specified category; NA = not applicable; PP = PharMetrics Plus; PY = person-years; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\pharmetrics plus_PP\Lilly Baricitinib Results_Top-Line_Pharmetrics Plus_v3.0.docx - page(s) 13

10.3.1.8.2. MACE

Within the unmatched eligible Pharmetrics Plus population, 4 of 473 patients in the baricitinib cohort and 8 of 6,579 patients in the TNFi cohort had a MACE (Table 54_PP). In the matched cohorts (n = 262 in each cohort), one patient had a MACE in the baricitinib cohort and no patients in the TNFi cohort. The rate of MACE in the baricitinib cohort was 0.7 (95% CI 0.1, 5) per 100 PY. Due to the absence of events within the TNFi cohort, the HR could not be estimated.

Table 54_PP Incidence Rate of MACE [PP]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 473)	TNFi (N = 6579)	Baricitinib[a] (N = 262)	TNFi (N = 262)	Total (N = 524)
Overall					
Person-Years	247	3856	141	155	296
MACE	4.0	8.0	1.0	0.0	1.0
MACE/100 PY	1.6	0.2	0.7	0.0	0.3
95% CI	(0.6, 4.3)	(0.1, 0.4)	(0.1, 5)	(0, 2.4)	(0, 2.4)
Rate difference events/100 PY	NA	NA	NA	NA	0.7
95% CI	NA	NA	NA	NA	(-0.7, 2.1)
MI					
MI	2	6	0	0	0
Person-Years	247.2	3855.7	140.9	155.2	296.1
IR /100 PY	0.8	0.2	0.0	0.0	0.0
95% CI	(0.2, 3.2)	(0.1, 0.3)	NA	NA	NA
Stroke, any					
Stroke	2	2	1	0	1
Person-Years	247.2	3855.7	140.9	155.2	296.1
IR/100 PY	0.8	0.1	0.7	0.0	0.3
95% CI	(0.2, 3.2)	(0, 0.2)	(0.1, 5)	NA	(0, 2.4)
Concomitant MTX Use					
MACE	0	1	0	0	0
Person-Years	0.0	0.4	0.0	0.0	0.0
IR/100 PY	0.0	272.6	0.0	0.0	0.0
95% CI	NA	(38.4, 1935.0)	NA	NA	NA
No Concomitant MTX Use					

Model	Unmatched		Matched		
	Baricitinib[a] (N = 473)	TNFi (N = 6579)	Baricitinib[a] (N = 262)	TNFi (N = 262)	Total (N = 524)
MACE	4	7	1	0	1
Person-Years	247.2	3855.3	140.9	155.2	296.1
IR/100 PY	1.6	0.2	0.7	0.0	0.3
95% CI	(0.6, 4.3)	(0.1, 0.4)	(0.1, 5)	NA	(0, 2.4)

Abbreviations: CI = confidence interval; IR = incidence rate; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; MI = myocardial infarction; MTX = methotrexate; N = number of patients in the specified category; NA = not applicable; PP = PharMetrics Plus; PY = person-years; TNFi = tumour necrosis factor inhibitor.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose when numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\pharmetrics plus_PP\Lilly Baricitinib Results_Top-Line_Pharmetrics Plus_v3.0.docx - page(s) 15

10.3.1.8.3. Serious infection

Within the unmatched eligible PharMetrics Plus cohorts, 6 of 478 patients in the baricitinib cohort and 54 of 6,688 patients in the TNFi cohort had a first serious infection (Table 59_PP). In the matched cohorts (n = 265 each), there were 3 patients with serious infection in each of the baricitinib and TNFi cohorts. The rate of serious infections in the baricitinib and TNFi cohorts were 2.1 (95% CI 0.7, 6.6) per 100 PY and 1.9 (95% CI 0.6, 5.8) per 100 PY, respectively. Patients treated with baricitinib had a small increase in risk of serious infection relative to those treated with TNFi (HR=1.17; 95% CI 0.2, 5.8) (Table 61_PP). Due to the small number of events, the CI is wide and interpretation of the result from this single data source is limited.

Table 59_PP Incidence Rate of First Serious Infection [PP]

Model	Unmatched		Matched		
	Baricitinib (N = 478)	TNFi (N = 6688)	Baricitinib (N = 265)	TNFi (N = 265)	Total (N = 530)
SI Events	6	54	3	3	6
Person-Years	249.5	3913.2	141.9	160.8	302.7
IR per 100 PY	2.4	1.4	2.1	1.9	2.0
95% CI	(1.1, 5.4)	(1.1, 1.8)	(0.7, 6.6)	(0.6, 5.8)	(0.9, 4.4)
Rate difference events/ 100 PY	NA	NA	NA	NA	0.2
95% CI	NA	NA	NA	NA	(-2.9, 3.4)

Abbreviations: CI = confidence interval; IR = incidence rate; N = number of patients in the specified category; NA = not applicable; PP = PharMetrics Plus; PY = person-years; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\pharmetrics plus_PP\Lilly Baricitinib Results_Top-Line_Pharmetrics Plus_v3.0.docx - page(s) 17

Table 61_PP Comparative Risk of First Serious Infection Event [PP]

Model	TNFi	Baricitinib		P-value
		HR	95% CI	
Base Model	Ref	1.17	(0.2, 5.8)	0.85

Abbreviations: CI = confidence interval; HR = hazard ratio; PP = PharMetrics Plus; Ref = Reference; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\pharmetrics plus_PP\Lilly Baricitinib Results_Top-Line_Pharmetrics Plus_v3.0.docx - page(s) 18

10.3.1.9. PS20

10.3.1.9.1. VTE

Within the unmatched eligible PS20 population, 6 of 933 patients in the baricitinib cohort had a VTE and 18 of 3,953 patients in the TNFi cohort had a VTE (Table 45_PS20). In the matched cohorts (n = 748 each), there were 6 patients with a VTE in the baricitinib cohort and 4 in the TNFi cohort. The rate of VTE in the baricitinib cohort was 2.55 (95% CI 0.94, 5.54) per 100 PY and in the TNFi cohort 1.06 (95% CI 0.29, 2.71) per 100 PY. Patients treated with baricitinib had more than a 2-fold increased risk of VTE relative to patients treated with TNFi, although the CI is wide resulting in an imprecise estimate (HR=2.15; 95% CI 0.60, 7.71) (Table 48_PS20).

Table 45_PS20 Incidence Rate of VTE, Primary Definition [PS20]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 933)	TNFi (N = 3953)	Baricitinib[a] (N = 748)	TNFi (N = 748)	Total (N = 1496)
Overall					
Person-Years	322.97	1940.61	235.54	377.49	613.03
VTE Events	6	18	6	4	10
VTE Events/100 PY	1.86	0.93	2.55	1.06	1.63
95% CI	0.68, 4.04	0.50, 1.36	0.94, 5.54	0.29, 2.71	0.62, 2.64
Concomitant MTX Use[b]					
Total, n	146 (15.6%)	939 (23.8%)	119 (15.9%)	141 (18.9%)	260 (17.4%)
Person-Years	77.32	620.21	57.98	97.38	155.36
VTE Events	1	3	1	1	2
VTE Events/100 PY	1.29	0.48	1.72	1.03	1.29
95% CI	0.03, 7.21	0.10, 1.41	0.04, 9.61	0.03, 5.72	0.16, 4.65
No Concomitant MTX Use[b]					
Total, n	787 (84.4%)	3014 (76.2%)	629 (84.1%)	607 (81.1%)	1236 (82.6%)
Person-Years	245.65	1,320.40	177.56	280.10	457.67

VTE Events	5	15	5	3	8
VTE Events/100 PY	2.04	1.14	2.82	1.07	1.75
95% CI	0.66, 4.75	0.56, 1.71	0.91, 6.57	0.22, 3.13	0.76, 3.44

Abbreviations: CI = confidence intervals; MTX = methotrexate; N = number of patients in the specified category; PS20 = HealthVerity Private Source 20; PY = person-years; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

[b] Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.45. Incidence Rate of Event - VTE, Primary Definition [HealthVerity, PS20].docx

Table 48_PS20 Comparative Risk of Incident VTE, Primary Definition [PS20]

		Baricitinib		
Model	**TNFi**	**HR**	**95% CI**	**P-value**
Base Model[a]	Ref	2.15	0.60, 7.71	0.24

Abbreviations: CI = confidence interval; HR = Hazard ratio; PS20 = HealthVerity Private Source 20; Ref = reference group; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Base model = propensity score-matched model with confounders, outcome and baricitinib exposure.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.48. Comparative Risk of Incident VTE, Primary Definition [HealthVerity, PS20], updated base model = PS matched.docx

10.3.1.9.2. MACE

Within the unmatched eligible PS20 population, 4 of 932 patients in the baricitinib cohort had a MACE and 10 of 3,952 patients in the TNFi cohort had a MACE (Table 54_PS20). In the matched cohorts (n = 743 in each cohort), there were 2 patients with a MACE in the baricitinib cohort and 4 in the TNFi cohort. The rate of MACE in the baricitinib and TNFi cohorts was 0.82 (95% CI 0.10, 2.97) per 100 PY and 1.13 (95% CI 0.31, 2.89) per 100 PY, respectively. Patients treated with baricitinib had an insignificantly lower risk of MACE compared to patients treated with TNFi, although the CI is wide, indicating an imprecise estimate (HR=0.73; 95% CI 0.13, 3.99) (Table 55_PS20). Due to the small number of events, the CI is wide and interpretation from this single data source is limited.

Table 54_PS20 Incidence Rate of MACE [PS20]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 932)	**TNFi (N = 3952)**	**Baricitinib[a] (N = 743)**	**TNFi (N = 743)**	**Total (N = 1486)**
Overall					
Person-Years	324.73	1942.05	243.69	354.02	597.71
MACE	4	10	2	4	6
MACE/100 PY	1.23	0.51	0.82	1.13	1.00

95% CI	0.34, 3.15	0.20, 0.83	0.10, 2.97	0.31, 2.89	0.37, 2.19
MI					
MI	2	4	1	2	3
Person-Years	325.12	1943.83	243.94	354.75	598.69
IR per 100 PY	0.62	0.21	0.41	0.56	0.50
95% CI	0.07, 2.22	0.06, 0.53	0.01, 2.28	0.07, 2.04	0.10, 1.46
Stroke, any					
Stroke	2	6	1	2	3
Person-Years	325.21	1942.68	243.73	354.26	597.99
IR per 100 PY	0.61	0.31	0.41	0.56	0.50
95% CI	0.07, 2.22	0.11, 0.67	0.01, 2.29	0.07, 2.04	0.10, 1.47
Concomitant MTX Use[b]					
MACE	1	3	0	1	1
Person-Years	77.57	623.24	52.67	102.15	154.82
IR per 100 PY	1.29	0.48	0.00	0.98	0.65
95% CI	0.03, 7.18	0.10, 1.41	0.00, 7.00	0.03, 5.46	0.02, 3.60
No Concomitant MTX Use[b]					
MACE	3	7	2	3	5
Person-Years	247.16	1318.81	191.02	251.88	442.89
IR per 100 PY	1.21	0.53	1.05	1.19	1.13
95% CI	0.25, 3.55	0.21, 1.09	0.13, 3.78	0.25, 3.48	0.37, 2.64

Abbreviations: CI = confidence interval; IR = incidence rate; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; MI = myocardial infarction; MTX = methotrexate; N = number of patients in the specified category; PS20 = HealthVerity Private Source 20; PY = person-years; TNFi = tumour necrosis factor inhibitor.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose, in which numbers of patients are sufficient to warrant separate reporting.

[b] Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.54. Incidence Rate of Event - MACE [HealthVerity, PS20].docx

Table 55_PS20 Comparative Risk of MACE [PS20]

Model		Baricitinib		
	TNFi	HR	95% CI	P-value
Base Model[a]	Ref	0.73	0.13, 3.99	0.71

Abbreviations: CI = confidence interval; HR = hazard ratio; MACE = major adverse cardiovascular event; PS20 = HealthVerity Private Source 20; Ref = reference group; TNFi = tumour necrosis factor inhibitor.

[a] Base model = propensity score-matched model with confounders, outcome, and baricitinib exposure.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.55. - Comparative Risk of MACE [HealthVerity, PS20].docx

10.3.1.9.3. Serious infection

Within the unmatched eligible PS20 cohorts, 7 of 930 patients in the baricitinib cohort had a first serious infection and 47 of 3,978 patients in the TNFi cohort had a serious infection (Table 59_PS20). In the matched cohorts (n = 748 each), there were 6 patients with serious infection in the baricitinib cohort and 10 in the TNFi cohort. The IR of serious infections in the baricitinib cohort and TNFi cohorts was 2.49 (95% CI 0.92, 5.43) per 100 PY and 2.76 (95% CI 1.05, 4.46) per 100 PY, respectively. No difference in risk was detected between the baricitinib and TNFi cohorts in the comparative analysis (HR=0.86; 95% CI 0.31, 2.28) (Table 61_PS20). Due to the small number of events, the CI is wide.

Table 59_PS20 Incidence Rate of Event - First Serious Infection [PS20]

Model	Unmatched		Matched		
	Baricitinib (N = 930)	TNFi (N = 3978)	Baricitinib (N = 748)	TNFi (N = 748)	Total (N = 1496)
SI Events	7	47	6	10	16
Person-Years	320.63	1937.44	240.64	362.97	603.62
IR per 100 PY	2.18	2.43	2.49	2.76	2.65
95% CI	0.88, 4.50	1.73, 3.12	0.92, 5.43	1.05, 4.46	1.35, 3.95

Abbreviations: CI = confidence interval; IR = incidence rate; N = number of patients in the specified category; PS20 = HealthVerity Private Source 20; PY = person-years; SI = serious infection; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.59. Incidence Rate of Event - First Serious Infection [HealthVerity, PS20 RA].docx

Table 61_PS20 Comparative Risk of First Serious Infection Event [PS20]

Model		Baricitinib		
	TNFi	HR	95% CI	P-value
Base Model[a]	Ref	0.86	0.31, 2.28	0.77

Abbreviations: CI = confidence interval; HR = hazard ratio; PS20 = HealthVerity Private Source 20; Ref = reference group; TNFi = tumour necrosis factor inhibitor.

[a] Base model = propensity score-matched model.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\ Table 6.61. Comparative Risk of First Serious Infection Event [HealthVerity, PS20].docx

10.3.2. Europe and Japan data sources

10.3.2.1. ARTIS

10.3.2.1.1. VTE

Within the unmatched eligible ARTIS population, 26 of 1,737 patients in the baricitinib cohort had a VTE and 45 of 6,230 patients in the TNFi cohort had a VTE (Table 45_ARTIS). In the matched cohorts (n = 1,685 in each), there were 23 patients with VTE in baricitinib cohort and 14 in the TNFi cohort. The rate of VTE in the baricitinib cohort was 0.99 (95% CI 0.66, 1.50) per 100 PY and 0.54 (95% CI 0.32, 0.91) per 100 PY in the TNFi cohort. The risk of VTE in patients treated with baricitinib was modestly increased relative to patients treated with TNFi, although the CI included the null (HR=1.83, 95% CI 0.95, 3.55) (Table 48_ARTIS).

Table 45_ARTIS Incidence rate of VTE, Primary Definition [ARTIS]

Model	Unmatched		Matched	
	Baricitinib[a] (N = 1737)	TNFi (N = 6230)	Baricitinib[a] (N = 1685)	TNFi (N = 1685)
Overall				
Person-Years	2387.2	9838.3	2313.6	2608.3
VTE Events	26	45	23	14
VTE Events/100 PY	1.09	0.46	0.99	0.54
95% CI	0.74, 1.60	0.34, 0.61	0.66, 1.50	0.32, 0.91

Abbreviations: ARTIS = antirheumatic therapy in Sweden; CI = confidence intervals; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be created for each dose when numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\ Table7_cruderate_08MAR22.xlsx

Table 48_ARTIS Comparative Risk of Incident VTE, Primary Definition [ARTIS]

Model	TNFi	Baricitinib		P-value
		HR	95% CI	
Base Model	Reference	1.83	0.95, 3.55	0.072

Abbreviations: ARTIS = antirheumatic therapy in Sweden; CI = confidence interval; HR = hazard ratio; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\ Table8_cox_08MAR22.xlsx

10.3.2.1.2. MACE

Within the unmatched eligible ARTIS population, 14 of 1,737 patients in the baricitinib cohort had a MACE and 58 of 6,230 patients in the TNFi cohort had a MACE (Table 54_ARTIS). In the matched cohorts (n = 1,681 in each), there were 13 patients with MACE in baricitinib cohort and 16 in the TNFi cohort. The rate of MACE in the baricitinib cohort was 0.56 (95% CI 0.33, 0.97) per 100 PY

and 0.60 (95% CI 0.37, 0.97) per 100 PY in the TNFi cohort. The risk of MACE in patients treated with baricitinib did not differ relative to the risk in patients treated with TNFi (HR=0.92, 95% CI 0.45, 1.90) (Table 55_ARTIS).

Table 54_ARTIS Incidence rate of MACE [ARTIS]

Model	Unmatched		Matched	
	Baricitinib[a] (N = 1737)	TNFi (N = 6230)	Baricitinib[a] (N = 1681)	TNFi (N = 1681)
Overall				
Person-Years	2396.8	9829.7	2315.1	2685.0
MACE Events	14	58	13	16
MACE Events/100 PY	0.58	0.59	0.56	0.60
95% CI	0.35, 0.99	0.46, 0.76	0.33, 0.97	0.37, 0.97

Abbreviations: ARTIS = antirheumatic therapy in Sweden; CI = confidence intervals; MACE = major adverse cardiovascular event; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose when numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\ Table7_cruderate_08MAR22.xlsx

Table 55_ARTIS Comparative Risk of MACE [ARTIS]

Model	TNFi	Baricitinib		P-value
		HR	95% CI	
Base Model	Reference	0.92	0.45, 1.90	0.831

Abbreviations: ARTIS = antirheumatic therapy in Sweden; CI = confidence interval; HR = hazard ratio; MACE = major adverse cardiovascular event; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\ Table8_cox_08MAR22.xlsx

10.3.2.1.3. Serious infection

Within the unmatched eligible ARTIS population, 105 of 1,737 patients in the baricitinib cohort had a first serious infection and 239 of 6,230 patients in the TNFi cohort had a serious infection (Table 59_ARTIS). In the matched cohorts (n = 1,683 in each), there were 94 patients with serious infection in baricitinib cohort and 66 in the TNFi cohort. The rate of serious infection in the baricitinib cohort was 4.21 (95% CI 3.44, 5.15) per 100 PY and 2.55 (95% CI 2.00, 3.24) per 100 PY in the TNFi cohort. The risk of serious infection in patients treated with baricitinib was modestly elevated relative to the risk in patients treated with TNFi (HR=1.72, 95% CI 1.24, 2.39). (Table 61_ARTIS).

Table 59_ARTIS Incidence Rate of First Serious Infection [ARTIS]

Model	Unmatched		Matched	
	Baricitinib[a] (N = 1737)	TNFi (N = 6230)	Baricitinib[a] (N = 1683)	TNFi (N = 1683)
Overall				
Person-Years	2295.3	9644.5	2234.3	2589.1

SI Events	105	239	94	66
SI Events/100 PY	4.57	2.48	4.21	2.55
95% CI	3.78, 5.54	2.18, 2.81	3.44, 5.15	2.00, 3.24

Abbreviations: ARTIS = antirheumatic therapy in Sweden; CI = confidence intervals; N = number of patients in the specified category; PY = person-years; SI = serious infection; TNFi = tumour necrosis factor inhibitor.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\ Table7_cruderate_08MAR22.xlsx

Table 61_ARTIS Comparative Risk of First Serious Infection Event [ARTIS]

Model	TNFi	Baricitinib		P-value
		HR	95% CI	
Base Model	Reference	1.72	1.24, 2.39	0.001

Abbreviations: ARTIS = antirheumatic therapy in Sweden; CI = confidence interval; HR = hazard ratio; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\ Table8_cox_08MAR22.xlsx

10.3.2.1.3.1. Sensitivity analysis: Serious infection adjusted disease activity

Additional information was available in this data source to evaluate the contribution of disease activity to the risk of serious infection associated with baricitinib. This sensitivity analysis could not be conducted for VTE or MACE because there were too few events across DAS28 categories.

To allow for a comparison to be made between the main result for serious infection and this sensitivity analysis result, patients with missing information were included in "DAS28 Missing" category. After controlling for DAS28 activity, the change to the overall result is negligible, as shown in Table 61_SA ARTIS. The result remains statistically significant and shifts slightly closer to the null from 1.72-fold to 1.61-fold greater risk of serious infection associated with baricitinib compared to TNFi treatment, when the model is adjusted for disease activity. Based on likelihood ratio testing of the covariate, addition of DAS28 to the model does not contribute meaningfully (p=0.29).

Table 61_SA ARTIS Comparative Risk of First Serious Infection Event , Adjusted for Disease Severity [ARTIS]

Model	Count (%) (baricitinib / TNFi)	TNFi	Baricitinib		P-value
			HR	95% CI	
Base Model	1683 / 1683	Reference	1.72	1.24, 2.39	0.001
Base Model, adj. for DAS28		Reference	1.61	1.15, 2.24	0.005
DAS28 Low	75 (4%) / 60 (4%)	Remission bari.: 61 (4%) TNFi: 99 (6%)	1.45	0.55, 3.82	0.29[a]
DAS28 Moderate	450 (27%) / 390 (23)%		0.75	0.33, 1.70	
DAS28 High	336 (20%) / 233 (14%)		1.38	0.61, 3.11	
DAS28 Missing	761 (45%) / 901 (54%)		0.90	0.41, 1.97	

Abbreviations: adj = adjusted; ARTIS = Anti-Rheumatic Therapy in Sweden; bari. = baricitinib; CI = confidence interval; DAS28 = Disease Activity Score 28; HR = hazard ratio; TNFi = tumour necrosis factor inhibitor.

[a] This p-value is based on a likelihood ratio test of the DAS28 covariate included in the base model.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\Table9_cox_SA_16MAY22_update.xlsx and lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\Table2_clinical_16MAY2022_update.xlsx

10.3.2.2. BKK

10.3.2.2.1. VTE

Within the unmatched eligible BKK population, 3 of 851 patients in the baricitinib cohort had a VTE and 21 of 3,332 patients in the TNFi cohort had a VTE (Table 45_BKK). In the matched cohorts (n = 765 each), there were 3 patients with a VTE in baricitinib cohort and 6 in the TNFi cohort. All 3 VTE events in the baricitinib cohort were among patients treated with 4mg, however, there were approximately 4.5 times more patients treated with 4 mg than with 2 mg (n = 628 vs n = 137, respectively). The rate of VTE in the overall baricitinib cohort was 0.6 (95% CI 0.1, 1.16) per 100 PY and 1.1 (95% CI 0.4, 2.4) per 100 PY in the TNFi cohort. Patients treated with baricitinib had approximately half the risk of VTE relative to patients treated with TNFi, (HR=0.49; 95% CI 0.1, 2.0), although the CIs were wide (Table 48_BKK).

Table 45_BKK Incidence Rate of VTE Primary Definition [BKK]

Model	Unmatched				Matched				
	Baricitinib[a] 4 mg N = 851	2 mg N = 699	TNFi N = 152		Baricitinib[a] 4 mg N = 765	2 mg N = 628	TNFi N = 137		Total N = 1530
				N = 3332				N = 765	
Overall									
Person-Years	595	492	103	2178	539	446	93	544	1083
VTE Events	3.0	3.0	0.0	21.0	3.0	3.0	0.0	6.0	9.0
VTE Events/100 PY	0.5	0.6	0.0	1.0	0.6	0.7	0.0	1.1	0.8
95% CI	(0.1, 1.5)	(0.1, 1.8)	(0, 3.6)	(0.6, 1.5)	(0.1, 1.6)	(0.1, 2.0)	(0.0, 3.9)	(0.4, 2.4)	(0.4, 1.6)
Rate difference events/100 PY	NA	NA	NA	NA	NA	NA	NA	NA	-0.5
95% CI	NA	NA	NA	NA	NA	NA	NA	NA	(-1.6, 0.5)
Concomitant MTX Use									
Total, n	209 (25%)	181 (26%)	28 (18%)	823 (25%)	181 (24%)	159 (25%)	22 (16%)	228 (30%)	409 (27%)
Person-Years	190	169	21	793	168	151	17	232	400
VTE Events	1.0	1.0	0.0	9.0	1.0	1.0	0.0	3.0	4.0
VTE Events/100 PY	0.5	0.6	0.0	1.1	0.6	0.7	0.0	1.3	1.0
95% CI	(0.0, 2.9)	(0.0, 3.3)	(0.0, 17.8)	(0.5, 2.2)	(0.0, 3.3)	(0.0, 3.7)	(0.0, 21.4)	(0.3, 3.8)	(0.3, 2.6)
No Concomitant MTX Use									
Total, n	642 (75%)	518 (74%)	124 (82%)	2509 (75%)	584 (76%)	469 (75%)	115 (84%)	537 (70%)	1121 (73%)
Person-Years	405	322	82	1385	372	295	76	312	683
VTE Events	2.0	2.0	0.0	12.0	2.0	2.0	0.0	3.0	5.0
VTE Events/100 PY	0.5	0.6	0.0	0.9	0.5	0.7	0.0	1.0	0.7
95% CI	(0.1, 1.8)	(0.1, 2.2)	(0, 4.5)	(0.4, 1.5)	(0.1, 1.9)	(0.1, 2.4)	(0, 4.8)	(0.2, 2.8)	(0.2, 1.7)

Abbreviations: BKK = Betriebskrankenkasse; CI = confidence intervals; MTX = methotrexate; N = number of patients in the specified category; NA = not applicable; PY = person-years; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

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Table 48_BKK Comparative Risk of Incident VTE, Primary Definition [BKK]

Model	Baricitinib			
	TNFi	HR	95% CI	P-value
Base Model	Ref	0.49	(0.1, 2.0)	0.31
Cochran-Mantel-Haenszel	Ref	0.50	(0.1, 2.0)	0.32

Abbreviations: BKK = Betriebskrankenkasse; CI = confidence interval; HR = hazard ratio; Ref = reference group; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

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10.3.2.2.2. MACE

Within the unmatched eligible BKK data, 8 of 853 patients in the baricitinib cohort had a MACE and 12 of the 3,340 patients in the TNFi cohort had a MACE (Table 54_BKK). In the matched cohorts (n = 757 in each), there were 8 patients with a MACE in baricitinib cohort and 4 in the TNFi cohort. The rate of MACE in the baricitinib cohort was 1.5 (95% CI 0.7, 3.0) per 100 PY and 0.7 (95% CI 0.2, 1.9) per 100 PY in the TNFi cohort. Because the individual doses were not propensity score matched with each other or the reference TNFi cohort, they should not be compared directly. Qualitatively, the point estimate for the IR of MACE was numerically higher in the 2-mg baricitinib cohort than the 4-mg cohort, but the event counts were low, and the CIs overlapped. While the CI included the null value, there was suggestion of a higher risk of MACE in patients treated with baricitinib relative to those treated with TNFi, with an approximately 2-fold greater risk (HR=2.09; 95% CI 0.6, 6.9) (Table 55_BKK).

Table 54_BKK Incidence Rate of MACE [BKK]

Model	Unmatched				Matched				
	Baricitinib[a] N = 853	4 mg N = 699	2 mg N = 154	TNFi N = 3340	Baricitinib[a] N = 757	4 mg N = 625	2 mg N = 132	TNFi N = 757	Total N = 1514
Overall									
Person-Years	592	491	102	2186	521	436	85	536	1057
MACE	8.0	5.0	3.0	12.0	8.0	5.0	3.0	4.0	12.0
MACE/100 PY	1.4	1.0	2.9	0.5	1.5	1.1	3.5	0.7	1.1
95% CI	(0.6, 2.7)	(0.3, 2.4)	(0.6, 8.6)	(0.3, 1.0)	(0.7, 3)	(0.4, 2.7)	(0.7, 10.3)	(0.2, 1.9)	(0.6, 2.0)
Rate difference events/100 PY	NA	NA	NA	NA	NA	NA	NA	NA	0.8
95% CI	NA	NA	NA	NA	NA	NA	NA	NA	(-0.5, 2.1)
MI									
MI	6	4	2	9	6	4	2	4	10
Person-Years	593.6	490.6	102.9	2187.6	521.7	435.5	86.2	536.4	1058.2
IR /100 PY	1.0	0.8	1.9	0.4	1.1	0.9	2.3	0.7	0.9
95% CI	(0.4, 2.2)	(0.2, 2.1)	(0.2, 7.0)	(0.2, 0.8)	(0.4, 2.5)	(0.3, 2.4)	(0.3, 8.4)	(0.2, 1.9)	(0.5, 1.7)
Stroke, any									
Stroke	2	1	1	3	2	1	1	0	2
Person-Years	596.3	492.8	103.5	2190.7	524.5	437.7	86.8	538.9	1063.4
IR/100 PY	0.3	0.2	1.0	0.1	0.4	0.2	1.2	0.0	0.2
95% CI	(0.0, 1.2)	(0.0, 1.1)	(0.0, 5.4)	(0.0, 0.4)	(0.0, 1.4)	(0.0, 1.3)	(0.0, 6.4)	(0.0, 0.7)	(0.0, 0.7)
Concomitant MTX Use									
MACE	2	2	0	5	2	2	0	2	4
Person-Years	189.3	168.6	20.8	801.3	161.6	143.6	18.1	229.8	391.5
IR/100 PY	1.1	1.2	0.0	0.6	1.2	1.4	0.0	0.9	1.0
95% CI	(0.1, 3.8)	(0.1, 4.3)	(0.0, 17.8)	(0.2, 1.5)	(0.1, 4.5)	(0.2, 5.0)	(0.0, 20.4)	(0.1, 3.1)	(0.3, 2.6)
No Concomitant MTX Use									
MACE	6	3	3	7	6	3	3	2	8
Person-Years	403.0	322.0	81.0	1384.4	358.9	291.9	67.0	306.6	665.5
IR/100 PY	1.5	0.9	3.7	0.5	1.7	1.0	4.5	0.7	1.2
95% CI	(0.5, 3.2)	(0.2, 2.7)	(0.8, 10.8)	(0.2, 1)	(0.6, 3.6)	(0.2, 3)	(0.9, 13.1)	(0.1, 2.4)	(0.5, 2.4)

Abbreviations: Betriebskrankenkasse; CI = confidence interval; IR = incidence rate; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; MI = myocardial infarction MTX = methotrexate; N = number of patients in the specified category; NA = not applicable; PY = person-years; TNFi = tumour necrosis factor inhibitor.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

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Table 55_BKK Comparative Risk of MACE [BKK]

Model	Baricitinib			
	TNFi	HR	95% CI	P-value
Base Model	Ref	2.09	(0.6, 6.9)	0.23
Cochran-Mantel-Haenszel	Ref	2.00	(0.6, 6.6)	0.25

Abbreviations: BKK = Betriebskrankenkasse; CI = confidence interval; HR = hazard ratio; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; Ref = Reference group; TNFi = tumour necrosis factor inhibitor.

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10.3.2.2.3. Serious infection

Within the unmatched eligible BKK cohorts, 20 of 965 patients in the baricitinib cohort had a first serious infection and 26 of 3,647 patients in the TNFi cohort had a serious infection (Table 59_BKK). In the matched cohorts (n = 859 each), there were 17 patients with serious infection in the baricitinib cohort and 12 in the TNFi cohort. The rate of serious infections in the baricitinib cohort and TNFi cohorts was 2.9 (95% CI 1.7, 4.6) per 100 PY and 2.0 (95% CI 1.0, 3.4) per 100 PY, respectively. Patients treated with baricitinib had a modestly increased risk of serious infection relative to patients treated with TNFi (HR=1.44, 95% CI 0.7, 3.0) (Table 61_BKK).

Table 59_BKK Incidence Rate of First Serious Infection [BKK]

Model	Unmatched				Matched				
	Baricitinib (N = 965)	4 mg (N = 772)	2 mg (N = 193)	TNFi (N = 3647)	Baricitinib (N = 859)	4 mg (N = 691)	2 mg (N = 168)	TNFi (N = 859)	Total (N = 1718)
SI Events	20	15	5	26	17	14	3	12	29
Person-Years	672.3	543.2	129.1	2397.9	596.4	486.4	110.0	607.8	1204.2
IR per 100 PY	3.0	2.8	3.9	1.1	2.9	2.9	2.7	2.0	2.4
95% CI	(1.8, 4.6)	(1.5, 4.6)	(1.3, 9)	(0.7, 1.6)	(1.7, 4.6)	(1.6, 4.8)	(0.6, 8)	(1.0, 3.4)	(1.6, 3.5)
Rate difference events/ 100 PY	NA	NA	NA	NA	NA	NA	NA	NA	0.9
95% CI	NA	NA	NA	NA	NA	NA	NA	NA	(-0.9, 2.6)

Abbreviations: Betriebskrankenkasse; CI = confidence interval; IR = incidence rate; N = number of patients in the specified category; NA = not available; PY = person-years; SI = serious infection; TNFi = tumour necrosis factor inhibitor.

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Table 61_BKK Comparative Risk of First Serious Infection Event [BKK]

Model	Baricitinib			
	TNFi	HR	95% CI	P-value
Base Model	Ref	1.44	(0.7, 3.0)	0.33
Cochran-Mantel-Haenszel	Ref	1.42	(0.7, 3.0)	0.35

Abbreviations: Betriebskrankenkasse; CI = confidence interval; HR = hazard ratio; Ref = reference group; TNFi = tumour necrosis factor inhibitor.

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10.3.2.3. French Cegedim THIN

Patients in the Cegedim data are also included in the national SNDS data, which includes all French residents. Analyses were executed (Annex 13) but results are not included in the meta-analysis for the reason above and will therefore not be discussed here.

10.3.2.4. CorEvitas Japan

10.3.2.4.1. VTE

Within the unmatched (ie., 'pre-matched') eligible CorEvitas Japan data, 0 of 210 patients in the baricitinib cohort had a VTE and 0 of 354 patients in the TNFi cohort had a VTE (Table 45_Cor_JP). There were 171 patients in each matched cohort, and consistent with the absence of VTE in the unmatched cohorts, there were no patients with VTE in the matched cohorts. The rate of VTE in the baricitinib cohort was 0.00 (95% CI 0.00, 1.8) per 100 PY and 0.00 (95% CI 0.00, 1.5) per 100 PY in the TNFi cohort. In the absence of VTE events, the hazard ratio was not estimated.

Table 45_Cor_JP Incidence rate of VTE, Primary Definition [Cor_JP]

Model	Pre-matched		Matched		
	Baricitinib (N = 210)	TNFi (N = 354)	Baricitinib (N = 171)	TNFi (N = 171)	Total (N = 342)
Overall					
VTE Events	0	0	0	0	0
Person-Years	231.6	537.0	199.5	247.8	447.3
VTE Events/100 PY	0.0	0.0	0.0	0.0	0.0
95% CI	0.0, 1.6	0.0, 0.7	0.0, 1.8	0.0, 1.5	0.0, 0.8
Incidence rate difference: baricitinib – TNFi (95% CI)					0.0 (0.0, 0.0)
Incidence rate ratio: baricitinib / TNFi (95% CI)					--
Concomitant MTX Use at Index Date					
N	110	254	94	103	197
VTE Events	0	0	0	0	0
Person-Years	120.7	398.7	108.5	155.6	264.0
VTE Events/100 PY	0.0	0.0	0.0	0.0	0.0
95% CI	0.0, 3.1	0.0, 0.9	0.0, 3.4	0.0, 2.4	0.0, 1.4

Model	Pre-matched		Matched		
	Baricitinib (N = 210)	TNFi (N = 354)	Baricitinib (N = 171)	TNFi (N = 171)	Total (N = 342)
Incidence rate difference: baricitinib – TNFi (95% CI)					0.0 (0.0, 0.0)
Incidence rate ratio: baricitinib / TNFi (95% CI)					--
No Concomitant MTX Use at Index Date					
N	100	100	77	68	145
VTE Events	0	0	0	0	0
Person-Years	110.8	138.2	91.0	92.2	183.2
VTE Events/100 PY	0.0	0.0	0.0	0.0	0.0
95% CI	0.0, 3.3	0.0, 2.7	0.0, 4.1	0.0, 4.0	0.0, 2.0
Incidence rate difference: baricitinib – TNFi (95% CI)					0.0 (0.0, 0.0)
Incidence rate ratio: baricitinib / TNFi (95% CI)					--

Abbreviations: CI = confidence interval; Cor_JP = CorEvitas RA registry, Japan; MTX = methotrexate; N = count of patients in specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

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10.3.2.4.2. MACE

Within the unmatched (ie., 'pre-matched') eligible CorEvitas Japan data, 1 of 210 patients in the baricitinib cohort had a MACE and 0 of the 354 patients in the TNFi cohort had a MACE (Table 54_Cor_JP). In the matched cohorts (n = 168 in each), there were 0 patients with a MACE both cohorts. The rate of MACE in the baricitinib cohort was 0.0 (95% CI 0.0, 1.9) per 100 PY and 0.0 (95% CI 0.0, 1.6) per 100 PY in the TNFi cohort. In the absence of MACE events, the hazard ratio was not estimated.

Table 54_Cor_JP Incidence Rate of MACE [Cor_JP]

Model	Pre-matched		Matched		
	Baricitinib (N = 210)	TNFi (N = 354)	Baricitinib (N = 168)	TNFi (N = 168)	Total (N = 336)
Overall					
MACE Events	1	0	0	0	0
Person-Years	231.3	537.0	194.3	233.7	427.9
MACE Events/100 PY	0.4	0.0	0.0	0.0	0.0
95% CI	0.0, 2.4	0.0, 0.7	0.0, 1.9	0.0, 1.6	0.0, 0.9
Incident rate difference: Baricitinib – TNFi (95% CI)		NA		NA	0.0 (0.0, 0.0)
Incidence rate ratio: baricitinib / TNFi (95% CI)		NA		NA	--
MI					
MI Events	0	0	0	0	0

Model	Pre-matched		Matched		
	Baricitinib (N = 210)	TNFi (N = 354)	Baricitinib (N = 168)	TNFi (N = 168)	Total (N = 336)
Person-Years	231.6	537.0	194.3	233.7	427.9
MI Events/100 PY	0.0	0.0	0.0	0.0	0.0
95% CI	0.0, 1.6	0.0, 0.7	0.0, 1.9	0.0, 1.6	0.0, 0.9
Incident rate difference: baricitinib – TNFi (95% CI)		NA		NA	0.0 (0.0, 0.0)
Incidence rate ratio: baricitinib / TNFi (95% CI)		NA		NA	--
Stroke					
Stroke Events	1	0	0	0	0
Person-Years	231.3	537.0	194.3	233.7	427.9
Stroke Events/100 PY	0.4	0.0	0.0	0.0	0.0
95% CI	0.0, 2.4	0.0, 0.7	0.0, 1.9	0.0, 1.6	0.0, 0.9
Incident rate difference: baricitinib – TNFi (95% CI)		NA		NA	0.0 (0.0, 0.0)
Incidence rate ratio: baricitinib / TNFi (95% CI)		NA		NA	--
Concomitant MTX Use at Index Date					
N	110	254	92	111	203
MACE Events	1	0	0	0	0
Person-Years	120.5	398.7	105.9	161.7	267.6
MACE Events/100 PY	0.8	0.0	0.0	0.0	0.0
95% CI	0.0, 4.6	0.0, 0.9	0.0, 3.5	0.0, 2.3	0.0, 1.4
Incident rate difference: baricitinib – TNFi (95% CI)		NA		NA	0.0 (0.0, 0.0)
Incidence rate ratio: baricitinib / TNFi (95% CI)		NA		NA	--
No Concomitant MTX Use at Index Date					
N	100	100	76	57	133
MACE Events	0	0	0	0	0
Person-Years	110.8	138.2	88.4	71.9	160.3
MACE Events/100 PY	0.0	0.0	0.0	0.0	0.0
95% CI	0.0, 3.3	0.0, 2.7	0.0, 4.2	0.0, 5.1	0.0, 2.3
Incident rate difference: baricitinib – TNFi (95% CI)		NA		NA	0.0 (0.0, 0.0)
Incidence rate ratio: baricitinib / TNFi (95% CI)		NA		NA	--

Abbreviations: CI = confidence interval; Cor_JP = CorEvitas RA registry, Japan; MI = myocardial infarction; MACE = major adverse cardiovascular event; MTX = methotrexate; N = number of patients in the analysis population; NA = not applicable; PY = person-years; TNFi = tumour necrosis factor inhibitor.

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10.3.2.4.3. Serious infection

Within the unmatched (ie., 'pre-matched') eligible CorEvitas Japan cohorts, 11 of the 210 patients in the baricitinib cohort had a first serious infection and 15 of 354 patients in the TNFi cohort had a serious infection (Table 59_Cor_JP). In the matched cohorts (n = 170 in each), there were 9 patients with serious infection in baricitinib cohort and 6 in the TNFi cohort. The rate of serious infection in the baricitinib cohort was 4.7 (95% CI 2.2, 9.0) per 100 PY and in the TNFi cohort 2.6 (95% CI 0.9, 5.6) per 100 PY. While the CI included the null value, there was a slightly elevated risk of serious infection in patients treated with baricitinib relative to those treated with TNFi ($HR_{adjusted\text{-}Model[1]}$=1.44; 95% CI 0.49, 4.23) (Table 61_Cor_JP).

Table 59_Cor_JP Incidence Rate of First Serious Infection [Cor_JP]

Model	Pre-matched		Matched		
	Baricitinib (N = 210)	TNFi (N = 354)	Baricitinib (N = 170)	TNFi (N = 170)	Total (N = 340)
Overall					
N	210	354	170	170	340
SI Events	11	15	9	6	15
Person-Years	225.1	524.5	190.8	232.9	423.7
SI Events/100 PY	4.9	2.9	4.7	2.6	3.5
95% CI	2.4, 8.7	1.6, 4.7	2.2, 9.0	0.9, 5.6	2.0, 5.8
Incidence rate difference: baricitinib – TNFi (95% CI)	NA	NA	NA	NA	2.14 (-1.57, 5.85)
Incidence rate ratio: baricitinib / TNFi (95% CI)	NA	NA	NA	NA	1.83 (0.58, 6.25)

Abbreviations: CI = confidence interval; Cor_JP = CorEvitas RA registry in Japan; N = count of patients in the specified category; NA = not applicable; PY = person-years; SI = serious infection defined as infection; TNFi = tumour necrosis factor inhibitor.

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Table 61_Cor_JP Comparative Risk of First Serious Infection Event [Cor_JP]

Model	TNFi	Baricitinib HR (95% CI)	P-Value
Base model	Ref	HR: 1.86 95% CI: [0.65, 5.32]	0.248
Adjusted - Model [1]	Ref	HR: 1.44 95% CI: [0.49, 4.23]	0.510
Adjusted - Model [2]	Ref	HR: 1.50 95% CI: [0.51, 4.42]	0.465
Non-mtx cDMARD use	Ref	HR: 0.45 95% CI: [0.06, 3.50]	0.447
Mtx cDMARD use	Ref	HR: 0.99 95% CI: [0.34, 2.88]	0.991
Prednisone use	Ref	HR: 1.68 95% CI: [0.57, 4.98]	0.347
Adjusted - Model [3]	Ref	HR: 1.49 95% CI: [0.51, 4.37]	0.469
Prednisone use	Ref	HR: 1.61 95% CI: [0.55, 4.76]	0.388
Adjusted - Model [4]	Ref	HR: 1.45 95% CI: [0.49, 4.27]	0.504
RA severity (CDAI)	Ref	HR: 1.00 95% CI: [0.96, 1.04]	0.892
Adjusted - Model [5]	Ref	HR: 1.44 95% CI: [0.49, 4.24]	0.510

Abbreviations: bDMARD = biologic disease-modifying anti-rheumatic drug; CDAI = clinical disease activity index; cDMARD = conventional disease-modifying anti-rheumatic drug; CI = confidence interval; Cor_JP = CorEvitas RA registry in Japan; HR = hazard ratio; mtx = methotrexate; RA = rheumatoid arthritis; Ref = referent group; TNFi = tumour necrosis factor inhibitor.
Base model: unadjusted model comparing propensity score matched cohorts.
Model [1]: adjusted by variables remaining unbalanced after propensity score matching (sex, number of prior bDMARDs used [0, 1, 2+ prior bDMARDs], and TNFi naïve at baseline).
Model [2]: Model [1] + time-varying concomitant non-methotrexate cDMARD use + time-varying concomitant methotrexate use + time-varying prednisone use.
Model [3]: Model [1] + time-varying prednisone use.
Model [4]: Model [1] + RA severity (CDAI).
Model [5]: Model [4] + BMI.
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10.3.2.5. CPRD (GOLD and Aurum)

No events were identified in eligible prematched patients treated with baricitinib. Exposure to baricitinib was limited (74 PY) and since propensity score matching substantially reduces the person-time available, analyses were discontinued. The CIs for the 0 per 100 PY incidence rates of MACE and VTE in the baricitinib cohort were (95% CI 0.0, 5.0).

10.3.2.6. JMDC

10.3.2.6.1. VTE

Within the unmatched JMDC data, 0 of 243 patients in the baricitinib cohort had a VTE and 3 of 1,721 patients in the TNFi cohort had a VTE (Table 45_JMDC). In the matched cohorts (n = 213 each), there were 0 patients with a VTE in the baricitinib cohort and 1 in the TNFi cohort. The IR of VTE in the baricitinib cohort was 0.00 (95% CI 0.00, 2.4) per 100 PY and 0.87 (95% CI 0.02, 4.84) per 100 PY in the TNFi cohort. In the absence of VTE events in the baricitinib cohort, the hazard ratio was not estimated.

Table 45_JMDC Incidence rate of VTE, Primary Definition [JMDC]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 243)	TNFi (N = 1721)	Baricitinib[a] (N = 213)	TNFi (N = 213)	Total (N = 426)
Overall					
Person-Years	170.96	865.47	154.02	115.01	269.03
VTE Events	0	3	0	1	1
VTE Events/100 PY	0.00	0.35	0.00	0.87	0.37
95% CI	0.00, 2.16	0.07, 1.01	0.00, 2.40	0.02, 4.84	0.01, 2.07
Concomitant MTX Use[b]					
Total, n	155 (63.8%)	1,024 (59.5%)	141 (66.2%)	132 (62.0%)	273 (64.1%)
Person-Years	122.36	637.45	113.96	81.93	195.88
VTE Events	0	2	0	1	1
VTE Events/100 PY	0.00	0.31	0.00	1.22	0.51

Model	Unmatched		Matched		
	Baricitinib[a] (N = 243)	TNFi (N = 1721)	Baricitinib[a] (N = 213)	TNFi (N = 213)	Total (N = 426)
95% CI	0.00, 3.02	0.04, 1.13	0.00, 3.24	0.03, 6.80	0.01, 2.84
No Concomitant MTX Use[b]					
Total, n	88 (36.2%)	697 (40.5%)	72 (33.8%)	81 (38.0%)	153 (35.9%)
Person-Years	48.60	228.03	40.06	33.08	73.15
VTE Events	0	1	0	0	0
VTE Events/100 PY	0.00	0.44	0.00	0.00	0.00
95% CI	0.00, 7.59	0.01, 2.44	0.00, 9.21	0.00, 11.15	0.00, 5.04

Abbreviations: CI = confidence intervals; JMDC = Japan Medical Data Center; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

[b] Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\jmdc_JMDC\3. Table 6.45. Incidence Rate of Event - VTE, Primary Definition [Japanese Medical Data Center Payer-Based].docx

10.3.2.6.2. MACE

Within the unmatched JMDC data, 0 of 246 patients in the baricitinib cohort had a MACE and 3 of the 1,720 patients in the TNFi cohort had a MACE (Table 54_JMDC). In the matched cohorts (n = 224 in each), there were 0 patients with a MACE both cohorts. The IR of MACE in the baricitinib cohort was 0.0 (95% CI 0.0, 2.33) per 100 PY and 0.0 (95% CI 0.0, 3.22) per 100 PY in the TNFi cohort. In the absence of MACE events, the hazard ratio was not estimated.

Table 54_JMDC Incidence Rate of MACE [JMDC]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 246)	TNFi (N = 1720)	Baricitinib[a] (N = 224)	TNFi (N = 224)	Total (N = 448)
Overall					
Person-Years	171.91	863.74	158.56	114.63	273.18
MACE	0	3	0	0	0
MACE/100 PY	0.00	0.35	0.00	0.00	0.00
95% CI	0.00, 2.15	0.07, 1.02	0.00, 2.33	0.00, 3.22	0.00, 1.35
MI					
MI	0	2	0	0	0
Person-Years	171.91	864.04	158.56	114.63	273.18
IR per 100 PY	0.00	0.23	0.00	0.00	0.00
95% CI	0.00, 2.15	0.03, 0.84	0.00, 2.33	0.00, 3.22	0.00, 1.35
Stroke, any					
Stroke	0	1	0	0	0
Person-Years	171.91	863.82	158.56	114.63	273.18
IR per 100 PY	0.00	0.12	0.00	0.00	0.00
95% CI	0.00, 2.15	0.00, 0.65	0.00, 2.33	0.00, 3.22	0.00, 1.35

Model	Unmatched		Matched		
	Baricitinib[a] (N = 246)	TNFi (N = 1720)	Baricitinib[a] (N = 224)	TNFi (N = 224)	Total (N = 448)
Concomitant MTX Use[b]					
MACE 0	0	1	0		0
Person-Years	122.99	634.80	110.25	80.76	191.01
IR per 100 PY	0.00	0.16	0.00	0.00	0.00
95% CI	0.00, 3.00	0.00, 0.88	0.00, 3.35	0.00, 4.57	0.00, 1.93
No Concomitant MTX Use[b]					
MACE	0	2	0	0	0
Person-Years	48.93	228.94	48.31	33.87	82.18
IR per 100 PY	0.00	0.87	0.00	0.00	0.00
95% CI	0.00, 7.54	0.11, 3.16	0.00, 7.64	0.00, 10.89	0.00, 4.49

Abbreviations: CI = confidence interval; IR = incidence rate; JMDC = Japan Medical Data Center; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; MI = myocardial infarction; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

[b] Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\jmdc_JMDC\3. Table 6.54. Incidence Rate of Event - MACE [JMDC].docx

10.3.2.6.3. Serious infection

Within the unmatched JMDC cohorts, 0 of the 246 patients in the baricitinib cohort had a first serious infection and 2 of 1,752 patients in the TNFi cohort had a serious infection (Table 59_JMDC). In the matched cohorts (n = 220 in each), there were 0 patients with serious infection in the baricitinib cohort and 1 in the TNFi cohort. The IR of serious infection in the baricitinib cohort was 0.0 (95% CI 0.0, 2.37) per 100 PY and in the TNFi cohort 0.78 (95% CI 0.02, 4.35) per 100 PY. In the absence of serious infection events in the baricitinib cohort, the hazard ratio was not estimated.

Table 59_JMDC Incidence Rate of First Serious Infection [JMDC]

Model	Unmatched		Matched		
	Baricitinib[a] (N = 246)	TNFi (N = 1752)	Baricitinib[a] (N = 220)	TNFi (N = 220)	Total (N = 440)
SI Events	0	2	0	1	1
Person-years	172.48	880.43	155.66	128.13	283.79
IR per 100 PY	0.00	0.23	0.00	0.78	0.35
95% CI	0.00, 2.14	0.03, 0.82	0.00, 2.37	0.02, 4.35	0.01, 1.96

Abbreviations: CI = confidence interval; IR = incidence rate; JMDC = Japan Medical Data Center; N = number of patients in the specified category; PY = person-years; SI = serious infection; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\jmdc_JMDC\3. [Updated 2022.03.15] Table 6.59. Incidence Rate of Event - First Serious Infection [Japanese Medical Data Center Payer-Based RA].docx

10.3.2.7. SNDS

10.3.2.7.1. VTE

Within the unmatched SNDS data, 23 of 3,242 patients in the baricitinib cohort had a VTE and 29 of 10,202 patients in the TNFi cohort had a VTE (Table 45_SNDS). In the matched cohorts (n = 2859 each), there were 20 patients with VTE in baricitinib cohort and 13 in the TNFi cohort. The rate of VTE in the baricitinib cohort was 1.1 (95% CI 0.7, 1.70) per 100 PY and 0.7 (95% CI 0.4, 1.2) per 100 PY in the TNFi cohort. Within the baricitinib cohort, 81% of patients received the 4-mg dose. The risk of VTE in patients treated with baricitinib was modestly increased relative to the risk in patients treated with TNFi, although the CI did include the null (HR=1.57, 95% CI 0.78, 3.18) (Table 48_SNDS).

Table 45_SNDS Incidence Rate of VTE, Primary Definition [SNDS]

	Unmatched				Matched				
		Baricitinib				Baricitinib			
VTE	Any[b] N = 3242	4 mg N = 2616	2 mg N = 622	TNFi N = 10202	Any[b] N = 2859	4 mg N = 2306	2 mg N = 551	TNFi[a] N = 2859	Total N = 5718
Overall									
Person-Years	2114	1734	377	6706	1855	1518	336	1923	3778
VTE	23	16	7	29	20	14	6	13	33
VTE/100 PY	1.1	0.9	1.9	0.4	1.1	0.9	1.8	0.7	0.9
95% CI	[0.7 ; 1.6]	[0.5 ; 1.5]	[0.7 ; 3.8]	[0.3 ; 0.6]	[0.7 ; 1.7]	[0.5 ; 1.5]	[0.7 ; 3.9]	[0.4 ; 1.2]	[0.6 ; 1.2]
IRD[d] /100 PY	0.7				0.4				
IRD[d] 95% CI	[0.3 ; 1.0]				[-0.2 ; 1.0]				
Concomitant[c] MTX Use, n (%)	1358 (41.9)	1148 (43.9)	208 (33.4)	5384 (52.8)	1226 (42.9)	1041 (45.1)	184 (33.4)	1336 (46.7)	2562 (44.8)
Person-Years	1009	860	148	4105	906	773	133	1034	1940
VTE	9	8	1	12	8	7	1	5	13
VTE/100 PY	0.9	0.9	0.7	0.3	0.9	0.9	0.8	0.5	0.7
95% CI	[0.4 ; 1.7]	[0.4 ; 1.8]	[0.0 ; 3.8]	[0.2 ; 0.5]	[0.4 ; 1.7]	[0.4 ; 1.9]	[0 ; 4.2]	[0.2 ; 1.1]	[0.4 ; 1.1]
IRD [d] /100 PY	0.6				0.4				
IRD [d] 95% CI	[0.2 ; 1.0]				[-0.3 ; 1.1]				
No concomitant[c] MTX Use, n (%)	1884 (58.1)	1468 (56.1)	414 (66.6)	4818 (47.2)	1633 (57.1)	1265 (54.9)	367 (66.6)	1523 (53.3)	3156 (55.2)
Person-Years	1105	875	228	2602	949	745	203	890	1839
VTE	14	8	6	17	12	7	5	8	20
VTE/100 PY	1.3	0.9	2.6	0.7	1.3	0.9	2.5	0.9	1.1
95% CI	[0.7 ; 2.1]	[0.4 ; 1.8]	[1.0 ; 5.7]	[0.4 ; 1.0]	[0.7 ; 2.2]	[0.4 ; 1.9]	[0.8 ; 5.7]	[0.4 ; 1.8]	[0.7 ; 1.7]
IRD[d] /100 PY	0.6				0.4				
IRD[d] 95% CI	[-0.03 ; 1.3]				[-0.6 ; 1.3]				

Abbreviations: CI = confidence intervals; IRD = incidence risk difference; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; SNDS = Système National des Données de Santé; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Matching ratio 1:1 is applied.

[b] n = 4 subjects were dispensed both baricitinib 4 mg and 2 mg at index date in unmatched cohort, are included in the overall « Baricitinib Any » group but not in the strata according to the dosage.

[c] Concomitance of MTX use with the initial treatment is defined as an overlap of continued exposure period of at least 28 days between both treatments. For each treatment, exposure period is considered as continued if the interval time between the end date of coverage period and the date of the new dispensing of the same treatment is ≤30 days.

[d] IRD = incidence risk difference between baricitinib group and TNFi group.

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Table 48_SNDS Comparative Risk of Incident VTE, Primary Definition [SNDS]

VTE	TNFi	Baricitinib, HR [95% CI]	P-value
Base model	Ref	1.57 [0.78 ; 3.18]	0.2055
Adjusted – Model [1]	Ref	1.57 [0.78 ; 3.18]	0.2055
Adjusted – Model [2]	Ref	1.55 [0.77 ; 3.13]	0.2234
Concomitant Glucocorticoid use	Ref	1.49 [0.74 ; 3.00]	0.2682
Concomitant cDMARD use	Ref	0.77 [0.39 ; 1.54]	0.4659
Adjusted – Model [3]	Ref	1.56 [0.77 ; 3.16]	0.2135
Concomitant Glucocorticoid use	Ref	1.47 [0.73 ; 2.97]	0.2858

Abbreviations: cDMARD = conventional disease-modifying antirheumatic drug; CI = confidence interval; HR = hazard ratio; Ref = referent group; SNDS = Système National des Données de Santé; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Model [1] = propensity score-matched model with outcome and baricitinib exposure, adjusted for any variables that remain unbalanced after propensity score matching. As no variable remains unbalanced, it is identical to Base model.

Model [2] = Model [1] + adjustment for time-dependent concomitant cDMARD use and glucocorticoid use.

Model [3] = Model [1] + adjustment for time-dependent concomitant glucocorticoid use.

For time-dependent cDMARD use, exposure period is considered as continued if the interval time between the end date of coverage period and the date of the new dispensing of the same treatment is ≤30 days. Concomitance with the initial treatment exposure is defined as overlap of continued exposure period of at least 28 days for cDMARD, and of at least 7 days for glucocorticoid.

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10.3.2.7.2. MACE

Within the unmatched SNDS data, 28 of 3,236 patients in the baricitinib cohort had a MACE and 34 of 10,175 patients in the TNFi cohort had a MACE (Table 54_SNDS). In the matched cohorts (n = 2864 in each), there were 25 patients with MACE in baricitinib cohort and 11 in the TNFi cohort. The rate of MACE in the baricitinib cohort was 1.4 (95% CI 0.9, 2.0) per 100 PY and 0.6 (95% CI 0.3, 1.0) per 100 PY in the TNFi cohort. The risk of MACE in patients treated with baricitinib was over 2-fold greater relative to the risk in patients treated with TNFi (adjusted HR=2.33, 95% CI 1.14, 4.77) (Table 55_SNDS).

Table 54_SNDS Incidence Rate of MACE [SNDS]

	Unmatched				Matched				
MACE	BARI Any[b] N = 3236	BARI 4 mg N = 2613	BARI 2 mg N = 619	TNFi N = 10175	BARI Any[b] N = 2864	BARI 4 mg N = 2314	BARI 2 mg N = 548	TNFi[a] N = 2864	Total N = 5728
Overall (MI or stroke)									
Person-Years	2102	1727	372	6681	1848	1521	326	1896	3744
MACE	28	19	9	34	25	16	9	11	36
MACE/100 PY	1.3	1.1	2.4	0.5	1.4	1.1	2.8	0.6	1.0
95% CI	[0.9 ; 1.9]	[0.7 ; 1.7]	[1.1 ; 4.6]	[0.4 ; 0.7]	[0.9 ; 2.0]	[0.6 ; 1.7]	[1.3 ; 5.2]	[0.3 ; 1.0]	[0.7 ; 1.3]
IRD[d] /100 PY	0.8			.	0.8				
IRD[d] 95% CI	[0.4 ; 1.2]				[0.1 ; 1.4]				
Overall (MI)									
Person-Years	2102	1727	372	6681	1848	1521	326	1896	3744
MI	16	12	4	23	13	9	4	6	19
MI/100 PY	0.8	0.7	1.1	0.3	0.7	0.6	1.2	0.3	0.5
95% CI	[0.4 ; 1.2]	[0.1 ; 1.2]	[0.3 ; 2.8]	[0.2 ; 0.5]	[0.4 ; 1.2]	[0.3 ; 1.1]	[0.3 ; 3.1]	[0.1 ; 0.7]	[0.3 ; 0.8]
IRD[d] /100 PY	0.4			.	0.4				
IRD[d] 95% CI	[0.1 ; 0.7]				[-0.1 ; 0.8]				
Overall (stroke)									
Person-Years	2102	1727	372	6681	1848	1521	326	1896	3744
Stroke	12	7	5	11	12	7	5	5	17
Stroke /100 PY	0.6	0.4	1.3	0.2	0.6	0.5	1.5	0.3	0.5
95% CI	[0.3 ; 1.0]	[0.2 ; 0.8]	[0.4 ; 3.1]	[0.1 ; 0.3]	[0.3 ; 1.1]	[0.2 ; 0.9]	[0.5 ; 3.6]	[0.1 ; 0.6]	[0.3 ; 0.7]
IRD[d] /100 PY	0.4			.	0.4				
IRD[d] 95% CI	[0.2 ; 0.7]				[-0.05 ; 0.8]				
Concomitant[c] MTX Use, n (%)	1357 (41.9)	1148 (43.9)	207 (33.4)	5376 (52.8)	1218 (42.5)	1031 (44.6)	185 (33.8)	1370 (47.8)	2588 (45.2)
Person-Years	1004	857	145	4093	895	764	130	1032	1927
MACE	9	6	3	23	7	4	3	4	11
MACE/100 PY	0.9	0.7	2.1	0.6	0.8	0.5	2.3	0.4	0.6
95% CI	[0.4 ; 1.7]	[0.3 ; 1.5]	[0.4 ; 6.0]	[0.4 ; 0.8]	[0.3 ; 1.6]	[0.1 ; 1.3]	[0.5 ; 6.7]	[0.1 ; 1.0]	[0.3 ; 1.0]
IRD[d] /100 PY	0.3			.	0.4				
IRD[d] 95% CI	[-0.2 ; 0.9]				[-0.3 ; 1.1]				
No concomitant[c] MTX Use, n (%)	1879 (58.1)	1465 (56.1)	412 (66.6)	4799 (47.2)	1646 (57.5)	1283 (55.4)	363 (66.2)	1494 (52.2)	3140 (54.8)

	Unmatched				Matched				
MACE	BARI Any[b] N = 3236	BARI 4 mg N = 2613	BARI 2 mg N = 619	TNFi N = 10175	BARI Any[b] N = 2864	BARI 4 mg N = 2314	BARI 2 mg N = 548	TNFi[a] N = 2864	Total N = 5728
Person-Years	1098	869	227	2589	953	757	196	864	1818
MACE	19	13	6	11	18	12	6	7	25
MACE/100 PY	1.7	1.5	2.6	0.4	1.9	1.6	3.1	0.8	1.4
95% CI	[1.0 ; 2.7]	[0.8 ; 2.6]	[1.0 ; 5.8]	[0.2 ; 0.8]	[1.1 ; 3.0]	[0.8 ; 2.8]	[1.1 ; 6.7]	[0.3 ; 1.7]	[0.9 ; 2.0]
IRD[d] /100 PY	1.3			.	1.1				
IRD[d] 95% CI	[0.7 ; 1.9]				[-0.001 ; 2.2]				

Abbreviations: CI = confidence interval; IRD = incidence risk difference; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; MI = myocardial infarction; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; SNDS = Système National des Données de Santé; TNFi = tumour necrosis factor inhibitor.

[a] Matching ratio 1:1 is applied.

[b] n = 4 subjects were dispensed both baricitinib 4 mg and 2 mg at index date in unmatched cohort, are included in the overall « Baricitinib Any » group but not in the strata according to the dosage.

[c] Concomitance of MTX use with the initial treatment is defined as overlap of continued exposure period of at least 28 days between both treatments. For each treatment, exposure period is considered as continued if the interval time between the end date of coverage period and the date of the new dispensing of the same treatment is ≤30 days.

[d] IRD = incidence risk difference between Baricitinib group and TNFi group.

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Table 55_SNDS Comparative Risk of MACE [SNDS]

MACE	TNFi	Baricitinib, HR [95% CI]	P-value
Base model	Ref	**2.33 [1.14 ; 4.77]**	0.0209
Adjusted – Model [1]	Ref	**2.33 [1.14 ; 4.77]**	0.0209
Adjusted – Model [2]	Ref	**2.27 [1.10 ; 4.69]**	0.0272
Concomitant Glucocorticoid use	Ref	0.88 *[0.41 ; 1.90]*	0.7532
Concomitant cDMARD use	Ref	0.55 [0.27 ; 1.14]	0.1071
Adjusted – Model [3]	Ref	**2.33 [1.14 ; 4.78]**	0.0207
Concomitant Glucocorticoid use	Ref	0.86 [0.41 ; 1.84]	0.7049

Abbreviations: cDMARD = conventional disease-modifying antirheumatic drug; CI = confidence interval; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; HR = hazard ratio; Ref = referent group; SNDS = Système National des Données de Santé; TNFi = tumour necrosis factor inhibitor.

Model [1] = propensity score-matched model with outcome and baricitinib exposure, adjusted for any variables that remain unbalanced after propensity score matching. As no variable remains unbalanced, it is identical to Base model.

Model [2] = Model [1] + adjustment for time-dependent concomitant cDMARD use and glucocorticoid use.

Model [3] = Model [1] + adjustment for time-dependent concomitant glucocorticoid use.

For time-dependent cDMARD use, exposure period is considered as continued if the interval time between the end date of coverage period and the date of the new dispensing of the same treatment is ≤30 days. Concomitance with the initial treatment exposure is defined as overlap of continued exposure period of at least 28 days for cDMARD, and of at least 7 days for glucocorticoid.

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10.3.2.7.3. Serious infection

Within the unmatched SNDS data, 44 of 3,366 patients in the baricitinib cohort had a first serious infection and 68 of 10,451 patients in the TNFi cohort experienced a first serious infection (Table 59_SNDS). In the matched cohorts (n = 2979 in each), there were 36 patients with serious infection in each of the baricitinib and TNFi cohorts. The rates of serious infection in the baricitinib and TNFi cohorts were not dissimilar; 1.9 (95% CI 1.3, 2.6) per 100 PY in baricitinib and 1.8 (95% CI 1.3, 2.5) per 100 PY in the TNFi cohort (HR=1.04, 95% CI 0.65, 1.66; Table 61_SNDS).

Table 59_SNDS Incidence Rate of First Serious Infection [SNDS]

	Unmatched				Matched				
SI	BARI Any[b] N = 3366	BARI 4 mg N = 2696	BARI 2 mg N = 666	TNFi N = 10451	BARI Any[b] N = 2979	BARI 4 mg N = 2385	BARI 2 mg N = 591	TNFi[a] N = 2979	Total N = 5958
Overall									
Person-Years	2188	1785	400	6867	1920	1561	357	1994	3914
SI	44	29	15	68	36	25	11	36	72
SI/100 PY	2.0	1.6	3.7	1.0	1.9	1.6	3.1	1.8	1.8
95% CI	[1.5 ; 2.7]	[1.1 ; 2.3]	[2.1 ; 6.2]	[0.8 ; 1.2]	[1.3 ; 2.6]	[1.0 ; 2.4]	[1.5 ; 5.5]	[1.3 ; 2.5]	[1.4 ; 2.2]
IRD[c] /100 PY	1.0			.	0.1				
IRD[c] 95% CI	[0.5 ; 1.6]				[-0.8 ; 0.9]				
Concomitant MTX Use, n (%)									
N	1403 (41.7)	1181 (43.8)	220 (33.0)	5508 (52.7)	1266 (42.5)	1064 (44.6)	200 (33.8)	1405 (47.2)	2671 (44.8)
Person-Years	1035	879	155	4194	941	797	143	1086	2027
SI	16	11	5	32	14	11	3	17	31
SI/100 PY	1.5	1.3	3.2	0.8	1.5	1.4	2.1	1.6	1.5
95% CI	[0.9 ; 2.5]	[0.6 ; 2.2]	[1.0 ; 7.5]	[0.5 ; 1.1]	[0.8 ; 2.5]	[0.7 ; 2.5]	[0.4 ; 6.1]	[0.9 ; 2.5]	[1.0 ; 2.2]
IRD[c] /100 PY	0.8			.	-0.1				
IRD[c] 95% CI	[0.1 ; 1.4]				[-1.2 ; 1.0]				
No concomitant MTX Use, n (%)									
N	1963 (58.3)	1515 (56.2)	446 (67.0)	4943 (47.3)	1713 (57.5)	1321 (55.4)	391 (66.2)	1574 (52.8)	3287 (55.2)
PY	1153	906	245	2673	979	764	214	908	1887
SI	28	18	10	36	22	14	8	19	41
SI/100 PY	2.4	2.0	4.1	1.3	2.2	1.8	3.7	2.1	2.2
95% CI	[1.6 ; 3.5]	[1.2 ; 3.1]	[2.0 ; 7.5]	[0.9 ; 1.9]	[1.4 ; 3.4]	[1.0 ; 3.1]	[1.6 ; 7.4]	[1.3 ; 3.3]	[1.6 ; 2.9]
IRD[c] /100 PY	1.1				0.2				
IRD[c] 95% CI	[0.2 ; 2.0]				[-1.2 ; 1.5]				

Abbreviations: CI = confidence interval; IRD = incidence risk difference; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; SI = serious infection; SNDS = Système National des Données de Santé; TNFi = tumour necrosis factor inhibitor.

[a] Matching ratio 1:1 is applied.

[b] n = 4 subjects were dispensed both baricitinib 4 mg and 2 mg at index date in unmatched cohort, are included in the overall « Baricitinib Any » group but not in the strata according to the dosage.

[c] IRD = incidence risk difference between baricitinib group and TNFi group.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\french snds_SNDS\BARICITINIB_RAS_SNDS_2019_Match_1_1_Point VII_V1.0 20220228.docx - pages 210-211

Table 61_SNDS Comparative Risk of First Serious Infection Event [SNDS]

Serious Infections	TNFi	Baricitinib, HR [95% CI]	P-value
Base Model	Ref	1.04 [0.65 ; 1.66]	0.8735
Adjusted – Model [1]	Ref	1.04 [0.65 ; 1.66]	0.8735
Adjusted – Model [2]	Ref	1.05 [0.66 ; 1.67]	0.8476
Concomitant Glucocorticoid use	Ref	1.03 [0.62 ; 1.70]	0.9228
Concomitant cDMARD use	Ref	1.19 [0.75 ; 1.89]	0.4640
Adjusted – Model [3]	Ref	1.04 [0.65 ; 1.66]	0.8757
Concomitant Glucocorticoid use	Ref	1.04 [0.62 ; 1.73]	0.8834

Abbreviations: cDMARD = conventional disease modifying anti-rheumatic drug; CI = confidence interval; HR = hazard ratio; Ref = referent group; SNDS = Système National des Données de Santé; TNFi = tumour necrosis factor inhibitor.

Model [1] = propensity score-matched model with outcome and baricitinib exposure, adjusted for any variables that remain unbalanced after propensity score matching. As no variable remains unbalanced, it is identical to Base model.

Model [2] = Model [1] + adjustment for time-dependent concomitant cDMARD use and glucocorticoid use.

Model [3] = Model [1] + adjustment for time-dependent concomitant glucocorticoid use.

For time-dependent cDMARD use, exposure period is considered as continued if the interval time between the end date of coverage period and the date of the new dispensing of the same treatment is ≤30 days. Concomitance with the initial treatment exposure is defined as overlap of continued exposure period of at least 28 days for cDMARD, and of at least 7 days for glucocorticoid.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\french snds_SNDS\BARICITINIB_RAS_SNDS_2019_Match_1_1_Point VII_V1.0 20220228.docx - pages 213

10.4. Outcome data

Data sources with more than 5 total patients in the baricitinib and TNFi cohorts combined, for at least one of the outcomes of interest, are as follows:

- **VTE**: PS20, ARTIS, BKK, and SNDS
- **MACE**: PS20, ARTIS, BKK, and SNDS
- **Incident Serious Infection**: Optum, Pharmetrics Plus, PS20, ARTIS, BKK, CorEvitas Japan, and SNDS

Clinical characteristics, patterns of RA medication use, and time to event are summarized for patients who experienced the respective event, by data source.

The number of events was low in most data sources; thus, caution must be exercised when considering these characteristics given the low sample sizes. Any trends or comparisons made between patients with the event to the overall cohort of RA patients are descriptive only.

Details for patients with events in the other data sources (ie, when patients with events ≤5) are in the respective Annexes and include information for unmatched patients. For some data sources, due to privacy policies and masking of patient information when counts are low, information is masked and cannot be presented.

10.4.1. VTE

Clinical characteristics of patients with VTE were generally the same as observed in the overall cohort of RA patients (as described in Section 10.2), except for age and gender. The mean age of patients with a VTE treated with baricitinib appeared higher than the overall age of the patients in VTE analyses, although sample sizes were small and no statistical comparison was made:

- PS20: The mean age of patients with a VTE treated with baricitinib (n = 6) was 60 years (Table 40_PS20), whereas the overall mean age was 55 years (Table 2_PS20).
- ARTIS: The mean age of patients with VTE treated with baricitinib (n = 23) was 63 years (Table 40_ARTIS), whereas the overall mean age was 59 years (Table 2_ARTIS).
- SNDS: The mean age of patients with a VTE treated with baricitinib (n = 20) was 68.6 years (Table 40_SNDS), while it was 58.4 years in the overall cohort (Table 2_SNDS).

The older age observed among patients with VTE was not present among patients in BKK.

In the BKK, ARTIS, and SNDS data, almost all patients with a VTE treated with baricitinib were male (2 of 3 in BKK; 18 of 23 in ARTIS; 19 of 20 in SNDS).

Clinical conditions at baseline and use of RA medications for these patients with VTE were as expected for the patient population. Notably within PS20, all 6 of the VTE events in patients treated with baricitinib had a recent hospitalization within the 4 weeks prior to VTE.

The distribution of time to VTE is variable. ARTIS and SNDS, which provided the 2 largest cohorts, had the most patients treated with baricitinib with a VTE. For the 23 baricitinib-treated patients with a VTE in ARTIS, the mean (median) time to event was 502 (454) days. For the 20 patients within SNDS, the mean (median) time to event was 239.9 (209) days.

Table 40_PS20 Clinical Characteristics of RA Patients with VTE, Primary Definition [PS20]

Characteristic[a,b]	Baricitinib[c] (N = 6)	TNFi (N = 4)	Total (N = 10)
Age (mean) [SD]	59.67 (9.22)	55.00 (6.38)	57.80 (8.16)
Sex			
Female	5 (83.3%)	3 (75.0%)	8 (80.0%)
Male	1 (16.7%)	1 (25.0%)	2 (20.0%)
Clinical Conditions during baseline			
Cancer	1 (16.7%)	0 (0.0%)	1 (10.0%)
NMSC	1 (16.7%)	0 (0.0%)	1 (10.0%)
Chronic Lung disease Disease	1 (16.7%)	1 (25.0%)	2 (20.0%)
Cardiovascular conditions			
Atrial arrhythmia/ fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)

Characteristic[a,b]	Baricitinib[c] (N = 6)	TNFi (N = 4)	Total (N = 10)
Congestive heart failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	2 (33.3%)	1 (25.0%)	3 (30.0%)
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	2 (33.3%)	1 (25.0%)	3 (30.0%)
Dyslipidaemia	4 (66.7%)	2 (50.0%)	6 (60.0%)
Hypertension	5 (83.3%)	1 (25.0%)	6 (60.0%)
Immune disorders	1 (16.7%)	2 (50.0%)	3 (30.0%)
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	1 (16.7%)	1 (25.0%)	2 (20.0%)
Primary Sjögren Syndrome	0 (0.0%)	1 (25.0%)	1 (10.0%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	1 (16.7%)	1 (25.0%)	2 (20.0%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	4.15 (1.87)	3.91 (0.85)	4.05 (1.48)
Smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)
Surgery, trauma, & hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medication			
Antibiotics	4 (66.7%)	2 (50.0%)	6 (60.0%)
Antidiabetic agents	3 (50.0%)	0 (0.0%)	3 (30.0%)
Insulins	1 (16.7%)	0 (0.0%)	1 (10.0%)
Non-insulins	2 (33.3%)	0 (0.0%)	2 (20.0%)
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			
Antihypertensives	5 (83.3%)	3 (75.0%)	8 (80.0%)
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anticoagulant	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiplatelet	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			
Oral contraceptives	0 (0.0%)	1 (25.0%)	1 (10.0%)
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERM	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)

Characteristic[a,b]	Baricitinib[c] (N = 6)	TNFi (N = 4)	Total (N = 10)
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	2 (33.3%)	1 (25.0%)	3 (30.0%)
Rheumatoid arthritis- related			
Cox-2 Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucocorticosteroid	4 (66.7%)	2 (50.0%)	6 (60.0%)
Vaccinations	1 (16.7%)	1 (25.0%)	2 (20.0%)
Post-index Occurrence[d]			
Cancer	1 (16.7%)	0 (0.0%)	1 (10.0%)
Hospitalization	6 (100.0%)	1 (25.0%)	7 (70.0%)
Surgery	0 (0.0%)	0 (0.0%)	0 (0.0%)
Trauma	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus;: HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; PS20 = HealthyVerity Private Source 20; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective oestrogen receptor modifier; SLE = systemic lupus erythematosus; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] All conditions and characteristics are measured during the 6 months prior to initiation of study medication until, and including, the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

[b] Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 (see Section 8.3.3, Annex 19) for each outcome (e.g., hospitalized congestive heart failure) for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias (e.g., Type I diabetes) for VTE.

[c] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

[d] Except for cancer diagnosed within 90 days of VTE diagnosis, events in this category must have occurred in the 4 weeks immediately prior to VTE (Sweetland et al 2009).

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.40. - Clinical Characteristics of RA Patients with VTE, Primary Definition [HealthVerity, PS20].docx

Table 40_ARTIS Clinical Characteristics of RA Patients with VTE, Primary Definition [ARTIS]

Characteristic[a,b]	Baricitinib[c] (N = 23)	TNFi (N = 14)	Total (N = 37)
Age (mean) [SD]	63 (10.4)	65 (11.0)	64 (10.5)
Sex			
Female	5 (22%)	<5	8 (22%)
Male	18 (78%)	11 (79%)	29 (78%)
Clinical Conditions During Baseline			
Cancer	<5	<5	<5
NMSC	<5	<5	<5

Characteristic[a,b]	Baricitinib[c] (N = 23)	TNFi (N = 14)	Total (N = 37)
Chronic lung disease			
Disease	<5	<5	<5
Cardiovascular conditions			
Atrial arrhythmia	<5	<5	<5
Cardiovascular revascularization	<5	<5	<5
Congestive heart failure	<5	<5	<5
Coronary artery disease	<5	<5	<5
Ischemic heart disease	<5	<5	<5
Unstable angina	<5	<5	<5
Ventricular arrhythmia	<5	<5	<5
Diabetes mellitus	<5	<5	<5
Type I	NA	NA	NA
Type II	NA	NA	NA
Dyslipidaemia	<5	<5	<5
Hypertension	<5	<5	<5
Immune disorders			
AIDS/HIV	NA	NA	NA
Antiphospholipid syndrome	NA	NA	NA
SLE	NA	NA	NA
Primary Sjögren Syndrome	<5	<5	<5
Liver disorder	<5	<5	<5
Obesity	NA	NA	NA
Pregnancy	<5	<5	<5
RA Severity (DAS28), mean (SD)	4.5 (1.27)	5.6 (0.86)	4.8 (1.25)
Smoking	15 (75%)	5 (56%)	20 (69%)
Surgery	18 (78%)	11 (79%)	29 (78%)
TIA	<5	<5	<5
Other Prescription Medications			
Antibiotics	5 (22%)	<5	9 (24%)
Antidiabetic agents	<5	<5	<5
Insulins	<5	<5	<5
Non-insulins	<5	<5	<5
Aspirin	5 (22%)	<5	7 (19%)
Cardiovascular			
Anticoagulant	<5	<5	<5
Antihypertensives	10 (43%)	<5	14 (38%)
Antiplatelet	5 (22%)	<5	7 (19%)
Nitrates	<5	<5	<5
Hormonal			
HRT	<5	<5	<5
Oral contraceptives	<5	<5	<5
SERM	<5	<5	<5
Lipid-lowering agents			
Bile acid binding	<5	<5	<5
Cholesterol absorption inhibitor	<5	<5	<5
Fibrates	<5	<5	<5
Niacin	NA	NA	NA

Characteristic[a,b]	Baricitinib[c] (N = 23)	TNFi (N = 14)	Total (N = 37)
Omega-3 fatty acids	NA	NA	NA
Statins	7 (30%)	<5	11 (30%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	<5	<5	<5
Glucocorticosteroid	19 (83%)	9 (64%)	28 (76%)
Vaccinations	NA	NA	NA
Post Index Occurrence[d]			
Cancer	<5	<5	<5

Abbreviations: AIDS = acquired immunodeficiency syndrome; ARTIS = Anti-Rheumatic Therapy in Sweden; DAS28 = Disease Activity Score 28; HIV = human immunodeficiency virus;: HRT = hormone replacement therapy; N = number of patients in the specified category; NA = not available; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective oestrogen receptor modifier; SLE = systemic lupus erythematosus; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until, and including, the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort. Clinical conditions are defined based on the "main diagnosis" in the National Patient Register

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 (see Section 8.3.3, Annex 19) for each outcome (e.g., hospitalized congestive heart failure) for VTE. Other factors that are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias (e.g., Type I diabetes) for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

d Except for cancer diagnosed within 90 days of VTE diagnosis, events in this category must have occurred in the 4 weeks immediately prior to VTE (Sweetland et al. 2009).

Source:
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Table 40_BKK Clinical Characteristics of RA Patients with VTE, Primary Definition [BKK]

Characterstic[a,b]	Baricitinib[c] (N = 3)	4 mg (N = 3)	2 mg (N = 0)	TNFi (N = 6)	Total (N = 9)
Age (mean) [SD]	53.7 (2)	53.7 (2)	0 (0)	58.5 (16)	56.9 (13)
Sex					
Female	1 (33%)	1 (33%)	0 (0%)	5 (83%)	6 (67%)
Male	2 (67%)	2 (67%)	0 (0%)	1 (17%)	3 (33%)
Clinical Conditions During Baseline					
Cancer	0 (0%)	0 (0%)	0 (0%)	3 (50%)	3 (33%)
NMSC	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Chronic lung disease	1 (33%)	1 (33%)	0 (0%)	1 (17%)	2 (22%)
Cardiovascular conditions	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Atrial arrhythmia/ fibrillation	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cardiovascular revascularization	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Characterstic[a,b]	Baricitinib[c] 4 mg (N = 3)	2 mg (N = 3)	TNFi (N = 0)	Total (N = 6)	(N = 9)
Congestive heart failure, hospitalized	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Coronary artery disease	0 (0%)	0 (0%)	0 (0%)	1 (17%)	1 (11%)
Ischemic heart disease	0 (0%)	0 (0%)	0 (0%)	1 (17%)	1 (11%)
Unstable angina	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Ventricular arrhythmia	1 (33%)	1 (33%)	0 (0%)	1 (17%)	2 (22%)
Diabetes mellitus	1 (33%)	1 (33%)	0 (0%)	2 (33%)	3 (33%)
Type I	1 (33%)	1 (33%)	0 (0%)	0 (0%)	1 (11%)
Type II	1 (33%)	1 (33%)	0 (0%)	2 (33%)	3 (33%)
Dyslipidaemia	0 (0%)	0 (0%)	0 (0%)	2 (33%)	2 (22%)
Hypertension	1 (33%)	1 (33%)	0 (0%)	3 (50%)	4 (44%)
Immune disorders	0 (0%)	0 (0%)	0 (0%)	1 (17%)	1 (11%)
AIDS/HIV	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Antiphospholipid syndrome	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SLE	0 (0%)	0 (0%)	0 (0%)	1 (17%)	1 (11%)
Primary Sjögren Syndrome	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Liver disorder	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Obesity	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pregnancy	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
RA severity (CIRAS), mean (SD)	8.4 (0)	8.4 (0)	0 (0)	6.9 (2)	7.4 (2)
Smoking	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Surgery, trauma, & hospitalization, recent	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Genetic coagulopathies	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
TIA	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Other Prescription Medications					
Antibiotics	1 (33%)	1 (33%)	0 (0%)	1 (17%)	2 (22%)
Antidiabetic agents	1 (33%)	1 (33%)	0 (0%)	1 (17%)	2 (22%)
Insulins	1 (33%)	1 (33%)	0 (0%)	0 (0%)	1 (11%)
Non-insulins	0 (0%)	0 (0%)	0 (0%)	1 (17%)	1 (11%)
Aspirin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cardiovascular					
Antihypertensives	2 (67%)	2 (67%)	0 (0%)	3 (50%)	5 (56%)
Nitrates	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Anticoagulant	1 (33%)	1 (33%)	0 (0%)	2 (33%)	3 (33%)
Antiplatelet	1 (33%)	1 (33%)	0 (0%)	1 (17%)	2 (22%)
Hormonal					
Oral contraceptives	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
HRT	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SERM	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Lipid-lowering agents					
Bile acid binding	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cholesterol absorption inhibitor	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Characterstic[a,b]	Baricitinib[c] (N = 3)	4 mg (N = 3)	2 mg (N = 0)	TNFi (N = 6)	Total (N = 9)
Fibrates	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Niacin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Omega-3 fatty acids	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Statins	1 (33%)	1 (33%)	0 (0%)	1 (17%)	2 (22%)
Rheumatoid arthritis-related					
Cox-2 inhibitor	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Glucocorticosteroid	1 (33%)	1 (33%)	0 (0%)	5 (83%)	6 (67%)
Vaccinations	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Postindex Occurrence[c]					
Cancer	0 (0%)	0 (0%)	0 (0%)	2 (33%)	2 (22%)
Hospitalization	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Surgery	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Trauma	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; cDMARD = conventional disease-modifying antirheumatic drug; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective oestrogen receptor modulator; SLE = systemic lupus erythematosus; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] All conditions and characteristics except for use of bDMARD and concomitant cDMARD are measured during the 6 months prior to initiation of study medication until, and including, the index date.

[b] Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 (see Section 8.3.3, Annex 19) for each outcome (e.g., hospitalized congestive heart failure) for VTE. Other factors that are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias (e.g., Type I diabetes) for VTE.

[c] Except for cancer diagnosed within 90 days of VTE diagnosis, events in this category must have occurred in the 4 weeks immediately prior to VTE (Sweetland et al. 2009).

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\BKK\Lilly Baricitinib Results_VTE_BKK_v1.0.docx -pages 14-15

Table 40_SNDS Clinical Characteristics of RA Patients with VTE, Primary Definition [SNDS]

Characteristics[b]	Baricitinib Any n = 20	Baricitinib 4 mg n = 14	Baricitinib 2 mg n ≤10	TNFi[a] n = 13	Total n = 33
Age [in years]					
N	20 (0)	14 (0)		13 (0)	33 (0)
Mean (SD)	68.6 (9.8)	65.8 (9.2)		66.2 (12.3)	67.6 (10.8)
Median	70.0	68.5		66.0	69.0
Min, Max	49.0, 87.0	49.0, 83.0		51.0, 88.0	49.0, 88.0
Sex, n (%)					
Female	≤10	≤10		≤10	≤10
Male	19 (95.0)	13 (92.9)		≤10	25 (75.8)

Characteristics[b]	Baricitinib Any n = 20	Baricitinib 4 mg n = 14	Baricitinib 2 mg n ≤10	TNFi[a] n = 13	Total n = 33
Clinical Conditions During Baseline Period, n (%)					
Cancer, excluding NMSC	≤10	≤10		0 (0.0)	≤10
NMSC	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Chronic lung disease, excluding cystic fibrosis[d]	≤10	≤10		≤10	≤10
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Cardiovascular revascularization	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Congestive heart failure, hospitalized	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Coronary artery disease	≤10	0 (0.0)		≤10	≤10
Unstable angina	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Ventricular arrhythmia	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Stroke	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Haemorrhagic	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Ischemic	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Unknown	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
TIA	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Diabetes mellitus[d]	≤10	≤10		≤10	≤10
Treated insulin dependent	NA	NA		NA	NA
Treated non-insulin dependent	NA	NA		NA	NA
Dyslipidaemia (not available in SNDS)	NA	NA		NA	NA
Hypertension (not available in SNDS)					
History of hypertension	NA	NA		NA	NA
Current hypertension	NA	NA		NA	NA
Immune disorders	≤10	≤10		0 (0.0)	≤10
AIDS/HIV	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Antiphospholipid syndrome	NA	NA		NA	NA
SLE	≤10	≤10		0 (0.0)	≤10
Primary Sjogren Syndrome	≤10	≤10		0 (0.0)	≤10
Liver or pancreatic disorder	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Obesity (not available in SNDS)	NA	NA		NA	NA
Recent pregnancy	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
RA Severity (CIRAS Index)					
Mean (± SD)	5.6 (0.6)	5.7 (0.6)		6.6 (1.6)	6.0 (1.2)
Smoking (not available in SNDS)	NA	NA		NA	NA
Surgery or trauma	≤10	≤10		≤10	≤10
Other Prescription Medications During Baseline Period, n (%)	≤10	≤10		≤10	≤10
Antibiotics	14 (70.0)	≤10		≤10	21 (63.6)
Antidiabetic agents	≤10	≤10		≤10	≤10
Insulins	≤10	≤10		0 (0.0)	≤10
Non-insulins	≤10	≤10		≤10	≤10
Cardiovascular					
Antithrombotic agents	≤10	≤10		≤10	≤10
Anticoagulant	≤10	≤10		≤10	≤10

Characteristics[b]	Baricitinib Any n = 20	Baricitinib 4 mg n = 14	Baricitinib 2 mg n ≤10	TNFi[a] n = 13	Total n = 33
Antiplatelet	≤10	≤10		≤10	≤10
Antihypertensives	≤10	≤10		≤10	13 (39.4)
Angiotensin converting enzyme inhibitors (ACE)	≤10	≤10		≤10	≤10
Angiotensin receptor blockers (ARB)	≤10	≤10		≤10	≤10
Beta blocker	≤10	0 (0.0)		≤10	≤10
Calcium channel blocker	≤10	≤10		≤10	≤10
Nitrates	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Acyclovir	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Valacyclovir	≤10	≤10		≤10	≤10
Hormonal	≤10	≤10		≤10	≤10
HRT	≤10	≤10		0 (0.0)	≤10
Oral Contraceptives	0 (0.0)	0 (0.0)		≤10	≤10
SERMs	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Topic with progestogens and/or oestrogens	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Lipid-lowering agents	≤10	≤10		≤10	13 (39.4)
HMG CoA reductase inhibitors	≤10	≤10		≤10	≤10
Fibrates	≤10	≤10		≤10	≤10
Bile acid sequestrants	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Other lipid-modifying agents	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Lipid-modifying agents, combinations	≤10	≤10		0 (0.0)	≤10
Rheumatoid arthritis-related					
Aspirin	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Cox-2 Inhibitor	0 (0.0)	0 (0.0)		≤10	≤10
NSAIDs	≤10	≤10		≤10	12 (36.4)
Glucocorticosteroid	18 (90.0)	12 (85.7)		≤10	28 (84.8)
Vaccines	14 (70.0)	≤10		≤10	21 (63.6)
Antineoplastic agents	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Post-index Occurrence[c], n (%)				-	
Cancer	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Hospitalization	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Surgery	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)

Abbreviations: ACE = Angiotensin converting enzyme inhibitors; AIDS = acquired immunodeficiency syndrome; ARB = Angiotensin receptor blockers; CIRAS = claims-based index for RA severity; CNAM = Caisse Nationale d'Assurance Maladie (French national health insurance); HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective oestrogen receptor modifier; SNDS = Système National des Données de Santé;TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Matching ratio 1:1 is applied.

[b] All conditions and characteristics are measured during the 6 months prior to initiation of study medication until, and including, the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort, index date excluded.

[c] Except for cancer diagnosed within 90 days of VTE diagnosis, events in this category must have occurred in the 4 weeks immediately prior to VTE (Sweetland et al. 2009).

[d] CNAM algorithm based on the year preceding the year of inclusion

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\french snds_SNDS\BARICITINIB_RAS_SNDS_2019_Match_1_1_Point VII_V1.0 20220228.docx - page 172-176

Table 41_PS20 Pattern of RA Medication Use in Patients with VTE, Primary Definition [PS20]

	Unmatched		Matched		
Characteristic[a]	Baricitinib[b] (N = 6)	TNFi (N = 18)	Baricitinib[b] (N = 6)	TNFi (N = 4)	Total (N = 10)
Baseline Medication					
cDMARDs, during baseline					
n, total	4 (66.7%)	11 (61.1%)	4 (66.7%)	3 (75.0%)	7 (70.0%)
Mean (SD)	1.67 (1.97)	0.78 (0.73)	1.67 (1.97)	0.75 (0.50)	1.30 (1.57)
Median	1.00 [0.00, 3.50]	1.00 [0.00, 1.00]	1.00 [0.00, 3.50]	1.00 [0.25, 1.00]	1.00 [0.00, 1.50]
Min, Max	0.0, 5.0	0.0, 3.0	0.0, 5.0	0.0, 1.0	0.0, 5.0
>1 cDMARD concomitantly	2 (33.3%)	1 (5.6%)	2 (33.3%)	0 (0.0%)	2 (20.0%)
Hydroxychloroquine	2 (33.3%)	3 (16.7%)	2 (33.3%)	1 (25.0%)	3 (30.0%)
Leflunomide	2 (33.3%)	2 (11.1%)	2 (33.3%)	0 (0.0%)	2 (20.0%)
Methotrexate	3 (50.0%)	6 (33.3%)	3 (50.0%)	2 (50.0%)	5 (50.0%)
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	2 (33.3%)	2 (11.1%)	2 (33.3%)	0 (0.0%)	2 (20.0%)
bDMARDs, during baseline					
n, total	1 (16.7%)	17 (94.4%)	1 (16.7%)	4 (100.0%)	5 (50.0%)
Mean (SD)	0.17 (0.41)	1.11 (0.32)	0.17 (0.41)	1.50 (0.58)	0.70 (0.82)
Median	0.00 [0.00, 0.25]	1.00 [1.00, 1.00]	0.00 [0.00, 0.25]	1.50 [1.00, 2.00]	0.50 [0.00, 1.25]
Min, Max	0.0, 1.0	0.0, 2.0	0.0, 1.0	1.0, 2.0	0.0, 2.0
cDMARDs, concomitant	1 (16.7%)	10 (55.6%)	1 (16.7%)	2 (50.0%)	3 (30.0%)
Abatacept	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adalimumab[c]	0 (0.0%)	7 (38.9%)	0 (0.0%)	1 (25.0%)	1 (10.0%)
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	2 (11.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Etanercept[c]	0 (0.0%)	5 (27.8%)	0 (0.0%)	1 (25.0%)	1 (10.0%)
Golimumab[c]	0 (0.0%)	1 (5.6%)	0 (0.0%)	1 (25.0%)	1 (10.0%)
Infliximab[c]	0 (0.0%)	2 (11.1%)	0 (0.0%)	1 (25.0%)	1 (10.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	1 (16.7%)	1 (5.6%)	1 (16.7%)	1 (25.0%)	2 (20.0%)
Post-index Medication[d]					
Methotrexate, concomitant	1 (16.7%)	3 (16.7%)	1 (16.7%)	1 (25.0%)	2 (20.0%)
Other Concomitant cDMARD	1 (16.7%)	4 (22.2%)	1 (16.7%)	0 (0.0%)	1 (10.0%)
Dose change, baricitinib	NA[d]	0 (0.0%)	NA[d]	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; PS20 = HealthVerity Private Source 20; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; US = United States; VTE = venous thromboembolism.

[a] All conditions and characteristics are measured during the 6 months prior to initiation of study medication until, and including, the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

[b] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

[c] TNF inhibitors.

[d] Only the baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked “NA” as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.41. - Pattern of RA Medication Use in Patients with VTE, Primary Definition [HealthVerity]].docx

Table 41_BKK Pattern of RA Medication Use in Patients with VTE, Primary Definition [BKK]

	Unmatched				Matched				
Characteristic[a]	Baricitinib (N = 3)	4 mg (N = 3)	2 mg (N = 0)	TNFi (N = 21)	Baricitinib (N = 3)	4 mg (N = 3)	2 mg (N = 0)	TNFi (N = 6)	Total (N = 9)
Baseline Medication									
csDMARDs, during baseline									
n, total	2 (67%)	2 (67%)	0 (0%)	15 (71%)	2 (67%)	2 (67%)	0 (0%)	4 (67%)	6 (67%)
Mean (SD)	1.3 (2)	1.3 (2)	0.0 (0)	0.8 (1)	1.3 (2)	1.3 (2)	0.0 (0)	0.8 (1)	1 (1)
Median	1.0	1.0	0.0	1.0	1.0	1.0	0.0	1.0	1.0
Min, Max	0.0, 3.0	0.0, 3.0	0.0, 0.0	0.0, 2.0	0.0, 3.0	0.0, 3.0	0.0, 0.0	0.0, 2.0	0.0, 3.0
>1 csDMARD concomitantly	1 (33%)	1 (33%)	0 (0%)	1 (5%)	1 (33%)	1 (33%)	0 (0%)	0 (0%)	1 (11%)
Hydroxychloroquine	1 (33%)	1 (33%)	0 (0%)	1 (5%)	1 (33%)	1 (33%)	0 (0%)	1 (17%)	2 (22%)
Leflunomide	1 (33%)	1 (33%)	0 (0%)	4 (19%)	1 (33%)	1 (33%)	0 (0%)	0 (0%)	1 (11%)
Methotrexate	1 (33%)	1 (33%)	0 (0%)	9 (43%)	1 (33%)	1 (33%)	0 (0%)	3 (50%)	4 (44%)
Minocycline	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Sulfasalazine	1 (33%)	1 (33%)	0 (0%)	2 (10%)	1 (33%)	1 (33%)	0 (0%)	1 (17%)	2 (22%)
bDMARDs, during baseline									
n, total	0 (0%)	0 (0%)	0 (0%)	4 (19%)	0 (0%)	0 (0%)	0 (0%)	3 (50%)	3 (33%)
Mean (SD)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.5 (1)	0.3 (1)
Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.0
Min, Max	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 1.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 1.0	0.0, 1.0
csDMARDs, concomitantly	0 (0%)	0 (0%)	0 (0%)	2 (10%)	0 (0%)	0 (0%)	0 (0%)	2 (33%)	2 (22%)
Abatacept	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Adalimumab[b]	0 (0%)	0 (0%)	0 (0%)	3 (14%)	0 (0%)	0 (0%)	0 (0%)	3 (50%)	3 (33%)
Anakinra	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Certolizumab pegol[b]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Etanercept[b]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Golimumab[b]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Infliximab[b]	0 (0%)	0 (0%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Rituximab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

	Unmatched				Matched				
Characteristic[a]	Baricitinib (N = 3)	4 mg (N = 3)	2 mg (N = 0)	TNFi (N = 21)	Baricitinib (N = 3)	4 mg (N = 3)	2 mg (N = 0)	TNFi (N = 6)	Total (N = 9)
Sarilumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Tocilizumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Post-index Medication[c]									
Methotrexate, concomitant	1 (33%)	1 (33%)	0 (0%)	9 (43%)	1 (33%)	1 (33%)	0 (0%)	3 (50%)	4 (44%)
Other Concomitant csDMARD	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Dose change, baricitinib	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; BKK = Betriebskrankenkasse; csDMARD = conventional synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; US = United States; VTE = venous thromboembolism.

[a] All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

[b] TNF inhibitors.

[c] Only baricitinib 2 mg dose is available in the US, so the baricitinib cells should be marked ‘NA’ as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\BKK\Lilly Baricitinib Results_VTE_BKK_v1.0.docx -pages 16-17

Table 41_SNDS Pattern of RA Medication Use in Patients with VTE, Primary Definition [SNDS]

Characteristics[b]	Unmatched				Matched				
	Baricitinib n = 23	BARI 4 mg n = 16	BARI 2 mg n ≤10	TNFi n = 29	Baricitinib n = 20	BARI 4 mg n = 14	BARI 2 mg n ≤10	TNFi n = 13	Total n = 33
Baseline Medication, n (%)			-						
cDMARDs, during baseline period									
n, total (%)	15 (65.2)	12 (75.0)		20 (69.0)	14 (70.0)	11 (78.6)		≤10	22 (66.7)
Mean (SD)	0.7 (0.6)	0.8 (0.4)		0.8 (0.6)	0.8 (0.6)	0.8 (0.4)		0.6 (0.5)	0.7 (0.5)
Median	1.0	1.0		1.0	1.0	1.0		1.0	1.0
Min, Max	0.0, 2.0	0.0, 1.0		0.0, 2.0	0.0, 2.0	0.0, 1.0		0.0, 1.0	0.0, 2.0
>1_cDMARD concomitantly	≤10	0 (0.0)		0 (0.0)	≤10	0 (0.0)		0 (0.0)	≤10
Hydroxychloroquine	≤10	≤10		≤10	≤10	≤10		0 (0.0)	≤10
Chloroquine	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Azathioprine	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Leflunomide	0 (0.0)	0 (0.0)		≤10	0 (0.0)	0 (0.0)		≤10	≤10
Methotrexate	13(56.5)	≤10		11 (37.9)	12 (60.0)	≤10		≤10	17 (51.5)
Mycophenolate mofetil	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Sulfasalazine	≤10	≤10		≤10	≤10	≤10		≤10	≤10
Cyclosporin	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Penicillamine	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
bDMARDs, during baseline period									
n, total (%)	14 (60.9)	11 (68.8)		≤10	11 (55.0)	≤10		≤10	17 (51.5)
Mean (SD)	0.7 (0.6)	0.8 (0.6)		0.3 (0.5)	0.6 (0.6)	0.7 (0.6)		0.5 (0.5)	0.5 (0.6)
Median	1.0	1.0		0.0	1.0	1.0		0.0	1.0
Min, Max	0.0, 2.0	0.0, 2.0		0.0, 1.0	0.0, 2.0	0.0, 2.0		0.0, 1.0	0.0, 2.0
cDMARDs, concomitant	≤10	≤10		≤10	≤10	≤10		≤10	≤10
Adalimumab[c]	≤10	≤10		≤10	≤10	≤10		≤10	≤10
Certolizumab pegol[c]	≤10	≤10		0 (0.0)	≤10	≤10		0 (0.0)	≤10
Etanercept[c]	≤10	≤10		≤10	≤10	≤10		≤10	≤10
Golimumab[c]	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)

Characteristics[b]	Unmatched				Matched				
	Baricitinib n = 23	BARI 4 mg n = 16	BARI 2 mg n ≤10	TNFi n = 29	Baricitinib n = 20	BARI 4 mg n = 14	BARI 2 mg n ≤10	TNFi n = 13	Total n = 33
Infliximab[c]	≤10	≤10		≤10	≤10	≤10		≤10	≤10
Rituximab	≤10	≤10		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Sarilumab	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Abatacept	≤10	≤10		≤10	≤10	≤10		≤10	≤10
Tocilizumab	≤10	≤10		0 (0.0)	≤10	≤10		0 (0.0)	≤10
Anakinra	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
TNFi naïve at baseline	16 (69.6)	≤10		24 (82.8)	14 (70.0)	≤10		≤10	24 (72.7)
Post-index Medication, n (%)									
Methotrexate, concomitant	≤10	≤10		12 (41.4)	≤10	≤10		≤10	13(39.4)
Other concomitant cDMARD	0 (0.0)	0 (0.0)		≤10	0 (0.0)	0 (0.0)		≤10	≤10
Dose change, baricitinib	≤10	≤10		NA	≤10	≤10		0 (0.0)	≤10

Abbreviations: BARI = baricitinib; bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; SNDS = Système National des Données de Santé; TNF = tumour necrosis factor; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Matching ratio 1:1 is applied.

[b] All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

[c] TNF inhibitors.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\french snds_SNDS\BARICITINIB_RAS_SNDS_2019_Match_1_1_Point VII_V1.0 20220228.docx - page 177-179

Table 42_PS20 Time to First VTE Event (Days), Primary Definition [PS20]

Time	Unmatched		Matched		
	Baricitinib[a,b] (N = 933)	TNFi (N = 3953)	Baricitinib[a,b] (N = 748)	TNFi (N = 748)	Total (N = 1496)
Mean (SD)	130.00 (157.42)	136.39 (144.32)	130.00 (157.42)	69.75 (37.96)	105.90 (123.35)
Median	57.00 [16.25, 274.75]	91.00 [68.25, 189.25]	57.00 [16.25, 274.75]	86.50 [31.25, 91.50]	76.00 [16.75, 127.50]
Min, Max	11.0, 406.0	3.0, 596.0	11.0, 406.0	13.0, 93.0	11.0, 406.0

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; PS20 = HealthVerity Private Source 20; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; US = United States; VTE = venous thromboembolism.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

[b] Only the baricitinib 2-mg dose is available in the US.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.42. Time to First Event Outcome (days) - VTE, Primary Definition [HV].docx

Table 42_ARTIS Time to First VTE Event (Days), Primary Definition [ARTIS]

Time	Unmatched		Matched	
	Baricitinib[a] (N = 1737)	TNFi (N = 6230)	Baricitinib[a] (N = 1685)	TNFi (N = 1685)
Mean (SD)	502 (346.6)	577 (418.9)	502 (345.7)	565 (423.5)
Median	456	482.5	454	454
Min, Max	1, 1310	3, 1460	1, 1310	9, 1458

Abbreviations: ARTIS = Anti-Rheumatic Therapy in Sweden; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\ Table6_time_to_outcome_08MAR22.xlsx

Table 42_BKK Time to First VTE Event (Days), Primary Definition [BKK]

Time	Unmatched				Matched				
	Baricitinib (N = 3)	4 mg (N = 3)	2 mg (N = 0)	TNFi (N = 21)	Baricitinib[a] (N = 3)	4 mg (N = 3)	2 mg (N = 0)	TNFi (N = 6)	Total (N = 9)
n	3	3	0	21	3	3	0	6	9
Mean (SD)	249.3 (215)	249.3 (215)	0.0 (0)	137.1 (141)	249.3 (215)	249.3 (215)	0.0 (0)	180.2 (171)	203.2 (176)
Median	272.0	272.0	0.0	88.0	272.0	272.0	0.0	120.5	124.0
Min, Max	24.0, 452.0	24.0, 452.0	0.0, 0.0	5.0, 518.0	24.0, 452.0	24.0, 452.0	0.0, 0.0	55.0, 518.0	24.0, 518.0

Abbreviations: BKK = Betriebskrankenkasse; Max = maximum; Min = minimum; N = number of patients in specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\BKK\Lilly Baricitinib Results_VTE_BKK_v1.0.docx -page 18

Table 42_SNDS Time to First VTE Event (Days), Primary Definition [SNDS]

	Unmatched			Matched			
	Baricitinib[b] n = 23	BARI 4 mg n = 16	TNFi n = 29	Baricitinib n = 20	BARI 4 mg n = 14	TNFi[a] n = 13	Total n = 33
Time to first VTE (days)							
N (missing)	23 (0)	16 (0)	29 (0)	20 (0)	14 (0)	13 (0)	33 (0)
Mean (SD)	239.9 (179.7)	261.6 (200.9)	197.7 (175.0)	227.0 (165.4)	245.1 (181.1)	181.4 (156.3)	209.0 (161.0)
Median	209.0	183.5	144.0	204.0	183.5	113.0	168.0
Min, Max	17.0, 650.0	75.0, 650.0	26.0, 624.0	17.0, 632.0	75.0, 632.0	28.0, 555.0	17.0, 632.0

Abbreviations: BARI = baricitinib; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; SNDS = Système National des Données de Santé; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Matching ratio 1:1 is applied.

[b] Only 4 mg details reported due to ≤10 patients in 2 mg for all categories.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\french snds_SNDS\BARICITINIB_RAS_SNDS_2019_Match_1_1_Point VII_V1.0 20220228.docx - page 180

10.4.2. MACE

Clinical characteristics and use of RA medications of patients with MACE were generally consistent with the overall cohort of RA patients (as described in Section 10.2). One exception was age. The mean age of patients with a MACE treated with baricitinib appeared higher than the overall age of the baricitinib cohort in MACE analyses, although sample sizes are low and no statistical comparison was made:

- PS20: The mean age of patients with MACE who were treated with baricitinib (n = 2) was 74.5 years (Table 51_PS20), whereas the overall mean age was 55 years (Table 3_PS20).
- ARTIS: The mean age of patients with MACE who were treated with baricitinib (n = 13) was 68 years (Table 51_ARTIS), whereas the overall mean age was 59 (Table 3_ARTIS).
- BKK: The mean age of patients with MACE who were treated with baricitinib (n = 8) was 61 years (Table 51_BKK), whereas the mean age of the overall cohort was 56 years (Table 3_BKK).
- SNDS: The mean age of patients with MACE who were treated with baricitinib (n = 25) was 67.5 years (Table 51_SNDS), whereas the mean age of the overall cohort was 58 years (Table 3_SNDS).

In PS20, both of the 2 patients with a MACE were female and had a record of atrial fibrillation, diabetes, and hypertension during baseline. In BKK, 6 of the 8 patients with MACE that were treated with baricitinib also had hypertension. Outside of those observations, clinical conditions at baseline and use of RA medications were as expected for the patient population.

The distribution of time to MACE is variable. ARTIS and SNDS are the 2 data sources with the greatest overall cohort sample sizes, and thus had the most observed number of patients treated with baricitinib with a MACE (n = 13 and 25, respectively). For the 13 baricitinib treated patients with a MACE in ARTIS, the mean (median) time to event was 503 (454) days. For the 25 patients within SNDS, the mean (median) time to event was 215.8 (171) days. The increased time to onset seen in ARTIS compared to SNDS patients occurs with a corresponding increase in the exposure time.

Table 51_PS20 Clinical Characteristics of RA Patients with MACE [PS20]

Characteristic[a,b]	Baricitinib[c] (N = 2)	TNFi (N = 4)	Total (N = 6)
Age (mean) [SD]	74.50 (24.75)	57.00 (13.09)	62.83 (17.52)
Sex			
Female	2 (100.0%)	4 (100.0%)	6 (100.0%)
Male	0 (0.0%)	0 (0.0%)	0 (0.0%)
Clinical Conditions during baseline			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic lung disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	2 (100.0%)	0 (0.0%)	2 (33.3%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	2 (50.0%)	2 (33.3%)
Ischemic heart disease	0 (0.0%)	2 (50.0%)	2 (33.3%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	2 (100.0%)	2 (50.0%)	4 (66.7%)
Type I	0 (0.0%)	1 (25.0%)	1 (16.7%)
Type II	2 (100.0%)	2 (50.0%)	4 (66.7%)
Dyslipidaemia	1 (50.0%)	3 (75.0%)	4 (66.7%)
Hypertension	2 (100.0%)	3 (75.0%)	5 (83.3%)
Immune disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Primary Sjögren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Disorder	1 (50.0%)	0 (0.0%)	1 (16.7%)
Obesity	0 (0.0%)	1 (25.0%)	1 (16.7%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	3.05 (3.12)	3.64 (1.38)	3.44 (1.78)
Smoking	0 (0.0%)	1 (25.0%)	1 (16.7%)
Surgery, Trauma, & Hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medications			
Antibiotics	1 (50.0%)	3 (75.0%)	4 (66.7%)
Antidiabetic agents	0 (0.0%)	1 (25.0%)	1 (16.7%)
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-insulins	0 (0.0%)	1 (25.0%)	1 (16.7%)
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			
Anticoagulant	2 (100.0%)	0 (0.0%)	2 (33.3%)
Antihypertensives	2 (100.0%)	3 (75.0%)	5 (83.3%)
Antiplatelet	0 (0.0%)	1 (25.0%)	1 (16.7%)
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			

Oral contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERM	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	1 (25.0%)	1 (16.7%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	1 (50.0%)	1 (25.0%)	2 (33.3%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucocorticosteroid	2 (100.0%)	2 (50.0%)	4 (66.7%)
Vaccinations	0 (0.0%)	1 (25.0%)	1 (16.7%)
Post-index Occurrence[d]			
Methotrexate, concomitant	0 (0.0%)	1 (25.0%)	1 (16.7%)

Abbreviations: AIDS = acquired immune deficiency syndrome; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus;: HRT = hormone replacement therapy; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; PS20 = HealthVerity Private Source 20; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective oestrogen receptor modifier; SLE = systemic lupus erythematosus; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

[b] Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 (see Section 8.3.3, Annex 19) for each outcome (e.g., hospitalized congestive heart failure) for VTE. Other factors that are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias (e.g., Type I diabetes) for VTE.

[c] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

[d] Events in this category must have occurred in the 7 days immediately prior to MACE.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.51. - Clinical Characteristics of RA Patients with MACE [HealthVerity, PS20]_.docx

Table 51_ARTIS Clinical Characteristics of RA Patients with MACE [ARTIS]

Characteristic[a,b]	Baricitinib[c] (N = 13)	TNFi (N = 16)	Total (N = 29)
Age (mean) [SD]	68 (11.1)	68 (7.6)	68 (9.1)
Sex			
Female	12 (92%)	13 (81%)	25 (86%)
Male	<5	<5	<5
Clinical Conditions during baseline			
Cancer	<5	<5	<5
NMSC	<5	<5	<5
Chronic Lung disease			
Disease	<5	<5	<5

Characteristic[a,b]	Baricitinib[c] (N = 13)	TNFi (N = 16)	Total (N = 29)
Cardiovascular conditions			
Atrial arrhythmia	<5	<5	<5
Cardiovascular revascularization	<5	<5	<5
Congestive heart failure	<5	<5	<5
Coronary artery disease	<5	<5	<5
Ischemic heart disease	<5	<5	<5
Unstable angina	<5	<5	<5
Ventricular arrhythmia	<5	<5	<5
Diabetes Mellitus	5 (38%)	<5	8 (28%)
Type I	NA	NA	NA
Type II	NA	NA	NA
Dyslipidaemia	<5	<5	<5
Hypertension	<5	<5	<5
Immune disorders			
AIDS/HIV	NA	NA	NA
Antiphospholipid syndrome	NA	NA	NA
SLE	NA	NA	NA
Primary Sjögren Syndrome	<5	<5	<5
Liver Disorder	<5	<5	<5
Obesity	NA	NA	NA
Pregnancy	<5	<5	<5
RA Severity (DAS28), mean (SD)	4.0 (1.18)	4.6 (1.21)	4.5 (1.18)
Smoking	6 (67%)	9 (82%)	15 (75%)
Surgery	9 (69%)	13 (81%)	22 (76%)
TIA	<5	<5	<5
Other Prescription Medication			
Antibiotics	6 (46%)	<5	8 (28%)
Antidiabetic agents	5 (38%)	<5	8 (28%)
Insulins	<5	<5	<5
Non-insulins	<5	<5	6 (21%)
Aspirin	<5	<5	6 (21%)
Cardiovascular			
Anticoagulant	<5	<5	<5
Antihypertensives	8 (62%)	11 (69%)	19 (66%)
Antiplatelet	<5	<5	6 (21%)
Nitrates	<5	<5	<5
Hormonal			
HRT	<5	<5	<5
Oral contraceptives	<5	<5	<5
SERM	<5	<5	<5
Lipid-lowering agents			
Bile acid binding	<5	<5	<5
Cholesterol absorption inhibitor	<5	<5	<5
Fibrates	<5	<5	<5
Niacin	NA	NA	NA
Omega-3 fatty acids	NA	NA	NA
Statins	5 (38%)	6 (38%)	11 (38%)

Characteristic[a,b]	Baricitinib[c] (N = 13)	TNFi (N = 16)	Total (N = 29)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	<5	<5	<5
Glucocorticosteroid	12 (92%)	13 (81%)	25 (86%)
Vaccinations	NA	NA	NA

Abbreviations: AIDS = acquired immunodeficiency syndrome; DAS28 = Disease Activity Score 28; HIV = human immunodeficiency syndrome; HRT = hormone replacement therapy; N = number of patients in the analysis population; NA = not applicable; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective oestrogen receptor modifier; SLE = systemic lupus erythematosus; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort. Clinical conditions are defined based on main diagnosis codes in the Swedish National Patient Register.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 (see Section 8.3.3, Annex 19) for each outcome (eg, hospitalized congestive heart failure) for VTE. Other factors are included for descriptive purposes only and may not be balanced across treatment groups but do not contribute to confounding bias (eg, Type I diabetes) for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\Table5_clinical_outcome_16May22_update.xlsx

Table 51_BKK Clinical Characteristics of RA Patients with MACE [BKK]

Characterstic[a,b]	Baricitinib (N = 8)	4 mg (N = 5)	2 mg (N = 3)	TNFi (N = 4)	Total (N = 12)
Age (mean) [SD]	61.0 (18)	56.4 (19)	68.7 (17)	62.0 (8)	61.3 (15)
Sex					
Female	4 (50%)	3 (60%)	1 (33%)	3 (75%)	7 (58%)
Male	4 (50%)	2 (40%)	2 (67%)	1 (25%)	5 (42%)
Clinical Conditions during baseline					
Cancer	2 (25%)	2 (40%)	0 (0%)	1 (25%)	3 (25%)
NMSC	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Chronic Lung disease	3 (38%)	2 (40%)	1 (33%)	0 (0%)	3 (25%)
Cardiovascular conditions	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Atrial arrhythmia/ fibrillation	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cardiovascular revascularization	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Characterstic[a,b]	Baricitinib (N = 8)	4 mg (N = 5)	2 mg (N = 3)	TNFi (N = 4)	Total (N = 12)
Congestive Heart Failure, Hospitalized	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Coronary artery disease	2 (25%)	2 (40%)	0 (0%)	1 (25%)	3 (25%)
Ischemic heart disease	2 (25%)	2 (40%)	0 (0%)	1 (25%)	3 (25%)
Unstable angina	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Ventricular arrhythmia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Diabetes Mellitus	2 (25%)	0 (0%)	2 (67%)	2 (50%)	4 (33%)
Type I	0 (0%)	0 (0%)	0 (0%)	1 (25%)	1 (8%)
Type II	2 (25%)	0 (0%)	2 (67%)	2 (50%)	4 (33%)
Dyslipidaemia	3 (38%)	3 (60%)	0 (0%)	2 (50%)	5 (42%)
Hypertension	6 (75%)	3 (60%)	3 (100%)	3 (75%)	9 (75%)
Immune disorders	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
AIDS/HIV	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Antiphospholipid syndrome	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SLE	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Primary Sjögren Syndrome	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Liver Disorder	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Obesity	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pregnancy	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
RA Severity (CIRAS), mean (SD)	5.7 (2)	6.1 (2)	5.1 (3)	7.0 (1)	6.1 (2)
Smoking	2 (25%)	1 (20%)	1 (33%)	1 (25%)	3 (25%)
Surgery, trauma, & hospitalization, recent	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
TIA	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Genetic Coagulopathies	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Other Prescription Medications					
Antibiotics	2 (25%)	1 (20%)	1 (33%)	1 (25%)	3 (25%)
Antidiabetic agents	0 (0%)	0 (0%)	0 (0%)	2 (50%)	2 (17%)
Insulins	0 (0%)	0 (0%)	0 (0%)	1 (25%)	1 (8%)
Non-insulins	0 (0%)	0 (0%)	0 (0%)	1 (25%)	1 (8%)
Aspirin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cardiovascular					
Anticoagulant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Antihypertensives	4 (50%)	2 (40%)	2 (67%)	3 (75%)	7 (58%)

Characterstic[a,b]	Baricitinib (N = 8)	4 mg (N = 5)	2 mg (N = 3)	TNFi (N = 4)	Total (N = 12)
Antiplatelet	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Nitrates	1 (13%)	0 (0%)	1 (33%)	0 (0%)	1 (8%)
Hormonal					
Oral contraceptives	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
HRT	1 (13%)	1 (20%)	0 (0%)	0 (0%)	1 (8%)
SERM	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Lipid-lowering agents					
Bile acid binding	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cholesterol absorption inhibitor	1 (13%)	1 (20%)	0 (0%)	0 (0%)	1 (8%)
Fibrates	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Niacin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Omega-3 fatty acids	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Statins	1 (13%)	1 (20%)	0 (0%)	0 (0%)	1 (8%)
Rheumatoid arthritis-related					
Cox-2 Inhibitor	1 (13%)	1 (20%)	0 (0%)	2 (50%)	3 (25%)
Glucocorticosteroid	7 (88%)	4 (80%)	3 (100%)	3 (75%)	10 (83%)
Vaccinations	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Post-index Occurrence[c]					
Methotrexate, concomitant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drug; BKK = Betriebskrankenkasse; CIRAS = claims-based index for RA severity; csDMARD = conventional synthetic disease-modifying antirheumatic drug; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; N = number of patients in the analysis population; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective oestrogen receptor modifier; SLE = systemic lupus erythematosus; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] All conditions and characteristics except for use of bDMARD and concomitant csDMARD are measured during the 6 months prior to initiation of study medication until and including the index date.

[b] Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 (see Section 8.3.3, Annex 19) for each outcome (eg, hospitalized congestive heart failure) for VTE. Other factors are included for descriptive purposes only and may not be balanced across treatment groups but do not contribute to confounding bias (eg, Type I diabetes) for VTE.

[c] Events in this category must have occurred in the 7 days immediately prior to MACE.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\BKK\Lilly Baricitinib Results_MACE_BKK_v1.0.docx -pages 9-10

Table 51_SNDS Clinical Characteristics of RA Patients with MACE [SNDS]

Characteristics[a]	Baricitinib Any N = 25	Baricitinib 4 mg N = 16	Baricitinib 2 mg N ≤10	TNFi[b] N = 11	Total N = 36
Age [in years]			-		
n (missing)	25 (0)	16 (0)		11 (0)	36 (0)
Mean (SD)	67.5 (8.6)	64.1 (5.8)		69.2 (11.8)	68.0 (9.5)
Median	65.0	64.0		66.0	65.5
Min, Max	48.0, 80.0	55.0, 79.0		52.0, 92.0	48.0, 92.0
Sex, n (%)					
Female	≤10	≤10		≤10	14 (38.9)
Male	16 (64.0)	11(68.8)		≤10	22(61.1)
Clinical conditions during baseline period, n (%)			-		
Cancer, excluding NMSC	≤10	≤10		0 (0.0)	≤10
NMSC	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Chronic lung disease, excluding cystic fibrosis[c]	≤10	≤10		≤10	≤10
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	0 (0.0)	0 (0.0)		≤10	≤10
Cardiovascular revascularization	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Congestive Heart Failure, hospitalized	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Coronary artery disease	≤10	≤10		≤10	≤10
Unstable angina	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Ventricular arrhythmia	≤10	≤10		0 (0.0)	≤10
Stroke	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Haemorrhagic	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Ischemic	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Unknown	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
TIA	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Diabetes Mellitus[c]	≤10	≤10		≤10	≤10
Treated insulin dependent	NA	NA		NA	NA
Treated non-insulin dependent	NA	NA		NA	NA
Dyslipidaemia (not available in SNDS)	NA	NA		NA	NA
Hypertension (not available in SNDS)	NA	NA		NA	NA
History of hypertension	NA	NA		NA	NA
Current hypertension	NA	NA		NA	NA
Immune disorders	≤10	0 (0.0)		≤10	≤10
AIDS/HIV	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Antiphospholipid syndrome	NA	NA		NA	NA
SLE	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Primary Sjogren Syndrome	≤10	0 (0.0)		≤10	≤10
Liver or pancreatic disorder[d]	≤10	≤10		0 (0.0)	≤10
Obesity (not available in SNDS)	NA	NA		NA	NA
Recent pregnancy	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
RA Severity (CIRAS Index)					
Mean (SD)	5.7 (0.9)	5.8 (0.8)		6.5 (1.8)	5.9 (1.3)
Smoking (not available in SNDS)	NA	NA		NA	NA

Characteristics[a]	Baricitinib Any N = 25	Baricitinib 4 mg N = 16	Baricitinib 2 mg N ≤10	TNFi[b] N = 11	Total N = 36
Surgery or trauma	≤10	≤10		0 (0.0)	≤10
Other prescription medications during baseline period, n (%)			-		
Antibiotics	11 (44.0)	≤10		≤10	18 (50.0)
Antidiabetic agents	≤10	≤10		≤10	≤10
Insulins	≤10	≤10		≤10	≤10
Non-insulins	≤10	≤10		≤10	≤10
Cardiovascular					
Antithrombotic agents	≤10	≤10		≤10	12 (33.3)
Anticoagulant	≤10	0 (0.0)		≤10	≤10
Antiplatelet	≤10	≤10		≤10	≤10
Antihypertensives	16 (64.0)	≤10		≤10	22 (61.1)
Angiotensin converting enzyme inhibitors (ACE)	≤10	≤10		≤10	≤10
Angiotensin receptor blockers (ARB)	≤10	≤10		≤10	≤10
Beta blocker	≤10	≤10		≤10	11 (30.6)
Calcium channel blocker	≤10	≤10		≤10	≤10
Nitrates	≤10	≤10		0 (0.0)	≤10
Acyclovir	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Valacyclovir	≤10	0 (0.0)		0 (0.0)	≤10
Hormonal	≤10	≤10		≤10	≤10
HRT	≤10	≤10		≤10	≤10
Oral Contraceptives	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
SERMs	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Topic with progestogens and/or oestrogens	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Lipid-lowering agents	≤10	≤10		≤10	≤10
HMG CoA reductase inhibitors	≤10	≤10		≤10	≤10
Fibrates	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Bile acid sequestrants	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Other lipid modifying agents	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Lipid modifying agents, combinations	≤10	≤10		0 (0.0)	≤10
Rheumatoid arthritis-related					
Aspirin	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Cox-2 Inhibitor	≤10	≤10		≤10	≤10
NSAIDs	≤10	≤10		≤10	≤10
Glucocorticosteroid	18(72.0)	12(75.0)		11 (100.0)	29(80.6)
Vaccines	≤10	≤10		≤10	15(41.7)
Antineoplastic agents	≤10	0 (0.0)		0 (0.0)	≤10
Post-index Occurrence[d], n (%)					
Cancer	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Hospitalization	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Surgery	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)

Abbreviations: AIDS = acquired immunodeficiency syndrome; CIRAS = claims-based index for RA severity;HIV = human immunodeficiency virus; HMG CoA reductase = statin; HRT = hormone replacement therapy; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the analysis population; n = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective oestrogen receptor modifier; SNDS = Système National des Données de Santé; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort, index date excluded.

[b] Matching ratio 1:1 is applied.

[c] CNAM algorithm based on the year preceding the year of inclusion.

[d] Events in this category must have occurred in the 7 days immediately prior to MACE.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\french snds_SNDS\BARICITINIB_RAS_SNDS_2019_Match_1_1_Point VII_V1.0 20220228.docx - pages 187-191

Table 52_PS20 Pattern of RA Medication Use in Patients with MACE [PS20]

Characteristic[a]	Unmatched		Matched		
	Baricitinib[b] (N = 4)	TNFi (N = 10)	Baricitinib[b] (N = 2)	TNFi (N = 4)	Total (N = 6)
Baseline Medication					
cDMARDs, during baseline					
n, total	3 (75.0%)	7 (70.0%)	1 (50.0%)	3 (75.0%)	4 (66.7%)
Mean (SD)	1.00 (0.82)	0.80 (0.42)	0.50 (0.71)	0.75 (0.50)	0.67 (0.52)
Median	1.00 [0.25, 1.75]	1.00 [0.75, 1.00]	0.50 [0.00, 1.00]	1.00 [0.25, 1.00]	1.00 [0.00, 1.00]
Min, Max	0.0, 2.0	0.0, 1.0	0.0, 1.0	0.0, 1.0	0.0, 1.0
>1 cDMARD concomitantly	1 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hydroxychloroquine	1 (25.0%)	1 (10.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Leflunomide	1 (25.0%)	0 (0.0%)	1 (50.0%)	0 (0.0%)	1 (16.7%)
Methotrexate	2 (50.0%)	6 (60.0%)	0 (0.0%)	3 (75.0%)	3 (50.0%)
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
bDMARDs, during baseline					
n, total	2 (50.0%)	9 (90.0%)	0 (0.0%)	3 (75.0%)	3 (50.0%)
Mean (SD)	0.50 (0.58)	1.10 (0.32)	0.00 (0.00)	1.25 (0.50)	0.83 (0.75)
Median	0.50 [0.00, 1.00]	1.00 [1.00, 1.00]	0.00 [0.00, 0.00]	1.00 [1.00, 1.75]	1.00 [0.00, 1.25]
Min, Max	0.0, 1.0	0.0, 2.0	0.0, 0.0	1.0, 2.0	0.0, 2.0
cDMARDs, concomitant	2 (50.0%)	8 (80.0%)	0 (0.0%)	3 (75.0%)	3 (50.0%)
Abatacept	1 (25.0%)	1 (10.0%)	0 (0.0%)	1 (25.0%)	1 (16.7%)
Adalimumab[c]	0 (0.0%)	5 (50.0%)	0 (0.0%)	2 (50.0%)	2 (33.3%)
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Etanercept[c]	0 (0.0%)	4 (40.0%)	0 (0.0%)	1 (25.0%)	1 (16.7%)
Golimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infliximab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Medication[d]					
Methotrexate, concomitant	2 (50.0%)	4 (40.0%)	0 (0.0%)	2 (50.0%)	2 (33.3%)
Other Concomitant cDMARD	2 (50.0%)	1 (10.0%)	1 (50.0%)	0 (0.0%)	1 (16.7%)
Dose change, baricitinib	NA[d]	0 (0.0%)	NA[d]	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; PS20 = Private Source 20; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

[a] All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

[b] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

[c] TNFi.

[d] Only the baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked “NA” as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.52. - Pattern of RA Medication Use in Patients with MACE [HV].docx

Table 52_BKK Pattern of RA Medication Use in Patients with MACE [BKK]

Characteristic[a]	Unmatched				Matched				
	Baricitinib (N = 8)	4 mg (N = 5)	2 mg (N = 3)	TNFi (N = 12)	Baricitinib (N = 8)	4 mg (N = 5)	2 mg (N = 3)	TNFi (N = 4)	Total (N = 12)
Baseline Medication									
csDMARDs, during baseline									
n, total	5 (63%)	4 (80%)	1 (33%)	8 (67%)	5 (63%)	4 (80%)	1 (33%)	4 (100%)	9 (75%)
Mean (SD)	0.9 (1)	1.0 (1)	0.7 (1)	0.9 (1)	0.9 (1)	1 (1)	0.7 (1)	1.3 (1)	1 (1)
Median	1.0	1.0	0.0	1.0	1.0	1.0	0.0	1.0	1.0
Min, Max	0.0, 2.0	0.0, 2.0	0.0, 2.0	0.0, 3.0	0.0, 2.0	0.0, 2.0	0.0, 2.0	1.0, 2.0	0.0, 2.0
>1 csDMARD concomitantly	0 (0%)	0 (0%)	0 (0%)	2 (17%)	0 (0%)	0 (0%)	0 (0%)	1 (25%)	1 (8%)
Hydroxychloroquine	0 (0%)	0 (0%)	0 (0%)	1 (8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Leflunomide	2 (25%)	1 (20%)	1 (33%)	2 (17%)	2 (25%)	1 (20%)	1 (33%)	1 (25%)	3 (25%)
Methotrexate	5 (63%)	4 (80%)	1 (33%)	7 (58%)	5 (63%)	4 (80%)	1 (33%)	4 (100%)	9 (75%)
Minocycline	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Sulfasalazine	0 (0%)	0 (0%)	0 (0%)	1 (8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
bDMARDs, during baseline									
n, total	2 (25%)	2 (40%)	0 (0%)	2 (17%)	2 (25%)	2 (40%)	0 (0%)	2 (50%)	4 (33%)
Mean (SD)	0.3 (0)	0.4 (1)	0 (0)	0.2 (0)	0.3 (0)	0.4 (1)	0 (0)	0.5 (1)	0.3 (0)
Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.0
Min, Max	0.0, 1.0	0.0, 1.0	0.0, 0.0	0.0, 1.0	0.0, 1.0	0.0, 1.0	0.0, 0.0	0.0, 1.0	0.0, 1.0
csDMARDs, concomitantly	2 (25%)	2 (40%)	0 (0%)	0 (0%)	2 (25%)	2 (40%)	0 (0%)	0 (0%)	2 (17%)
Abatacept	0 (0%)	0 (0%)	0 (0%)	1 (8%)	0 (0%)	0 (0%)	0 (0%)	1 (25%)	1 (8%)
Adalimumab[b]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Anakinra	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Certolizumab pegol[b]	1 (13%)	1 (20%)	0 (0%)	0 (0%)	1 (13%)	1 (20%)	0 (0%)	0 (0%)	1 (8%)
Etanercept[b]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Golimumab[b]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Infliximab[b]	0 (0%)	0 (0%)	0 (0%)	1 (8%)	0 (0%)	0 (0%)	0 (0%)	1 (25%)	1 (8%)

Characteristic[a]	Unmatched				Matched				
	Baricitinib (N = 8)	4 mg (N = 5)	2 mg (N = 3)	TNFi (N = 12)	Baricitinib (N = 8)	4 mg (N = 5)	2 mg (N = 3)	TNFi (N = 4)	Total (N = 12)
Rituximab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Sarilumab	1 (13%)	1 (20%)	0 (0%)	0 (0%)	1 (13%)	1 (20%)	0 (0%)	0 (0%)	1 (8%)
Tocilizumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Post-index Medication									
Concomitant Methotrexate	2 (25%)	2 (40%)	0 (0%)	5 (42%)	2 (25%)	2 (40%)	0 (0%)	2 (50%)	4 (33%)
Other Concomitant csDMARD	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Dose change, baricitinib[c]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; BKK = Betriebskrankenkasse; csDMARD = conventional synthetic disease-modifying antirheumatic drug; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the analysis population; n = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor

[a] All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

[b] TNFi.

[c] Only the baricitinib 2-mg dose is available in the US, so the baricitinib dose change should be marked 'NA' in US data.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\BKK\Lilly Baricitinib Results_MACE_BKK_v1.0.docx -pages 11-12

Table 52_SNDS Pattern of RA Medication Use in Patients with MACE [SNDS]

Characteristics[b]	Unmatched				Matched[a]				
	Baricitinib N = 28	BARI 4 mg N = 19	BARI 2 mg N ≤10	TNFi N = 34	Baricitinib N = 25	BARI 4 mg N = 16	BARI 2 mg N ≤10	TNFi N = 11	Total N = 36
Baseline Medication, n (%)									
cDMARDs, during baseline period									
n, total (%)	17 (60.7)	11 (57.9)		25 (73.5)	14(56.0)	≤10		≤10	21 (58.3)
Mean (SD)	0.6 (0.6)	0.6 (0.5)		0.8 (0.5)	0.6 (0.6)	0.5 (0.5)		0.7 (0.6)	0.6 (0.6)
Median	1.0	1.0		1.0	1.0	0.5		1.0	1.0
Min, Max	0.0, 2.0	0.0, 1.0		0.0, 2.0	0.0, 2.0	0.0, 1.0		0.0, 2.0	0.0, 2.0
>1 cDMARD concomitantly	≤10	0 (0.0)		≤10	≤10	0 (0.0)		0 (0.0)	≤10
Hydroxychloroquine	≤10	≤10		≤10	≤10	≤10		0 (0.0)	≤10
Chloroquine	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Azathioprine	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Leflunomide	≤10	≤10		≤10	≤10	≤10		≤10	≤10
Methotrexate	≤10	≤10		23 (67.6)	≤10	≤10		≤10	15 (41.7)
Mycophenolate mofetil	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Sulfasalazine	≤10	≤10		0 (0.0)	≤10	≤10		0 (0.0)	≤10
Cyclosporin	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Penicillamine	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.)		0 (0.)	0 (0.0)
bDMARDs, during baseline period									
n, total (%)	19 (67.9)	14 (73.7)		≤10	16 (64.0)	11 (68.8)		≤10	21 (58.3)
Mean (SD)	0.8 (0.6)	0.9 (0.7)		0.2 (0.4)	0.6 (0.5)	0.7 (0.5)		0.5 (0.5)	0.6 (0.5)
Median	1.0	1.0		0.0	1.0	1.0		0.0	1.0
Min, Max	0.0, 2.0	0.0, 2.0		0.0, 1.0	0.0, 1.0	0.0, 1.0		0.0, 1.0	0.0, 1.0

Characteristics[b]	Unmatched				Matched[a]				
	Baricitinib N = 28	BARI 4 mg N = 19	BARI 2 mg N ≤10	TNFi N = 34	Baricitinib N = 25	BARI 4 mg N = 16	BARI 2 mg N ≤10	TNFi N = 11	Total N = 36
cDMARDs, concomitant	11 (39.3)	≤10		≤10	≤10	≤10		≤10	11 (30.6)
Adalimumab[c]	≤10	≤10		≤10	≤10	≤10		≤10	≤10
Certolizumab pegol[c]	≤10	≤10		0 (0.0)	≤10	≤10		0 (0.0)	≤10
Etanercept[c]	≤10	≤10		≤10	≤10	≤10		≤10	≤10
Golimumab[c]	≤10	0 (0.0)		0 (0.0)	≤10	0 (0.0)		0 (0.0)	≤10
Infliximab[c]	≤10	≤10		0 (0.0)	≤10	≤10		0 (0.0)	≤10
Rituximab	≤10	≤10		0 (0.0)	≤10	≤10		0 (0.0)	≤10
Sarilumab	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Abatacept	≤10	≤10		≤10	≤10	≤10		≤10	≤10
Tocilizumab	≤10	≤10		≤10	≤10	≤10		≤10	≤10
Anakinra	≤10	0 (0.)		0 (0.0)	≤10	0 (0.0)		0 (0.0)	≤10
TNFi naïve at baseline	17 (60.7)	≤10		29 (85.3)	17 (68.0)	≤10		≤10	25 (69.4)
Post-index Medication, n (%)									
Methotrexate, concomitant	≤10	≤10		23 (67.6)	≤10	≤10		≤10	11 (30.6)
Other Concomitant cDMARD	≤10	≤10		≤10	≤10	≤10		0 (0.0)	≤10
Dose change, baricitinib	≤10	≤10		0 (0.0)	≤10	≤10		0 (0.0)	≤10

Abbreviations: BARI = baricitinib; bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; Max = maximum; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; Min = minimum; N = number of patients in the analysis population; n = number of patients in the specified category; RA = rheumatoid arthritis; SD = standard deviation; SNDS = Système National des Données de Santé; TNFi = tumour necrosis factor inhibitor.

[a] Matching ratio 1:1 is applied.

[b] All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

[c] TNFi.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\french snds_SNDS\BARICITINIB_RAS_SNDS_2019_Match_1_1_Point VII_V1.0 20220228.docx - pages 192-194.

Table 53_PS20 Time to First MACE (Days) [PS20]

	Unmatched		Matched		
	Baricitinib[a,b] (N = 932)	TNFi (N = 3952)	Baricitinib[a,b] (N = 743)	TNFi (N = 743)	Total (N = 1486)
n	932	3,952	743	743	1,486
Mean (SD)	171.75 (150.44)	135.00 (140.87)	266.00 (166.88)	73.00 (39.27)	137.33 (128.17)
Median	136.50 [53.75, 325.00]	93.00 [28.25, 208.00]	266.00 [148.00, 384.00]	72.50 [35.75, 110.75]	100.50 [55.25, 207.00]
Min, Max	30.0, 384.0	8.0, 473.0	148.00, 384.00	26.0, 121.0	26.0, 384.0

Abbreviations: MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis code of acute myocardial infarction or ischemic or haemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; PS20 = Private Source 20; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

[b] Only the baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked NA as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.53. - Time to First MACE (Days) [HV].docx

Table 53_ARTIS Time to First MACE (Days) [ARTIS]

Time	Unmatched		Matched	
	Baricitinib[a] (N = 1737)	TNFi (N = 6230)	Baricitinib[a] (N = 1681)	TNFi (N = 1681)
n	1737	6230	1681	1681
Mean (SD)	504 (347.1)	576 (418.4)	503 (346.4)	583 (425.6)
Median	457	485	454	484
Min, Max	1, 1310	3, 1460	1, 1310	3, 1460

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; VTE = venous thromboembolism.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\ Table6_time_to_outcome_08MAR22.xlsx

Table 53_BKK Time to First MACE (Days) [BKK]

	Unmatched				Matched				
	Baricitinib (N = 8)	4 mg (N = 5)	2 mg (N = 3)	TNFi (N = 12)	Baricitinib (N = 8)	4 mg (N = 5)	2 mg (N = 3)	TNFi (N = 4)	Total (N = 12)
n	8	5	3	12	8	5	3	4	12
Mean (SD)	185.0 (190)	206.2 (242)	149.7 (83)	123.6 (93)	185.0 (190)	206.2 (242)	149.7 (83)	164.8 (122)	178.3 (165)
Median	105.0	105.0	105.0	79.0	105.0	105.0	105.0	133.5	105.0
Min, Max	24.0, 622.0	24.0, 622.0	99.0, 245.0	12.0, 334.0	24.0, 622.0	24.0, 622.0	99.0, 245.0	58.0, 334.0	24.0, 622.0

Abbreviations: BKK = Betriebskrankenkasse; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis code of acute myocardial infarction or ischemic or haemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the analysis population; n = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

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Table 53_SNDS Time to First MACE (Days) [SNDS]

	Unmatched				Matched				
	Baricitinib N = 28	BARI 4 mg N = 19	BARI 2 mg N ≤10	TNFi N = 34	Baricitinib N = 25	BARI 4 mg N = 16	BARI 2 mg N ≤10	TNFi[a] N = 11	Total N = 36
Time to first MACE (in days)									
n (missing)	28 (0)	19 (0)		34 (0)	25 (0)	16 (0)		11 (0)	36 (0)
Mean (SD)	211.5 (180.3)	192.6 (162.0)		281.2 (238.1)	215.8 (179.6)	195.9 (157.5)		226.1 (176.9)	218.9 (176.3)
Median	156.0	141.0		197.5	171.0	156.0		174.0	172.5
Min, Max	4.0, 710.0	7.0, 586.0		1.0, 807.0	4.0, 710.0	16.0, 586.0		1.0, 522.0	1.0, 710.0

Abbreviations: BARI = baricitinib; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis code of acute myocardial infarction or ischemic or haemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the analysis population; n = number of patients in the specified category; SD = standard deviation; SNDS = Système National des Données de Santé; TNFi = tumour necrosis factor inhibitor.

[a] Matching ratio 1:1 is applied.

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10.4.3. Serious infections

Clinical characteristics, RA medication use, and time to event for patients with serious infections are detailed in Tables 56, 57, and 58 within the Annex for each respective data source. As described in Section 10.4, there were 7 data sources with more than 5 patients (when considering the matched cohorts combined) with a serious infection event. Clinical characteristics of patients with serious infections were generally the same as observed in the overall cohort of RA patients (as described in Section 10.2), or simply too small of sample sizes to be informative. The 3 data sources with the greatest number of serious infection events (consistent with their large overall sample sizes) were ARTIS (n = 160 serious infections overall), SNDS (n = 72), and BKK (n = 29). Within these three largest data sources, there was a suggestion that patients with serious infection may be older and more often male than patients in the overall cohorts. The mean age of baricitinib patients with serious infection (Table 56 in the respective Annex for each data source) was approximately 66 years old in each of these 3 cohorts. The proportion of male patients with serious infection ranged from 50-70% in these cohorts, whereas in the overall data approximately 20-25% of patients were male. It is important to note that these are qualitative observations rather than statistically tested. In ARTIS, smoking (69%) and diabetes (18%) were common among baricitinib patients with serious infection.

The distribution of time to serious infection is variable. Optum and BKK reported the shortest mean (median) time to serious infection among baricitinib patients with the event: 79.67 (79) days in Optum (where there were 3 baricitinib patients in matched cohort with a serious infection) and 107.3 (100) days in BKK (where there were 17 baricitinib patients in matched cohort with serious infection). ARTIS (with 94 baricitinib patients with serious infection in matched cohort) reported the longest mean (median) time to serious infection: 485 (428) days.

10.5. Other analyses: Quantitative bias analysis

Bias analysis quantifies the impact of systematic error on the measure of association estimated in a study. This provides information for interpreting the results, specifically the confidence that they correctly estimate the risk. In this study there are three important sources of potential confounding that cannot be addressed in the large majority of data sources included: smoking status, obesity, and disease severity. Results of the array approach to bias analysis (Schneeweiss 2006) are presented in this section for all three covariates with respect to the IRR estimated for VTE and MACE outcomes.

For important confounding bias to exist three conditions must be met:

(1) a factor must be associated with the outcome under investigation and it must be an independent risk factor above and beyond the population under study,
(2) the prevalence of that risk factor must differ between the comparison groups, and
(3) the bias introduced must be large enough to meaningfully alter the results; in practice, causing a change of more than 10% in the estimated relative risk is often used.

Simply stated, the array approach considers an array of possible strengths of the risk factor across the range of possible differences in prevalence that could exist between comparison

groups. This approach quantifies the influence of bias in the absence of external information. For context, the prevalence of obesity, smoking, and high-disease activity is reported in real-world patients treated for RA.

For each the bias analysis, the strength of the confounder-VTE association (RR_{CD}) was varied from 1.0 to 5.5, while the prevalence of the potential confounder was varied from 0 to 50%. The aggregate US IRR (VTE: Figure 10.19 and MACE: Figure 10.23) was used as the starting point for the bias analyses in US data, due to the small numbers of events and exposures in individual US data sources. The analysis in French data used the IRR from Table 48_SNDS in the bias analysis for VTE and Table 55_SNDS for MACE. The full range of adjusted IRRs, that consider the extent of possible bias due to each unmeasured risk factor, are presented graphically.

Information from real-world patients was provided for context, for comparison with the range of prevalences and strengths of risk factors evaluated in the bias analysis. In US patients, the prevalence of obesity and smoking was estimated from medical charts of patients with RA treated with b/tsDMARDs in the Optum claims data. There were 164 patients with information on BMI and 145 with known smoking status. The prevalence of obesity (categorised using WHO ranges) and smoking status in the general population are also reported for reference purposes, from the 2017–2018 National Health and Nutrition Examination Survey (Hales et al. 2020) and CDC, respectively (Cornelius et al 2022). In French patients, BMI and smoking prevalences in patients with RA is based on information from the CORPUS and ESPOIR cohorts. Prevalences are also available for the French general population (van Gelder 2022; WHO 2013).

Context for the prevalence of high disease activity (ie, DAS28 >5.2) is based on information from the CorEvitas and ARTIS registries for US and French patients, respectively, recognizing that information from Swedish patients in ARTIS may not necessarily reflect the experience of French patients with RA but the bias analysis does not depend on external information. Instead, information from RA populations is provided as context for the prevalences assessed in the analysis.

Finally, for comparison with the range of risk factor strengths evaluated in the bias analyses, the magnitude of increase in risk of VTE (or MACE) associated with each risk factor was obtained from the literature.

Table 10.6. Prevalence of Obesity and Smoking in the US

Population	Prevalence	Source
BMI		
Optum RA Population		
Non-VTE patients (n = 164 valid)	Underweight 1.2% Healthy weight 24.3% Overweight 28.7% Obese 45.7%	Optum Patients with RA (B029 Study Report, Annex 17)
Patients with VTE (n = 141)	Underweight 0.7% Healthy weight 23.4% Overweight 29.1% Obese 46.8%	Optum Patients with RA (B029 Study Report, Annex 17)
General US Population	Obese 42.4%	National Health and Nutrition Examination Survey (Hales et al. 2020)
Smoking		
Optum RA Population		
Patients who did not experience VTE (n = 145 valid)	Current smoker 21% Former smoker 26% Never smoked 54%	Optum Patients with RA (B029 Study Report, Annex 17)
Patients who later experienced VTE (n = 147)	Current smoker 16% Former smoker 40% Never smoked 44%	Optum Data (B029 Study Report, Annex 17)
General US population	Current smoker 12.5%	CDC MMWR (Cornelius et al. 2022)

Table 10.7. France: Prevalence of Obesity and Smoking in France

Population	Prevalence	Source
BMI		
RA Population		
Derived from first-line treatment table (n = 180 valid)	Underweight 2.2% Healthy weight 51.7% Overweight 30.0% Obese 16.1%	ESPOIR Report
Derived from first-line treatment table (n = 166 valid)	Underweight 3.0% Healthy weight 47.0% Overweight 27.1% Obese 19.3%	CORPUS Report
French General Population	Underweight/ Healthy weight 31.1% Overweight 50.7% Obese 18.2%	WHO Country Profile (WHO 2013)

Smoking		
RA Population		
Derived from first-line treatment table (n = 180 valid)	Current smoker 19.4% Former smoker 27.2% Never smoked 53.3%	ESPOIR Report
Derived from first-line treatment table (n = 166 valid)	Current smoker 21.7% Former smoker 19.3% Never smoked 58.4%	CORPUS Report
General French Population (RFI)	Current smoker 25.0%	RFI French Survey
General French Population (van Gelder 2022)	Current smoker 28.0%	Statista (van Gelder 2022)

Abbreviations: BMI = body mass index; CORPUS = Cohorte d'Observation Rheumatologique des Pratiques et des Usages; ESPORI = Etude et Suivi des Polyarthrites Indifférenciées Récentes; n = number of patients in the specified category; RA = rheumatoid arthritis; WHO = World Health Organisation.

10.5.1. QBA: VTE

In the general population, BMI is an established risk factor for VTE (Eichinger et al 2008) and some studies have observed an increased risk of VTE among smokers (Enga et al. 2012). Although information about the association between RA disease severity and VTE is sparse from studies of patients with RA, the biological pathway linking inflammation and VTE is clear (Colling et al. 2021; Vaszque-Garza et al. 2017).

10.5.1.1. Smoking

US Patients

The prevalence of smoking assumed for the 'unexposed' reference TNFi cohort is indicated with a solid line in Figure 10.7 and presented in Table 10.8. Information about the strength of smoking as a risk factor for VTE (RR_{CD} in the figure) is also included, for context. The unadjusted or observed IRR ('ARR' in the figure) is based on the meta-analysis of US data in Figure 10.19

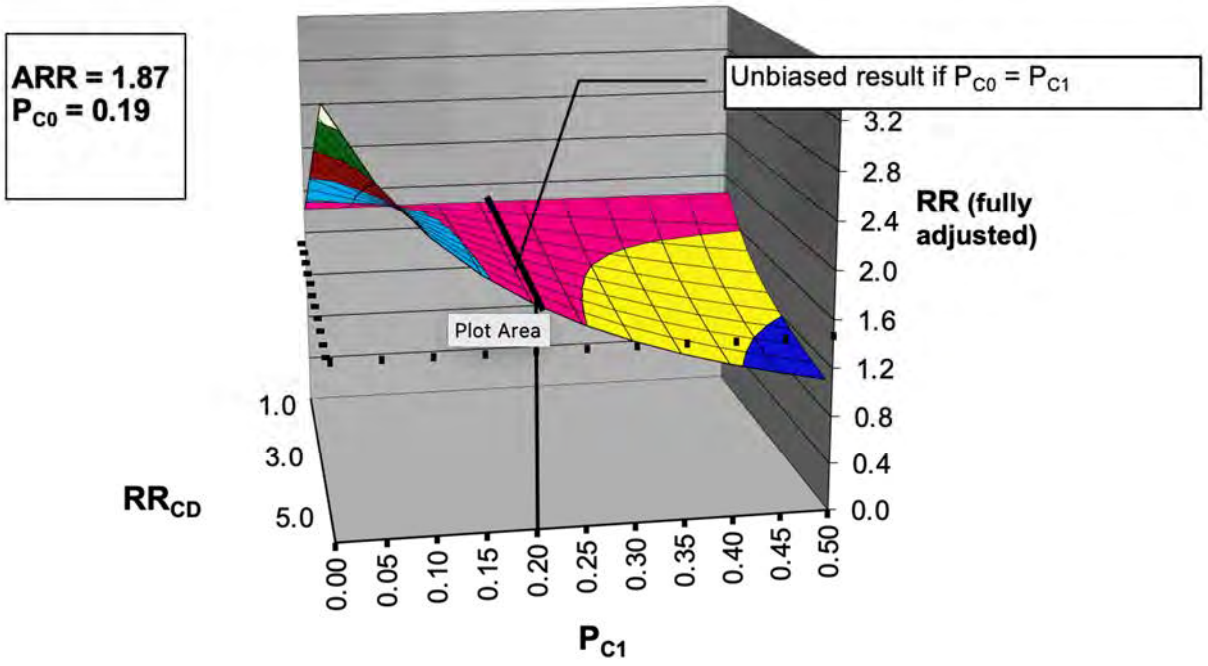
Table 10.8. Values Used in Bias Analysis of Smoking and VTE, US Data Meta-Analysis

	Prevalence of Smoking in Unexposed Patients with RA[a]	RR Between Smoking and VTE[b]	ARR Point Estimate we Observed	ARR LCL	ARR UCL
Non-VTE patients	21.0%	1.9	1.87	0.63	5.59
VTE patients	16.0%	1.9	1.87	0.63	5.59
Average	19.0%	1.9	1.87	0.63	5.59

Abbreviations: ARR = apparent relative risk, referring to the IRR estimated from meta-analysis of US data; LCL = lower confidence limit; RA = rheumatoid arthritis; RR = relative risk referring to the strength of association between the risk factor and the outcome; UCL = upper confidence limit; VTE = venous thromboembolism.

a Based on prevalence estimated from patients with RA in Study B029 (Annex 17).

b Nakanishi et al. 2015.



Abbreviations: ARR = apparent relative risk (ie, incidence rate ratio, IRR); PC_0 = prevalence in unexposed (ie, TNFi reference group); PC_1 = prevalence in exposed (ie, baricitinib group); RA = rheumatoid arthritis; RR = relative risk (ie, IRR after adjusting for potential bias); RR_{CD} = relative risk between potential confounder and outcome (ie, smoking and VTE); VTE = venous thromboembolism.

Figure 10.7. Sensitivity analysis of unmeasured confounding by smoking on the effect of baricitinib on VTE in US patients with RA.

Across all scenarios, the RR adjusted to remove the effect of bias ranged from 1.1 to 3.4. In the strongest bias scenario, 77.4%, when the RR_{CD}=5.5 and the prevalence of the confounder in the exposed baricitinib group is 50%, the RR adjusted for bias =1.1. The scenario where the adjusted RR was 3.4 included an RR_{CD}=5.5 and the prevalence of the confounder in the exposed group was 0%. Compared with the range of potential values of the adjusted RR from this analysis, the CI of the ARR includes both of these values.

If the RR_{CD} or strength of the risk factor reported in the literature is used instead (ie, RR_{CD}=1.9), an adjusted RR=2.2 occurs when the prevalence of smoking in the exposed group is 0% and an adjusted RR=1.5 when the prevalence of smoking in the exposed cohort is 50%. These values are well within the 95% CIs of the ARR.

Thus, unmeasured confounding by smoking is unlikely to meaningfully impact the observed findings in US patients.

French Patients in SNDS

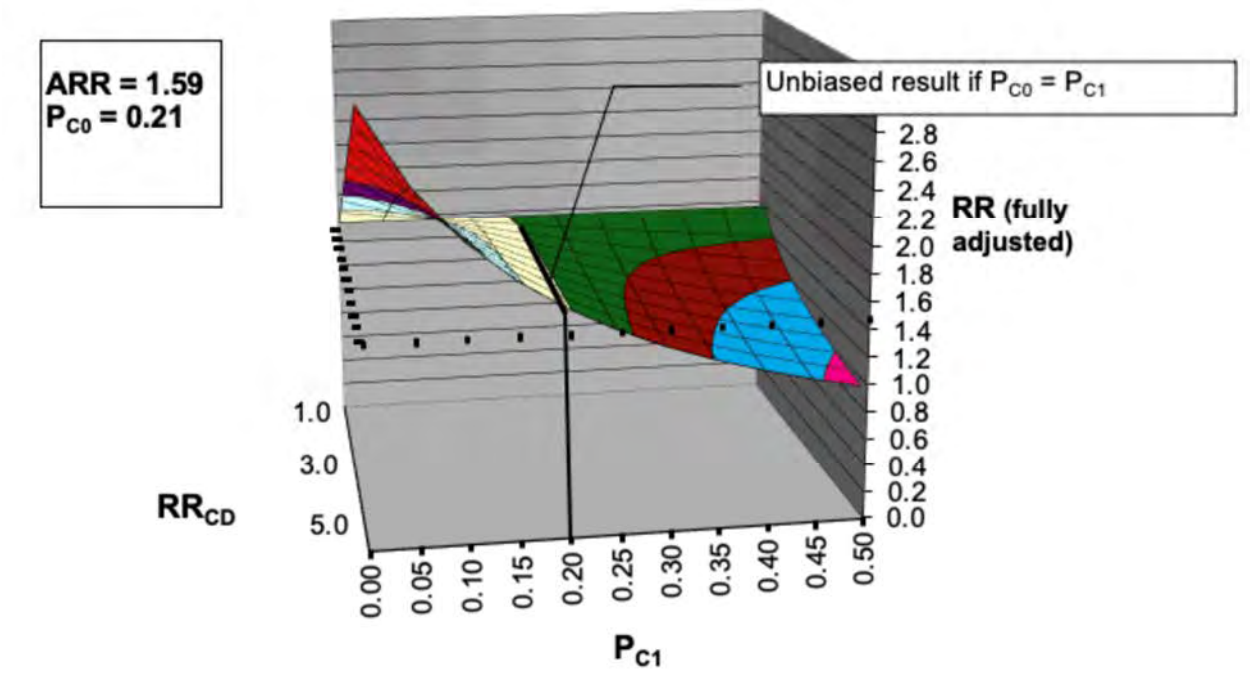
The prevalence of smoking assumed for the reference TNFi cohort is indicated with a solid line in Figure 10.8 and presented in Table 10.9. Information from the literature about the strength of smoking as a risk factor for VTE (RR_{CD} in the figure) is also included, for context. The unadjusted or observed IRR ('ARR' in the figure) is based on the comparative analysis of French patients from Table 48_SNDS.

Table 10.9. Prevalence of Smoking Among French Patients

RA Population Sample	Prevalence of Smoking in the Unexposed Patients with RA	RR Between Smoking and VTE	ARR VTE Point Estimate we Observed, any BARI Dose	ARR LCL	ARR UCL
ESPOIR	19.4%	1.19[a]	1.59	0.79	3.21
CORPUS	21.7%	1.19[a]	1.59	0.79	3.21
Average	21.0%	1.19[a]	1.59	0.79	3.21

Abbreviations: ARR = apparent relative risk; BARI = baricitinib; CORPUS = Cohorte d'Observation Rheumatologique des Pratiques et des Usages; ESPOIR = Etude et Suivi des Polyarthrites Indifférenciées Récentes; LCL = lower confidence limit; RA = rheumatoid arthritis; RR = relative risk; UCL = upper confidence limit; VTE = venous thromboembolism.

[a] Anand 2017.



Abbreviations: ARR = apparent relative risk (ie, incidence rate ratio, IRR); PC_0 = prevalence in unexposed (ie, TNFi reference group); PC_1 = prevalence in exposed (ie, baricitinib group); RA = rheumatoid arthritis; RR = relative risk (ie, IRR after adjusting for potential bias); RR_{CD} = relative risk between potential confounder and outcome (ie, smoking and VTE); VTE = venous thromboembolism.

Figure 10.8. Sensitivity analysis of unmeasured confounding by smoking on the effect of baricitinib on VTE in French patients with RA.

Across all scenarios, the RR adjusted for the effect of bias ranged from 0.9 to 3.1. In the strongest bias scenario, 69%, when RR_{CD}=5.5 and the prevalence of the confounder in the exposed baricitinib group is 50%, the adjusted RR is 0.9. The scenario where the adjusted RR was 3.1 included an RR_{CD} = 5.5 and the prevalence of the confounder in the exposed group = 0%. Compared with the range of potential values of the adjusted IRR from this analysis, the CI of the ARR is almost the same, including when the strength between the confounder and disease is the greater, RR_{CD} = 5.5. If RR_{CD} from the literature is used instead (ie, RR_{CD}=1.19) an adjusted RR=1.7 when the prevalence of smoking in the exposed is 0% and an RR=1.5 when the prevalence of smoking in the exposed cohort is 50%. These values are included in the 95% CI for the ARR.

Thus, unmeasured confounding by smoking is unlikely to meaningfully impact the results observed in French patients.

10.5.1.2. Obesity

The prevalence of obesity assumed for the reference TNFi cohort and, for context, the strength of obesity as a risk factor for VTE ('RR_{CD}' in the figure) are presented in Table 10.10. The unadjusted or observed IRR ('ARR' in the figure) is based on the meta-analysis of US data in Figure 10.19

US Patients

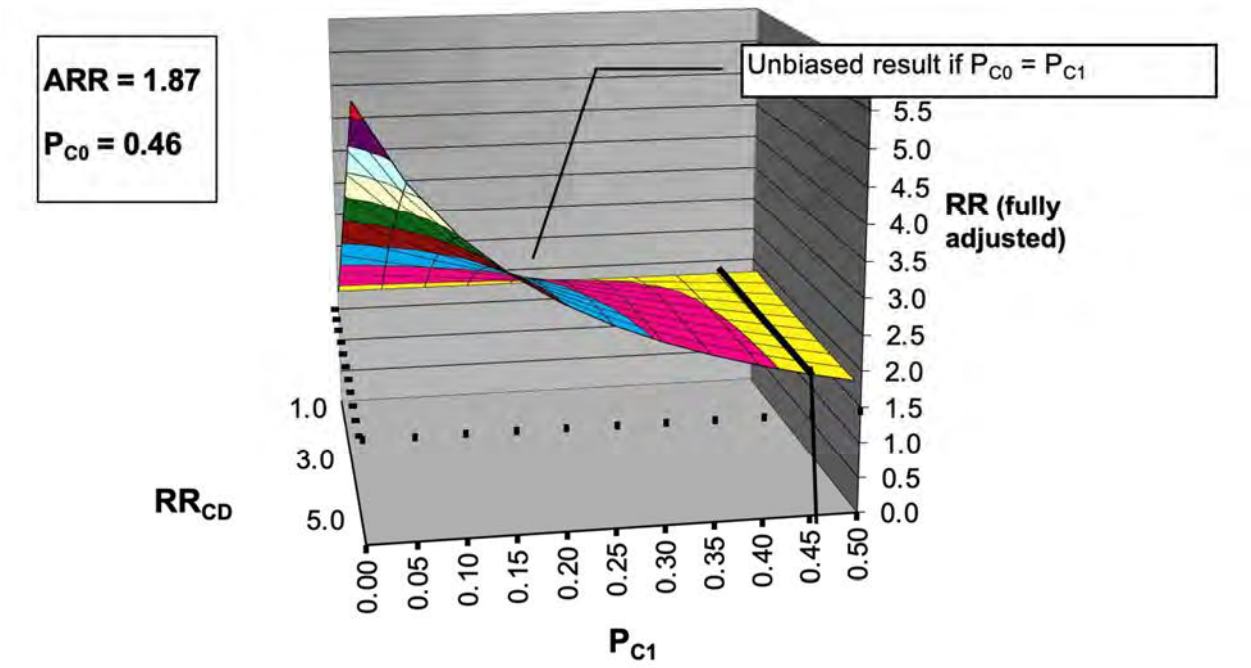
Table 10.10. Prevalence QBA for Obesity and VTE, US Data Meta-Analysis

	Prevalence of Obesity in the Unexposed Patients with RA[a,b]	RR Between Obesity and VTE	ARR Point Estimate we Observed	ARR LCL	ARR UCL
Non-VTE patients	45.9%	2	1.87	0.63	5.59
VTE patients	46.8%	2	1.87	0.63	5.59
Average	46.0%	2	1.87	0.63	5.59

Abbreviations: ARR = apparent relative risk; LCL = lower confidence limit; QBA = quantitative bias analysis; RA = rheumatoid arthritis; RR = relative risk; UCL = upper confidence limit ; venous thromboembolism.

[a] The prevalence of obesity in US patients is based on abstracted information from medical charts from US patients with RA linked to the Optum claims data.

[b] Eichinger et al. 2008.



Abbreviations: ARR = apparent relative risk (ie, incidence rate ratio, IRR); PC_0 = prevalence in unexposed (ie, TNFi reference group); PC_1 = prevalence in exposed (ie, baricitinib group); RA = rheumatoid arthritis; RR = relative risk (ie, IRR after adjusting for potential bias); RR_{CD} = relative risk between potential confounder and outcome (ie, obesity and VTE); RA = rheumatoid arthritis; VTE = venous thromboembolism.

Figure 10.9. Sensitivity analysis of unmeasured confounding by obesity on the effect of baricitinib on VTE in US patients with RA

Across all scenarios, the RR adjusted to remove the effect of bias ranged from 1.8 to 5.8. In the strongest bias scenario, -68%, when the RR_{CD}=5.5 and the prevalence of the confounder in the exposed baricitinib group is 50%, the RR adjusted for bias =5.8. The scenario where the adjusted RR was 1.8 included an RR_{CD}=5.5 and the prevalence of the confounder in the exposed group at 50%. Compared with the range of potential values of the adjusted RR from this analysis, the CI of the ARR is largely overlapping, although the upper bound of the 95% CI is less than in the strongest bias scenario with RR_{CD} = 5.5 and the prevalence of the confounder in the exposed group is 0%. For this scenario to be true, no one in the exposed baricitinib would be obese. Given that 42% of the general population (Hales et al. 2020) and 46% of US patients with RA in Optum are obese, this is highly unlikely.

If the RR_{CD} or strength of the risk factor reported in the literature is used instead (ie, RR_{CD}=2.04), an adjusted RR=2.7 occurs when the prevalence of smoking in the exposed group is 0% and an adjusted RR=1.8 when the prevalence of obesity in the exposed cohort is 50%. These values are in the 95% CI of the ARR.

Thus, unmeasured confounding by obesity is unlikely to meaningfully impact the observed findings in US patients.

French Patients in SNDS

The prevalence of obesity assumed for the reference TNFi cohort is indicated with a solid line in Figure 10.10 and presented in Table 10.11. The strength of obesity as a risk factor for VTE ('RR_{CD}' in the figure) in French patients is also included, for context. The unadjusted or observed IRR ('ARR' in the figure) is based on the IRR for French patients from Table 48_SNDS.

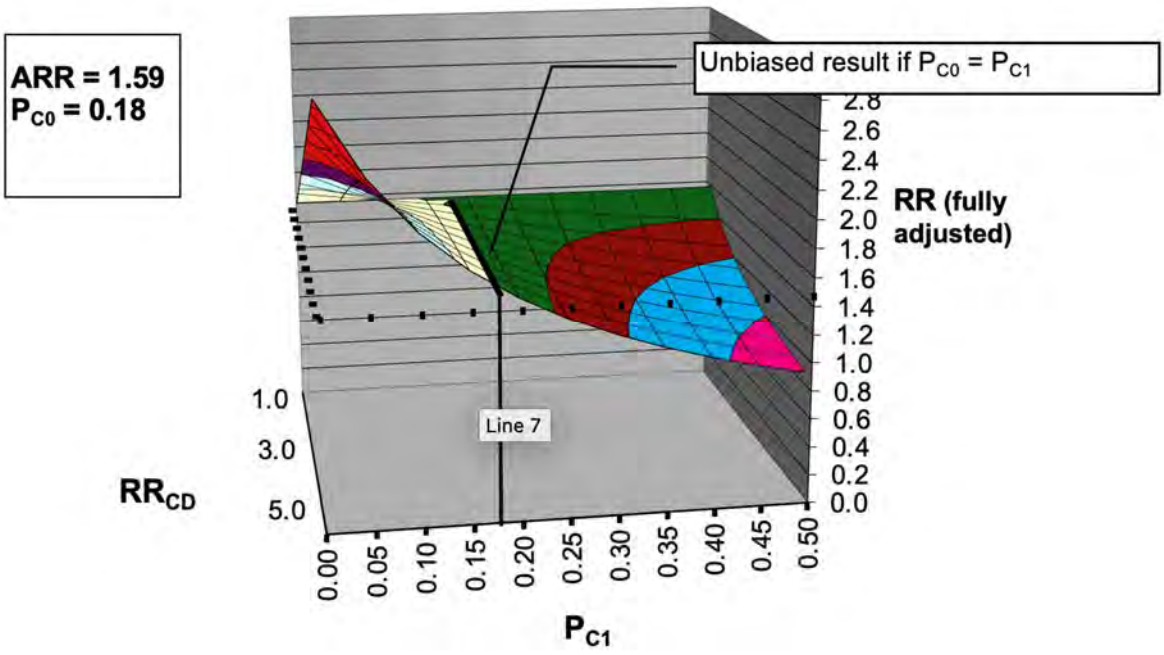
Table 10.11. Prevalence of Obesity and Strength of Obesity as a Risk Factor for VTE – French Patients

RA Population Sample	Prevalence of Obesity in the Unexposed Patients with RA[a,b]	RR Between Obesity and VTE	ARR Point Estimate Observed for VTE, any BARI Dose	ARR LCL	ARR UCL
ESPOIR	16.1%	2	1.59	0.79	3.21
CORPUS	20.0%	2	1.59	0.79	3.21
Average	18.0%	2	1.59	0.79	3.21

Abbreviations: ARR = apparent relative risk; BARI = baricitinib; CORPUS = Cohorte d'Observation Rheumatologique des Pratiques et des Usages; ESPORI = Etude et Suivi des Polyarthrites Indifférenciées Récentes; LCL = lower confidence limit; RA = rheumatoid arthritis; RR = relative risk; UCL = upper confidence limit; VTE = venous thromboembolism.

[a] The prevalence of obesity in French patients is based on information from patients with RA included in the ESPOIR or CORPUS cohorts.

[b] Eichinger et al. 2008.



Abbreviations: ARR = apparent relative risk (ie, incidence rate ratio, IRR); PC_0 = prevalence in unexposed (ie, TNFi reference group); PC_1 = prevalence in exposed (ie, baricitinib group); RA = rheumatoid arthritis; RR = relative risk (ie, IRR after adjusting for potential bias); RR_{CD} = relative risk between potential confounder and outcome (ie, obesity and VTE); RA = rheumatoid arthritis; VTE = venous thromboembolism.

Figure 10.10 Sensitivity analysis of unmeasured confounding by obesity on the effect of baricitinib on VTE in French patients with RA.

Across all scenarios, the RR adjusted to remove the effect of bias ranged from 0.9 to 2.9. In the strongest bias scenario, 79%, when RR_{CD}=5.5 and the prevalence of the confounder in the exposed baricitinib group is 50%, the RR adjusted for bias is 0.9. The scenario where the adjusted RR was 2.9 included an RR_{CD} = 5.5 and the prevalence of the confounder in the exposed group = 0%. Compared with the range of potential values of the adjusted RR from this analysis, the CI of the ARR is almost identical. If a value of RR_{CD} from the literature (ie, RR_{CD}=2.0), is used instead, an adjusted RR=1.9 occurs when the prevalence of obesity in the exposed is 0% and an adjusted RR=1.3 when the prevalence of obesity in the exposed population is 50%. These values are in the 95% CI for the ARR.

Thus, it is unlikely that unmeasured confounding by obesity meaningfully impacts the results observed.

10.5.1.3. Disease severity

US Patients

The prevalence of high disease activity (ie, DAS28 >5.2), assumed for the reference TNFi cohort is indicated with a solid line in Figure 10.11 and presented in Table 10.12. For context, the strength of high disease activity as a risk factor for VTE ('RR_{CD}' in the figure) is also included. The unadjusted or observed IRR ('ARR' in the figure) is based on the meta-analysis of US data in Figure 10.19.

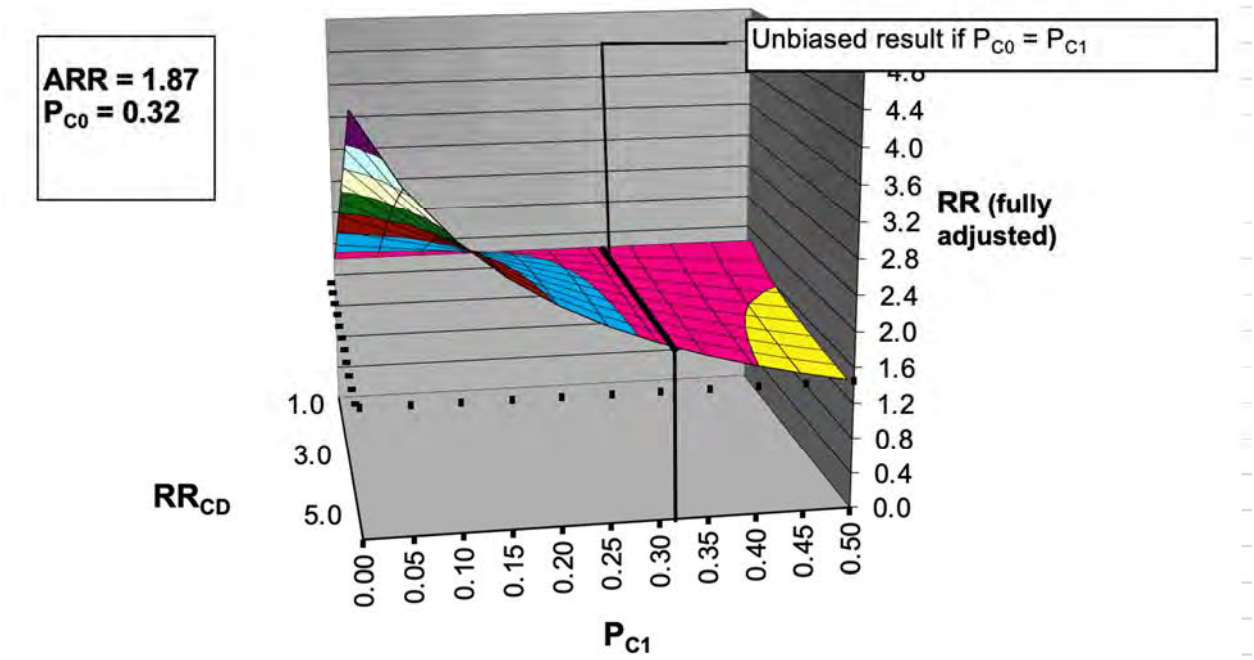
Table 10.12. Values Used in RA Disease Severity and VTE, US Data Meta-Analysis

	Prevalence of High Disease Activity in Unexposed Patients with RA	RR Between High Disease Activity and VTE[a]	ARR Point Estimate we Observed	ARR LCL	ARR UCL
In RA patients	32.0%	2.03[b]	1.87	0.63	5.59

Abbreviations: ARR = apparent relative risk; DAS28 = Disease Activity Score 28; LCL = lower confidence limit; RA = rheumatoid arthritis; RR = relative risk; UCL = upper confidence limit; VTE = venous thromboembolism.

[a] High disease activity is defined as DAS28 ≥5.2.

[b] Molander et al. 2021.



Abbreviations: ARR = apparent relative risk (ie, incidence rate ratio, IRR); PC_0 = prevalence in unexposed (ie, TNFi reference group); PC_1 = prevalence in exposed (ie, baricitinib group); RA = rheumatoid arthritis; RR = relative risk (ie, IRR after adjusting for potential bias); RR_{CD} = relative risk between potential confounder and outcome (ie, disease severity and VTE); RA = rheumatoid arthritis; VTE = venous thromboembolism.

Figure 10.11. Sensitivity analysis of unmeasured confounding by RA disease severity on the effect of baricitinib on VTE in US patients with RA.

Across all scenarios, the RR adjusted to remove the effect of bias ranged from 1.4 to 4.5. In the strongest bias scenario, -59%, when the RR_{CD}=5.5 and the prevalence of the confounder in the exposed baricitinib group is 50%, the RR adjusted for bias =4.5. The scenario where the adjusted RR was 1.4 included an RR_{CD}=5.5 and the prevalence of the confounder in the exposed group is 50%. Compared with the range of potential values of the adjusted RR from this analysis, the CI of the ARR includes both of these values.

If the RR_{CD}, or strength of the risk factor, reported in the literature is used instead (ie, RR_{CD}=2.03), an adjusted RR=2.5 occurs when the prevalence of high disease activity in the exposed group is 0% and an adjusted RR=1.6 when the prevalence of smoking in the exposed cohort is 50%. These values are well within the 95% CIs of the ARR.

Thus, unmeasured confounding by high disease activity, DAS28 ≥5.2, is unlikely to meaningfully impact the observed findings in US patients.

French Patients in SNDS

The prevalence of high disease activity assumed for the reference TNFi cohort is indicated with a solid line in Figure 10.12 and presented in Table 10.13. The strength of obesity as a risk factor for VTE in French patients ('RR_{CD}' in the figure) is also included, for context. The unadjusted or observed IRR ('ARR' in the figure) is based on the IRR for French patients from Table 48_SNDS.

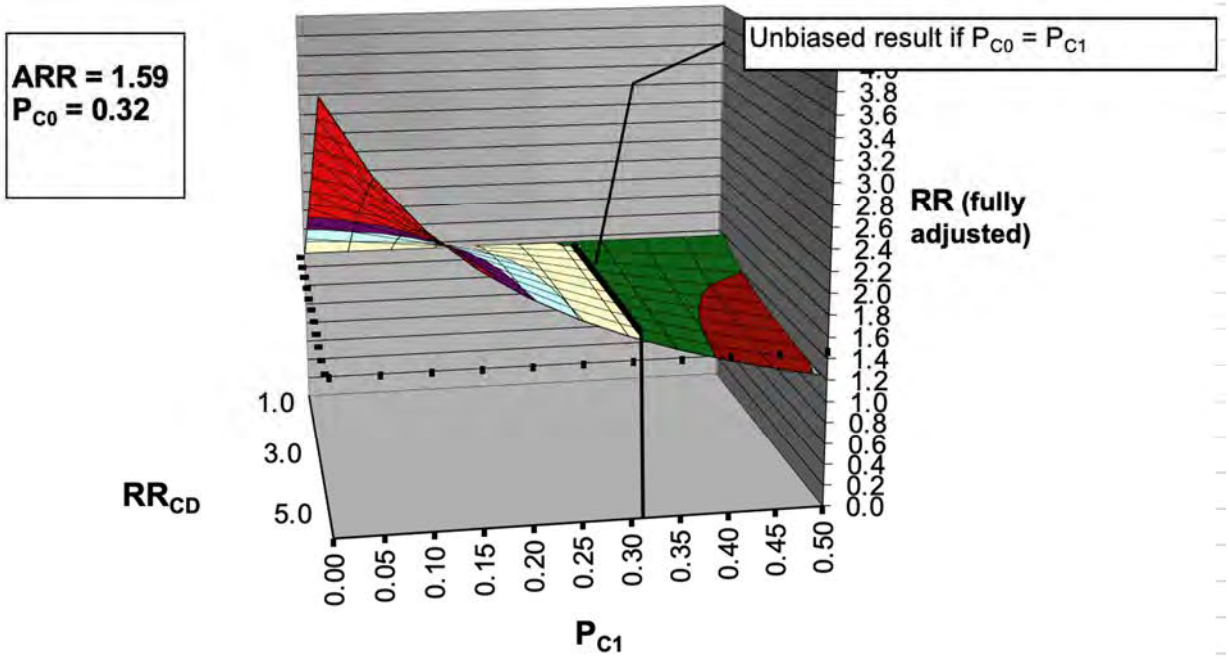
Table 10.13. Values Used in RA Disease Severity and VTE, SNDS Analysis

High RA Disease Activity in the Unexposed Patients with RA	RR Between High Disease Activity[a] and VTE[b]	ARR Point Estimate we Observed, any BARI Dose	ARR LCL	ARR UCL
32.0%	2.03	1.59	0.79	3.21

Abbreviations: ARR = apparent relative risk; BARI = baricitinib; DAS28 = Disease Activity Score 28; LCL = lower confidence limit; RA = rheumatoid arthritis; RR = relative risk; SNDS = Système National des Données de Santé; UCL = upper confidence limit; VTE = venous thromboembolism.

[a] High disease activity is defined as DAS28 ≥5.2.

[b] Molander et al. 2021.



Abbreviations: ARR = apparent relative risk (ie, incidence rate ratio, IRR); PC_0 = prevalence in unexposed (ie, TNFi reference group); PC_1 = prevalence in exposed (ie, baricitinib group); RA = rheumatoid arthritis; RR = relative risk (ie, IRR after adjusting for potential bias); RR_{CD} = relative risk between potential confounder and outcome (ie, disease severity and VTE); VTE = venous thromboembolism.

Figure 10.12. Sensitivity analysis of unmeasured confounding by RA disease severity on the effect of baricitinib on VTE in French patients with RA.

Across all scenarios, the RR adjusted to remove the effect of bias ranged from 1.2 to 3.9. In the strongest bias scenario, -59%, when the RR_{CD}=5.5 and the prevalence of the confounder in the exposed baricitinib group is 0%, the RR adjusted for bias =3.9. The scenario where the adjusted RR was 1.2 included RR_{CD}=5.5 and the prevalence of the confounder in the exposed group is 50%. Compared with the range of potential values of the adjusted RR from this analysis, the CI of the ARR includes the lower bound of the 95% CI and is close to, though higher than, the upper bound of the 95% CI of the ARR at 3.21. For the RR=3.9 to be true, the prevalence of high disease activity must be 50% in the TNFi reference group and 0% in the baricitinib group. This is an unlikely scenario and contrary to the expectation that patients treated with baricitinib may have more refractory, severe disease.

If the RR_{CD} or strength of the risk factor reported in the literature is used instead (ie, RR_{CD}=2.03), an adjusted RR=2.1 occurs when the prevalence of high disease activity in the exposed group is 0% and an adjusted RR=1.4 when the prevalence of high disease activity in the exposed cohort is 50%. These values are well within the 95% CIs of the ARR.

Thus, unmeasured confounding by high disease activity is unlikely to meaningfully impact the observed findings in French patients.

10.5.2. QBA MACE

BMI and smoking are established risk factors for MACE and disease severity (eg, DAS28) is also a risk factor for MACE (Liao et al. 2013). Similar to the bias analysis for unmeasured confounding in the analysis of VTE, context for this bias analysis came from abstracted charts from Optum patients for information on BMI and smoking, from the CORPUS and ESPOIR cohorts for similar information for French patients, and from the CorEvitas and ARTIS registries for information about disease severity for US and French patients, respectively.

10.5.2.1. Smoking

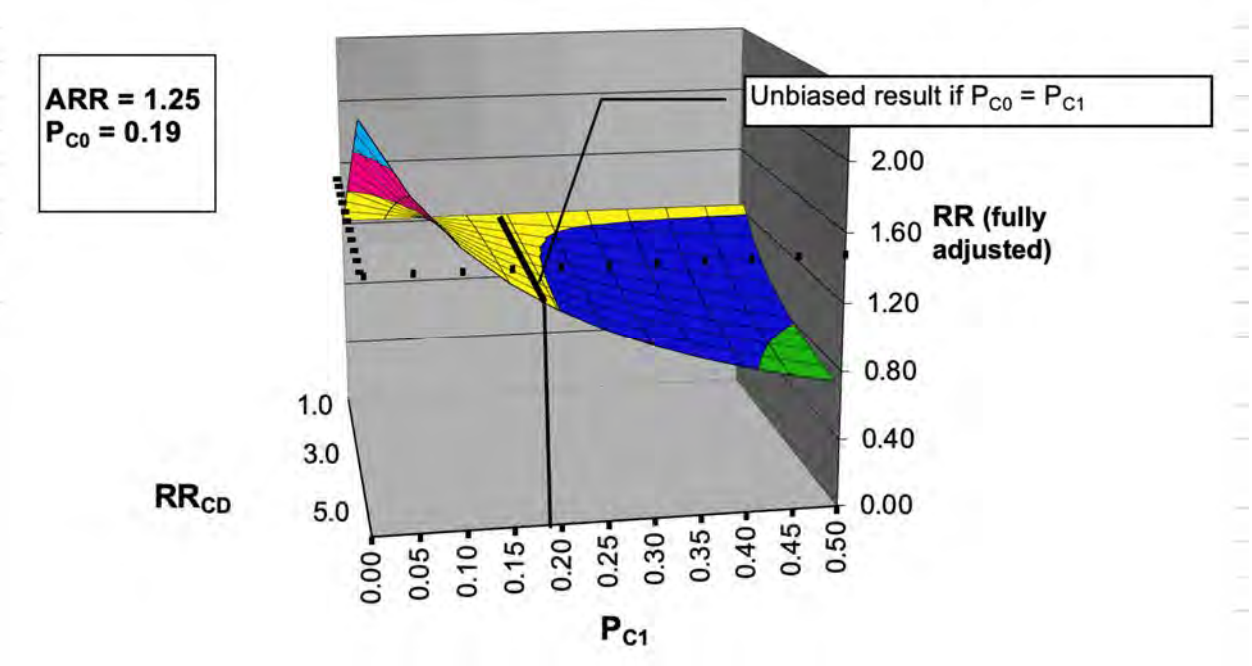
US Patients

The prevalence of smoking assumed for the reference TNFi cohort and, for context, the strength of smoking as a risk factor for MACE ('RR_{CD}' in the figure), are provided in Table 10.14. The unadjusted or observed IRR ('ARR' in the figure) is based on the meta-analysis of US data in Figure 10.23.

Table 10.14. Values Used in Smoking and MACE, US Data Meta-Analysis

	Prevalence of Smoking in the Unexposed Patients with RA	RR Between Smoking and MACE	ARR Point Estimate we Observed for MACE	ARR LCL	ARR UCL
Non-VTE patients	21.0%	1.9	1.25	0.52	3.05
VTE patients	16.0%	1.9	1.25	0.52	3.05
Average	19.0%	1.9	1.25	0.52	3.05

Abbreviations: ARR = apparent relative risk; LCL = lower confidence limit; MACE = major adverse cardiovascular event; RA = rheumatoid arthritis; UCL = upper confidence limit; VTE = venous thromboembolism.



Abbreviations: ARR = apparent relative risk (ie, incidence rate ratio, IRR); MACE = major adverse cardiovascular events; PC_0 = prevalence in unexposed (ie, TNFi reference group); PC_1 = prevalence in exposed (ie, baricitinib group); RA = rheumatoid arthritis; RR = relative risk (ie, IRR after adjusting for potential bias); RR_{CD} = relative risk between potential confounder and outcome (ie, smoking and MACE); .

Figure 10.13. Sensitivity analysis of unmeasured confounding by smoking on the effect of baricitinib on MACE in US patients with RA.

Across all scenarios, the RR adjusted to remove the effect of bias ranged from 0.7 to 2.3. In the strongest bias scenario, 77.4%, when the RR_{CD}=5.5 and the prevalence of the confounder in the exposed baricitinib group is 50%, the RR adjusted for bias =0.7. The scenario where the adjusted RR was 2.3 included an RR_{CD}=5.5 and the prevalence of the confounder in the exposed group is 0%. Compared with the range of potential values of the adjusted RR from this analysis, the CI of the ARR is overlapping.

If the RR_{CD} or strength of the risk factor reported in the literature is used instead (ie, RR_{CD}=1.9), an adjusted RR=1.5 occurs when the prevalence of smoking in the exposed group is 0% and an adjusted RR=1.0 when the prevalence of smoking in the exposed cohort is 50%. These values are in the 95% CIs of the ARR.

Thus, unmeasured confounding by smoking is unlikely to meaningfully impact the observed findings in US patients.

French Patients

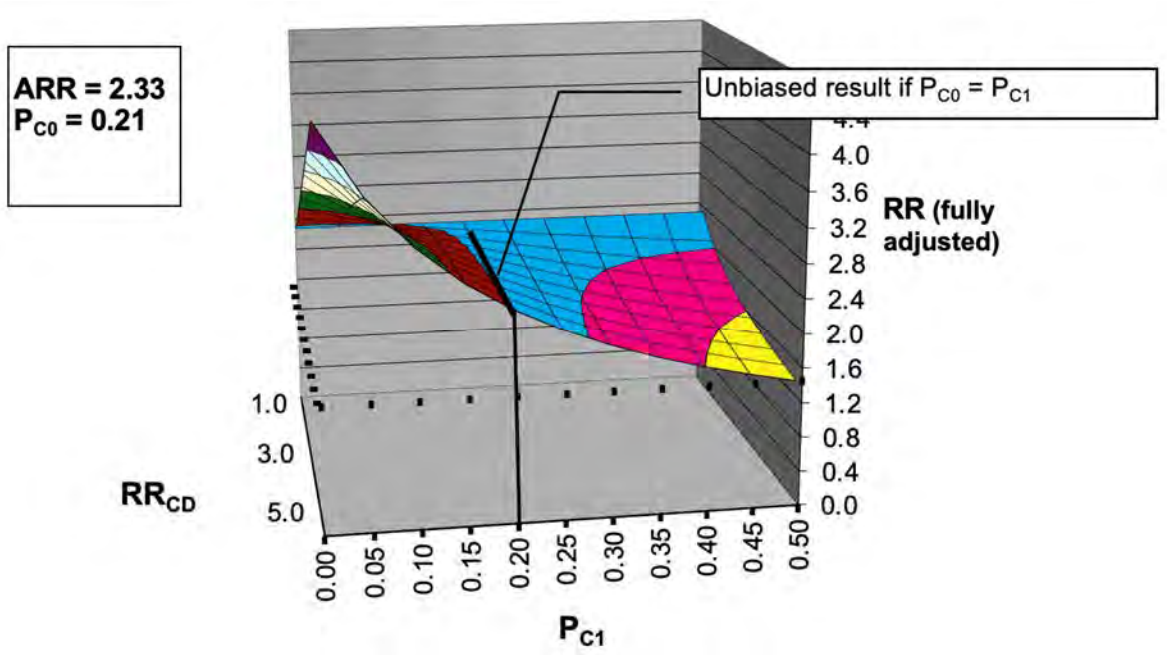
The prevalence of smoking assumed for the reference TNFi cohort and, for context, the strength of smoking as a risk factor for MACE ('RR_{CD}' in the figure), are provided in Table 10.15. The unadjusted or observed IRR ('ARR' in the figure) is based on the comparative analysis results for SNDS patients reported in Table 55_SNDS.

Table 10.15. Prevalence of Smoking Among RA Patients and Strength of Smoking as a Risk Factor for MACE

RA Population Sample	Prevalence of Smoking in the Unexposed Patients with RA	RR Between Smoking and MACE	ARR Point Estimate we Observed, any BARI Dose	ARR LCL	ARR UCL
ESPOIR	19.4%	1.9[a]	2.33	1.15	4.74
CORPUS	21.7%	1.9[a]	2.33	1.15	4.74
Average	21.0%	1.9[a]	2.33	1.15	4.74

Abbreviations: ARR = apparent relative risk; BARI = baricitinib; LCL = lower confidence limit; MACE = major adverse cardiovascular event; RA = rheumatoid arthritis; RR = relative risk; UCL = upper confidence limit.

[a] Nakanishi et al. 2015.



Abbreviations: ARR = apparent relative risk (ie, incidence rate ratio, IRR); MACE = major adverse cardiovascular events; PC_0 = prevalence in unexposed (ie, TNFi reference group); PC_1 = prevalence in exposed (ie, baricitinib group); RA = rheumatoid arthritis; RR = relative risk (ie, IRR after adjusting for potential bias); RR_{CD} = relative risk between potential confounder and outcome (ie, smoking and MACE).

Figure 10.14. Sensitivity analysis of unmeasured confounding by smoking on the effect of baricitinib on MACE in French patients with RA

Across all scenarios, the RR adjusted to remove the effect of bias ranged from 1.4 to 4.5. In the strongest bias scenario, 69%, when the RR_{CD}=5.5 and the prevalence of the confounder in the exposed baricitinib group is 50%, the RR adjusted for bias =1.4. The scenario where the adjusted RR was 4.5 included an RR_{CD}=5.5 and the prevalence of the confounder in the exposed group is 0%. Compared with the range of potential values of the adjusted RR from this analysis, the CI of the ARR is almost identical.

If the RR_{CD} or strength of the risk factor reported in the literature is used instead (ie, RR_{CD}=1.9 [rounded to 2.0]), an adjusted RR=2.8 occurs when the prevalence of smoking in the exposed group is 0% and an adjusted RR=1.9 when the prevalence of smoking in the exposed cohort is 50%. These values are well within the 95% CIs of the ARR.

Thus, unmeasured confounding by smoking is unlikely to meaningfully impact the observed findings in French patients.

10.5.2.2. Obesity

US Patients

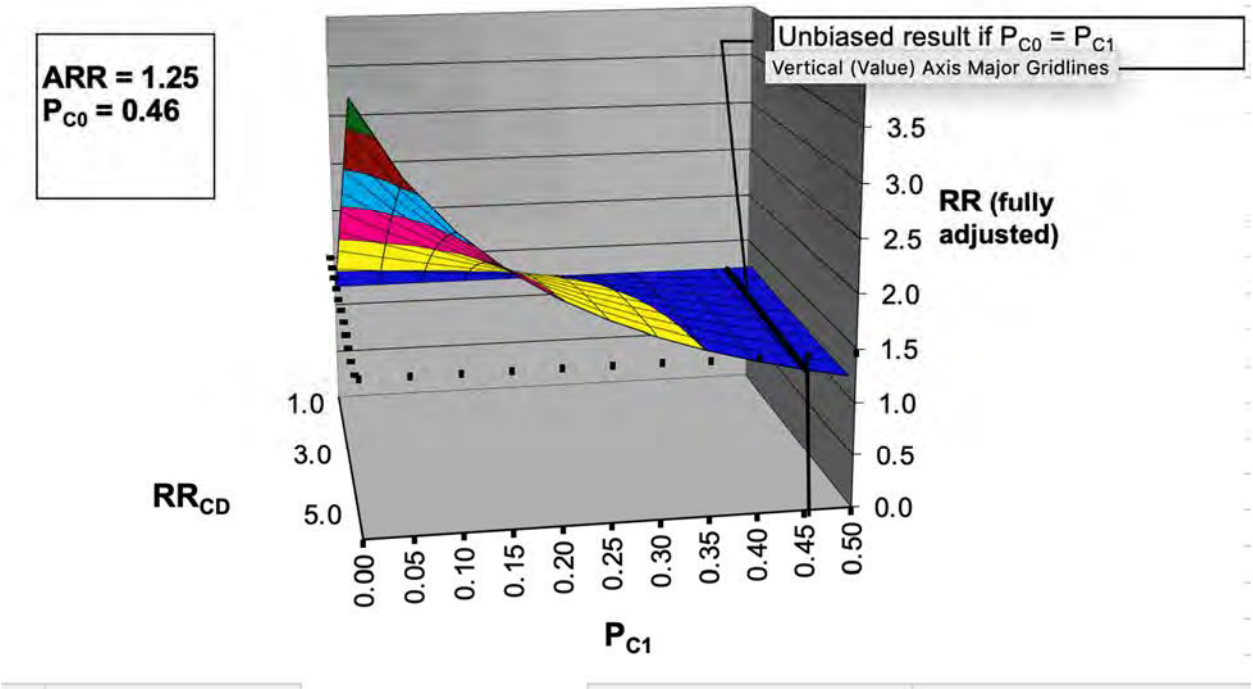
The prevalence of obesity assumed for the reference TNFi cohort and, for context, the strength of obesity as a risk factor for MACE ('RR_{CD}' in the figure) is presented in Table 10.16. The unadjusted or observed IRR ('ARR' in the figure) is based on meta-analysis of US data in Figure 10.23.

Table 10.16. Values used in Obesity and MACE, US Data Meta-Analysis

	Prevalence of Obesity in the Unexposed Patients with RA	RR Between Obesity and MACE[a]	ARR Point Estimate we Observed, MACE	ARR LCL	ARR UCL
Non-VTE patients	45.9%	2.04	1.25	0.52	3.05
VTE patients	46.8%	2.04	1.25	0.52	3.05
Average	46.0%	2.04	1.25	0.52	3.05

Abbreviations: ARR = apparent relative risk; LCL = lower confidence limit; MACE = major adverse cardiovascular event; RA = rheumatoid arthritis; RR = relative risk; UCL = upper confidence limit; VTE = venous thromboembolism.

[a] Thomsen et al. 2014.



Abbreviations: ARR = apparent relative risk (ie, incidence rate ratio, IRR); MACE = major adverse cardiovascular events; PC_0 = prevalence in unexposed (ie, TNFi reference group); PC_1 = prevalence in exposed (ie, baricitinib group); RA = rheumatoid arthritis; RR = relative risk (ie, IRR after adjusting for potential bias); RR_{CD} = relative risk between potential confounder and outcome (ie, obesity and MACE).

Figure 10.15. Sensitivity analysis of unmeasured confounding by obesity on the effect of baricitinib on MACE in US patients with RA.

Across all scenarios, the RR adjusted to remove the effect of bias ranged from 1.2 to 3.9. In the strongest bias scenario, -68%, when the RR_{CD}=5.5 and the prevalence of the confounder in the exposed baricitinib group is 0%, the RR adjusted for bias =3.9. The scenario where the adjusted RR was 1.2 included an RR_{CD}=5.5 and the prevalence of the confounder in the exposed group of 50%. Compared with the range of potential values of the adjusted RR from this analysis, the CI of the ARR is largely overlapping, although the upper bound of the 95% CI is less than in the strongest bias scenario with RR_{CD} = 5.5 and a prevalence of the confounder in the exposed group of 0%. For this scenario to be true, no one in the exposed baricitinib cohort could be obese. Given that 42% of the general population (Hales et al. 2020) and 46% of US patients with RA in Optum are obese, this is highly unlikely.

If the RR_{CD} or strength of the risk factor reported in the literature is used instead (ie, RR_{CD}=2.04), an adjusted RR=1.8 occurs when the prevalence of smoking in the exposed group is 0% and an adjusted RR=1.2 when the prevalence of obesity in the exposed cohort is 50%. These values are in the 95% CI of the ARR.

Thus, unmeasured confounding by obesity is unlikely to meaningfully impact the observed findings in US patients.

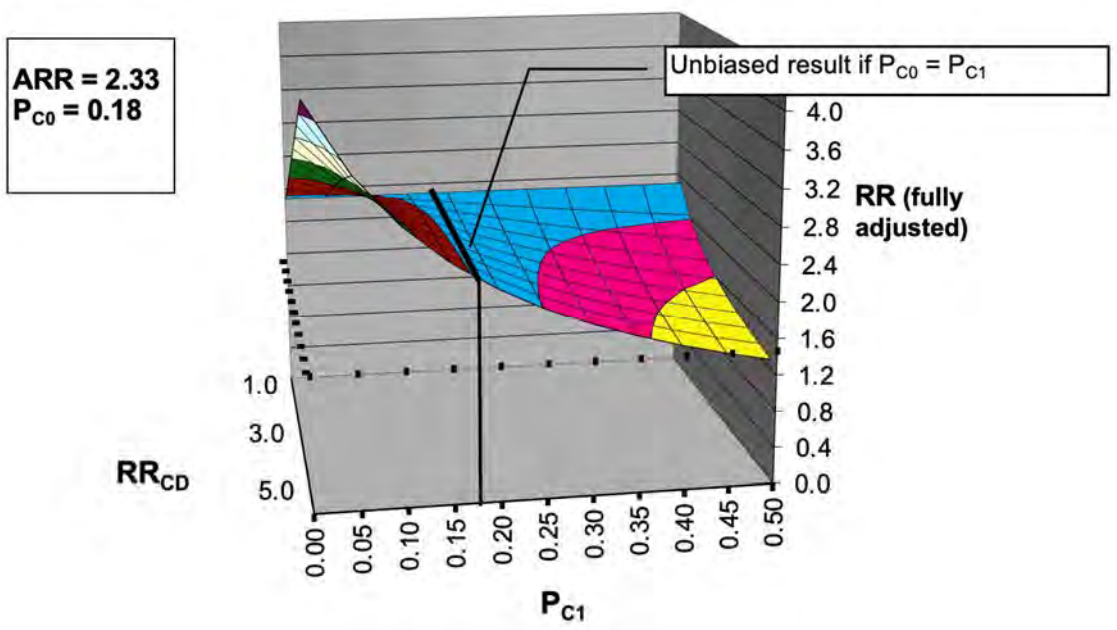
French Patients

The prevalence of obesity assumed for the reference TNFi cohort and, for context, the strength of obesity as a risk factor for MACE ('RR_{CD}' in the figure), are presented in Table 10.17. The unadjusted or observed IRR ('ARR' in the figure) is based on the comparative analysis of French patients reported in Table 55_SNDS.

Table 10.17. Prevalence of Obesity Among RA Patients and Strength of Obesity as a Risk Factor for MACE

RA Population Sample	Prevalence of Obesity in the Unexposed Patients with RA	RR Between Obesity and MACE	ARR Point Estimate we Observed, any BARI Dose	ARR LCL	ARR UCL
ESPOIR	16.1%	2.04	2.33	1.15	4.74
CORPUS	20.0%	2.04	2.33	1.15	4.74
Average	18.0%	2.04	2.33	1.15	4.74

Abbreviations: ARR = apparent relative risk (ie, the incidence rate ratio); BARI = baricitinib; CORPUS = Cohorte d'Observation Rheumatologique des Pratiques et des Usages; ESPOIR = Etude et Suivi des Polyarthrites Indifférenciées Récentes LCL = lower confidence limit; MACE = major adverse cardiovascular event; RA = rheumatoid arthritis; RR = relative risk; UCL = upper confidence limit.



Abbreviations: ARR = apparent relative risk (ie, incidence rate ratio, IRR); MACE = major adverse cardiovascular events; PC_0 = prevalence in unexposed (ie, TNFi reference group); PC_1 = prevalence in exposed (ie, baricitinib group); RA = rheumatoid arthritis; relative risk (ie, IRR after adjusting for potential bias); RR_{CD} = relative risk between potential confounder and outcome (ie, obesity and MACE).

Figure 10.16. Sensitivity analysis for unmeasured confounding by obesity on the effect of baricitinib on MACE in French patients with RA.

Across all scenarios, the RR adjusted to remove the effect of bias ranged from 1.3 to 4.2. In the strongest bias scenario, 79%, when RR_{CD}=5.5 and the prevalence of the confounder in the exposed baricitinib group is 50%, the RR adjusted for bias is 1.3. The scenario where the adjusted RR was 4.2 included an RR_{CD} = 5.5 and the prevalence of the confounder in the exposed group = 0%. Compared with the range of potential values of the adjusted RR from this analysis, the CI of the ARR is largely overlapping.

If a value of RR_{CD} from the literature (ie, RR_{CD}=2.04), is used instead, an adjusted RR=2.8 occurs when the prevalence of obesity in the exposed is 0% and an adjusted RR=1.8 when the prevalence of obesity in the exposed population is 50%. These values are in the 95% CI for the ARR.

Thus, it is unlikely that unmeasured confounding by obesity meaningfully impacts the results observed.

10.5.2.3. Disease severity

US Patients

The prevalence of high disease activity (ie, DAS28 >5.2), assumed in the reference TNFi cohort and, for context, the strength of high disease activity as a risk factor for MACE ('RR_{CD}' in the figure) are in Table 10.18. The unadjusted or observed IRR ('ARR' in the figure) is based on the meta-analysis of US data in Figure 10.23.

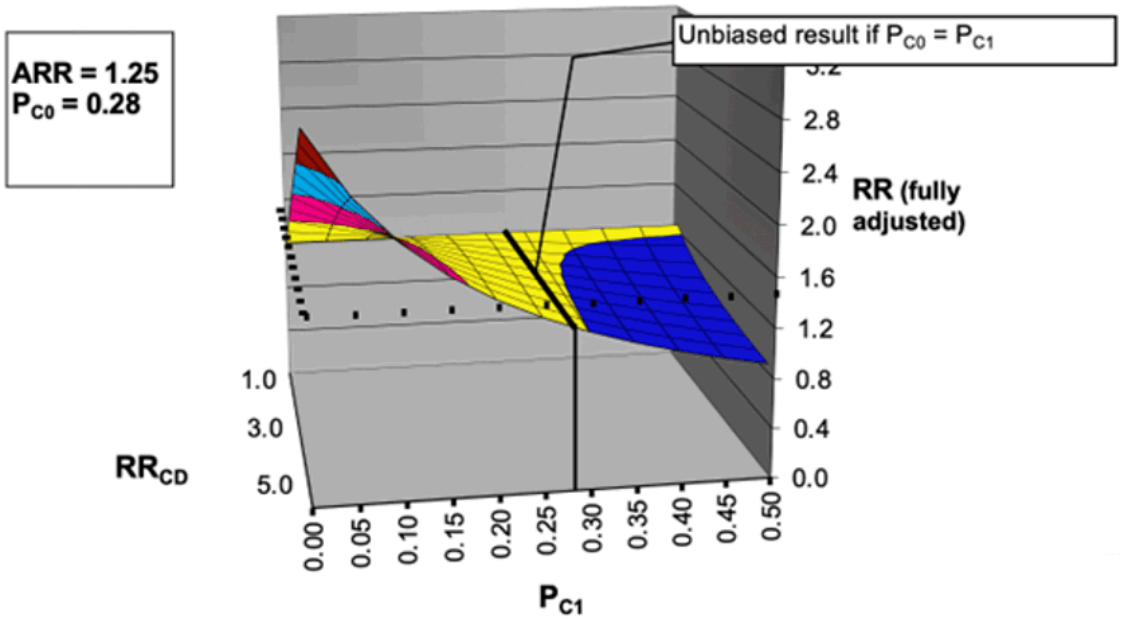
Table 10.18. Values Used in RA Disease Severity and MACE, US Data Meta-Analysis

Prevalence of High Disease Activity in Patients with RA (CDAI[a])	RR Between High Disease Activity and VTE	ARR Point Estimate we Observed	ARR LCL	ARR UCL
28.0%	2.99[b]	1.25	0.52	3.05

Abbreviations: ARR = apparent relative risk; CDAI = clinical disease activity index; LCL = lower confidence limit; MACE = major adverse cardiovascular event; RA = rheumatoid arthritis; RR = relative risk; UCL = upper confidence limit; VTE = venous thromboembolism.

[a] High disease activity is defined as CDAI >22.1.

[b] Yoshida et al. 2022.



Abbreviations: ARR = apparent relative risk (ie, incidence rate ratio, IRR); MACE = major adverse cardiovascular events; PC_0 = prevalence in unexposed (ie, TNFi reference group); PC_1 = prevalence in exposed (ie, baricitinib group); RA = rheumatoid arthritis; RR = relative risk (ie, IRR after adjusting for potential bias); RR_{CD} = relative risk between potential confounder and outcome (ie, disease severity and MACE).

Figure 10.17. Sensitivity analysis of unmeasured confounding by RA disease severity for the effect of baricitinib on MACE in US patients with RA.

Across all scenarios, the RR adjusted to remove the effect of bias ranged from 0.9 to 2.8. In the strongest bias scenario, -56%, when the RR_{CD}=5.5 and the prevalence of the confounder in the exposed baricitinib group is 0%, the RR adjusted for bias =2.8. The scenario where the adjusted RR was 0.9 included an RR_{CD}=5.5 and the prevalence of the confounder in the exposed group is 50%. Compared with the range of potential values of the adjusted RR from this analysis, the CI of the ARR includes both of these values.

If the RR_{CD}, or strength of the risk factor, reported in the literature is used instead (ie, RR_{CD}=2.99), an adjusted RR=2.0 occurs when the prevalence of high disease activity in the exposed group is 0% and an adjusted RR=1.0 when the prevalence of smoking in the exposed cohort is 50%. These values are well within the 95% CIs of the ARR.

Thus, unmeasured confounding by high disease activity (ie, CDAI >22.1), is unlikely to meaningfully impact the observed findings in US patients.

French Patients

The prevalence of high disease activity assumed for the reference TNFi cohort is indicated with a solid line in Figure 10.18 and presented in Table 10.19. The strength of high disease activity as a risk factor for MACE in French patients ('RR_{CD}' in the figure) is also included, for context. The unadjusted or observed IRR ('ARR' in the figure) is based on the IRR for French patients from Table 55_SNDS.

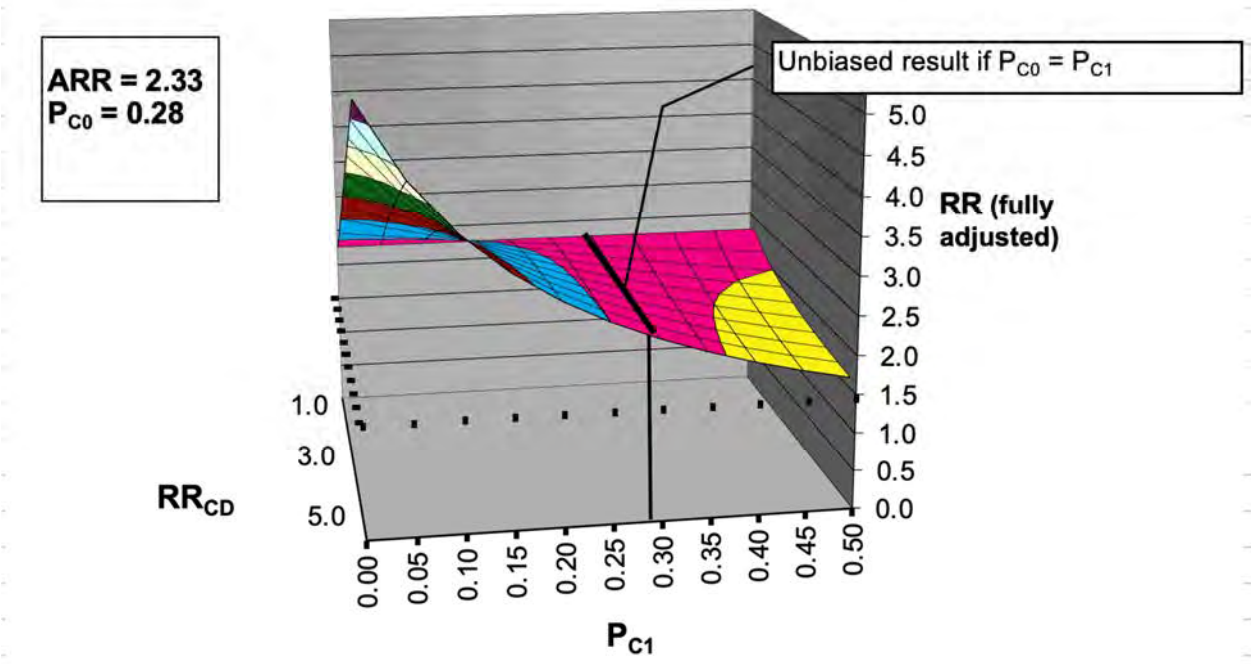
Table 10.19. Values Used in RA Disease Severity and MACE, French Analysis

Prevalence of High RA Disease Activity[a] in Patients with RA (CDAI)	RR Between Disease Activity and MACE	ARR Point Estimate we Observed, Any BARI Dose	ARR LCL	ARR UCL
28.0%	2.99[b]	2.33	1.15	4.74

Abbreviations: ARR = apparent relative risk; BARI = baricitinib; CDAI = clinical disease activity index; LCL = lower confidence limit; MACE = major adverse cardiovascular event; RA = rheumatoid arthritis; RR = relative risk; UCL = upper confidence limit.

[a] High disease activity is defined as CDAI >22.1.

[b] Yoshida et al. 2022.



Abbreviations: ARR = apparent relative risk (ie, incidence rate ratio, IRR); MACE = major adverse cardiovascular events; PC_0 = prevalence in unexposed (ie, TNFi reference group); PC_1 = prevalence in exposed (ie, baricitinib group); RA = rheumatoid arthritis; RR = relative risk (ie, IRR after adjusting for potential bias); RR_{CD} = relative risk between potential confounder and outcome (ie, obesity and VTE).

Figure 10.18. Sensitivity analysis of unmeasured confounding by RA disease severity for the effect of baricitinib on MACE in French patients with RA.

Across all scenarios, the RR adjusted to remove the effect of bias ranged from 1.6 to 5.3. In the strongest bias scenario, -56%, when the RR_{CD}=5.5 and the prevalence of the confounder in the exposed baricitinib group is 0%, the RR adjusted for bias =5.3. The scenario where the adjusted RR was 1.6 included RR_{CD}=5.5 and the prevalence of the confounder in the exposed group is 50%. Compared with the range of potential values of the adjusted RR from this analysis, the CI of the ARR includes the lower bound of the 95% CI and is close to, though higher than, the upper bound of the 95% CI of the ARR at 4.74. In order for the RR=5.3 to be true, the prevalence of high disease activity must be 28.4% in the 'unexposed' TNFi group and 0% in the 'exposed' baricitinib group. This is an unlikely scenario and contrary to the expectation that patients treated with baricitinib may have more refractory, severe disease.

If the RR_{CD} or strength of the risk factor reported in the literature is used instead (ie, RR_{CD}=2.99), an adjusted RR=3.7 occurs when the prevalence of high disease activity in the exposed group is 0% and an adjusted RR=1.8 when the prevalence of high disease activity in the exposed cohort is 50%. These values are well within the 95% CIs of the ARR.

Thus, unmeasured confounding by high disease activity is unlikely to meaningfully impact the observed findings in French patients.

10.6. Meta-analysis

Results from 14 data sources on the comparative risk of VTE, MACE, or serious infection are summarized using 2 measures. First, a modified Poisson regression was conducted to generate an $IRR_{meta\text{-}analysis}$ summarizing comparative results from all 14 data sources. This option was selected rather than a summary of Cox regression results (see Section 9.9.6) since it allowed inclusion of person-time from all data sources, even those with 0 events overall or 0 events in the TNFi cohort. Second, a supplemental analysis was adopted to report the difference in risk, $IRD_{meta\text{-}analysis}$, between treatment cohorts. These measures provide distinct but complementary information. The ratio of incidence rates is used most often in epidemiological studies evaluating risk due to an exposure, while the incidence rate difference may be considered as a measure of the excess (or reduced) number of cases that would be expected if treatment with baricitinib was truly associated with the outcome under investigation. RD may also be expressed as the number needed to treat (NNT), but Lilly reserves this presentation for exposure/outcome associations that are established as being causal.

The 3 largest data sources, ARTIS, SNDS, and BKK, contributed approximately 80% of the total exposures and events (VTE 80%, MACE 85%) for the study. Due to the limited exposures and wide CIs from the majority of data sources, the only sensitivity analysis conducted was to stratify analyses by the region of the data (ie, US or OUS (Section 10.6.1).

Comparative Meta-Analysis Results

VTE

Meta-analysis of VTE based on individual results from 14 data sources estimated a summary IRR = 1.51 (95% 1.10, 2.08) and IRD = 0.26 (-0.04, 0.57), shown in Figure 10.1 and Figure 10.2, respectively. Table 10.3 also lists results by data source, as available based on the number of events. HR could be estimated from 6 and IRR from 8 data sources. There were no meaningful differences between HR and IRR estimated from a given data source. Results from the Swedish ARTIS data and the French SNDS, with 39% and 32% of total baricitinib exposure, respectively, had point estimates that were numerically greater for baricitinib vs. TNFi treatment (IRR_{ARTIS} = 1.85; 95% CI 0.95, 3.60 and IRR_{SNDS} = 1.59; 95% CI 0.79, 3.21). With 9% of total baricitinib exposure, the IRR from German BKK data was 0.50, but the CI was wide (95% CI 0.13, 2.02).

MACE

Meta-analysis of MACE based on individual results from 14 data sources estimated a summary IRR = 1.54 (95% 0.93, 2.54) and IRD = 0.22 (95% CI -0.07, 0.52), and are shown in Figures Figure 10.3 and Figure 10.4. Table 10.3 also lists results by data source, as available based on the number of events. HR were estimable from 6 data sources and IRR from 7. There were no meaningful differences between HR and IRR estimated from a given data source. Results from

the French SNDS data, with 32% of total baricitinib exposure, suggest a significant increase in risk (IRR_{SNDS} = 2.33; 95% CI 1.15, 4.74). In the Swedish ARTIS data, with 39% of total baricitinib exposure, no increase in risk is observed (IRR_{ARTIS} = 0.94; 95% CI 0.45, 1.96).

Serious infections

Meta-analysis of serious infections based on individual results from 14 data sources estimated a summary IRR = 1.36 (95% CI 0.86, 2.13) and IRD = 0.57 (95% CI -0.07, 1.21), and are shown in Figure 10.5 and Figure 10.6, respectively. Table 10.4 also lists results by data source, as available based on the number of events. HR could be estimated from 6 and IRR from 7 data sources. There were not meaningful differences between HR and IRR estimated from a given data source. In the Swedish ARTIS data (38% of total baricitinib exposure) and the smaller German data (10% of baricitinib exposure), results suggest a larger (and significant: ARTIS) increase in risk (IRR_{ARTIS} = 1.65; 95% CI 1.20, 2.26 and IRR_{BKK} = 1.44; 95% CI 0.69, 3.02). In French patients, with the second greatest baricitinib exposure (32% of total) no increase in risk was observed (ie, IRR_{SNDS}=1.04; 95% CI 0.65, 1.65), IRD_{SNDS} = 0.07; 95% CI -0.77, 0.91).

10.6.1. Sensitivity analysis: Meta-analysis by geographic region

Additional meta-analyses were executed to estimate overall risk of VTE (Section 10.6.1.1), MACE (Section 10.6.1.2), and serious infection (Section 10.6.1.3) in data from US patients and from non-US data. Table 10.20 summarizes results presented in Figure 10.19 through Figure 10.30.

Overall, based on the meta-analysis for VTE, exposures contributed by US data sources (818.22 PY) represent only a fraction (13.9%) of the total evaluated in the study, especially compared to exposures contributed by European data sources (5061.12 PY). This is important to consider when assessing results from each region. Given the range of uncertainty estimated for each outcome in the 2 regions, differences in the point estimates for IRR and IRD between regions are not meaningful.

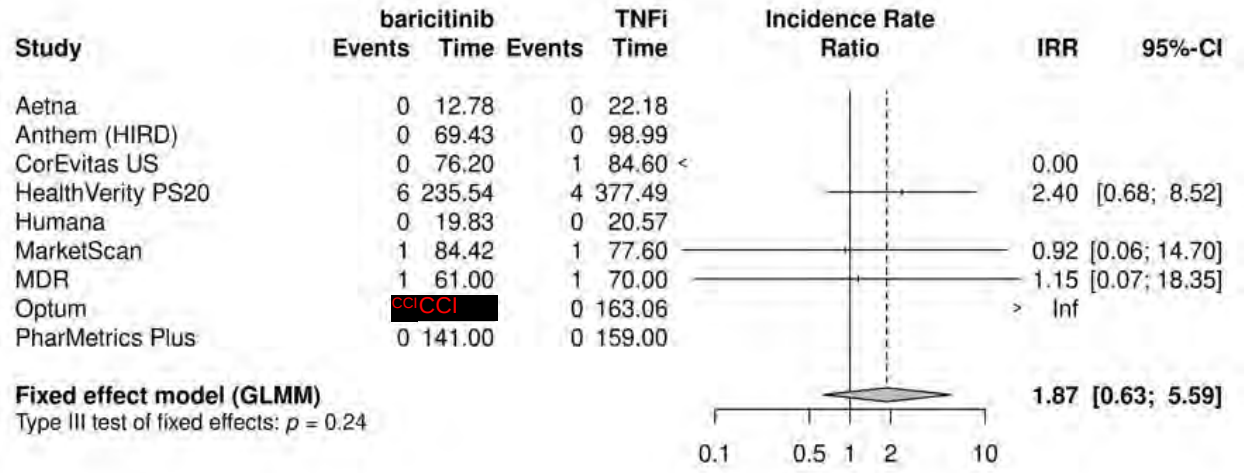
Table 10.20. Summary of Meta-Analysis Results (IRD and IRR), by Geographic Region

Outcome	US (818.22 PY of baricitinib exposure)[a]		Europe and Japan (5061.12 PY of baricitinib exposure)[a]	
	IRD (95% CI) per 100 PY	IRR (95% CI)	IRD (95% CI) per 100 PY	IRR (95% CI)
VTE	0.31 (-0.55, 1.17)	1.87 (0.63, 5.59)	0.24 (-0.11, 0.59)	1.45 (1.02, 2.08)
MACE	0.28 (-0.60, 1.17)	1.25 (0.52, 3.05)	0.27 (-0.16, 0.71)	1.61 (0.86, 3.01)
Serious infection	0.24 (-1.05, 1.53)	1.07 (0.67, 1.73)	0.68 (-0.34, 1.69)	1.40 (0.80, 2.47)

Abbreviations: CI = confidence interval; IRD = incidence rate difference; IRR = incidence rate ratio; MACE = major adverse cardiovascular event; PY = person-years; VTE = venous thromboembolism.

[a] Baricitinib exposure is based on the propensity score-matched cohort generated for analysis of VTEs. Baricitinib exposure was similar in analyses of other outcomes.

10.6.1.1. VTE



Abbreviations: CI = confidence interval; GLMM = generalised linear mixed model; HIRD = HealthCore Integrated Research Database; IRR = incidence rate ratio; MDR = Military Data Repository; PS20 = Private Source 20; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

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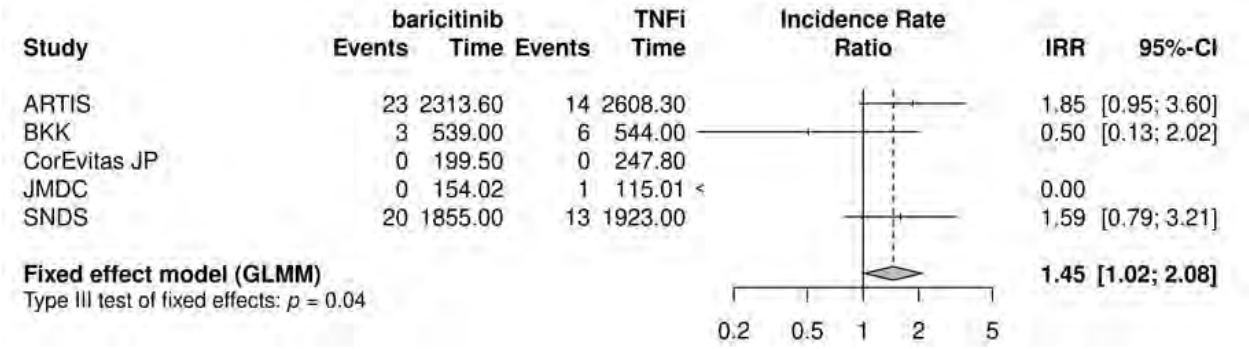
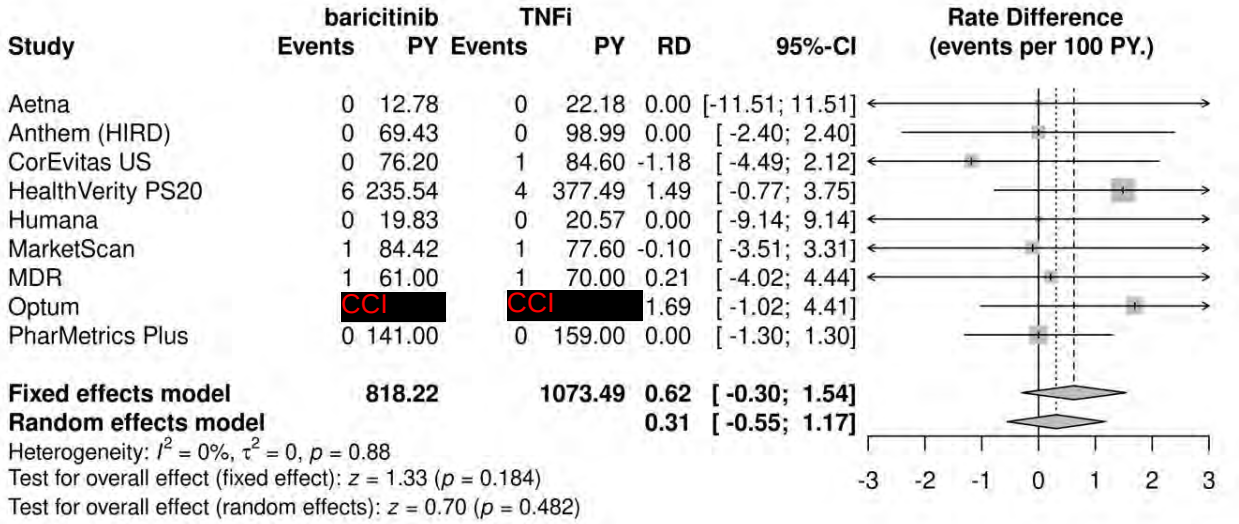
Figure 10.19. Incidence rate ratios comparing VTE in US patients treated with baricitinib versus TNFi.



Abbreviations: BKK = Brietriebskrankenkasse; CI = confidence interval; GLMM = generalised linear mixed model; IRR = incidence rate ratio; JMDC = Japanese Medical Data Center, Inc.'s claims database; JP = Japan; SNDS = Système National des Données de Santé; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.
Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\irr_vte_14ds_OUS.png

Figure 10.20. Incidence rate ratios comparing VTE in non-US patients treated with baricitinib versus TNFi.

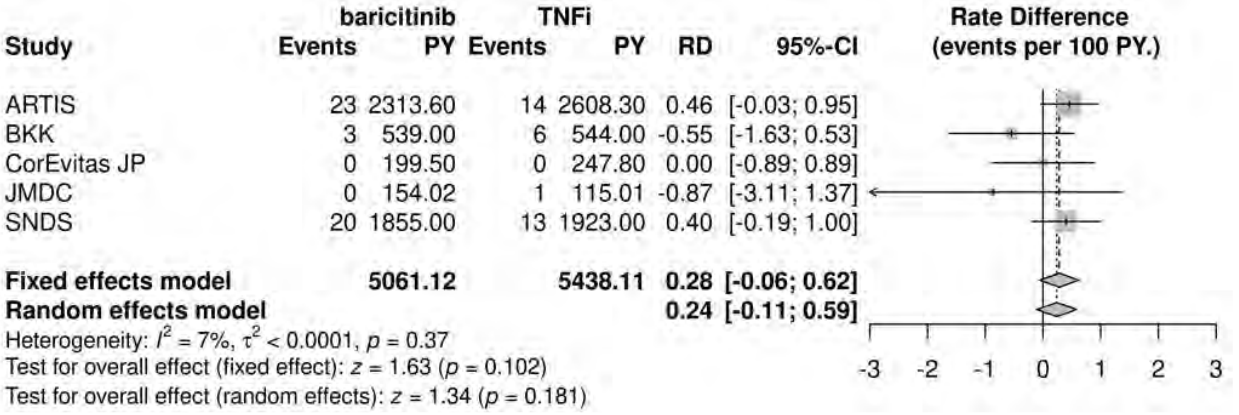


Abbreviations: CI = confidence interval; HIRD = HealthCore Integrated Research Database;MDR = Military Data Repository; PS20 = Private Source 20; PY = person-years; RD = incidence rate difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Any differences between CIs for the individual incidence rate differences reported here and in Section 10.3 are due to different methods used for the calculation.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\final_ird_vte3_us.png

Figure 10.21. Differences in VTE incidence rates between US patients treated with baricitinib and TNFi.



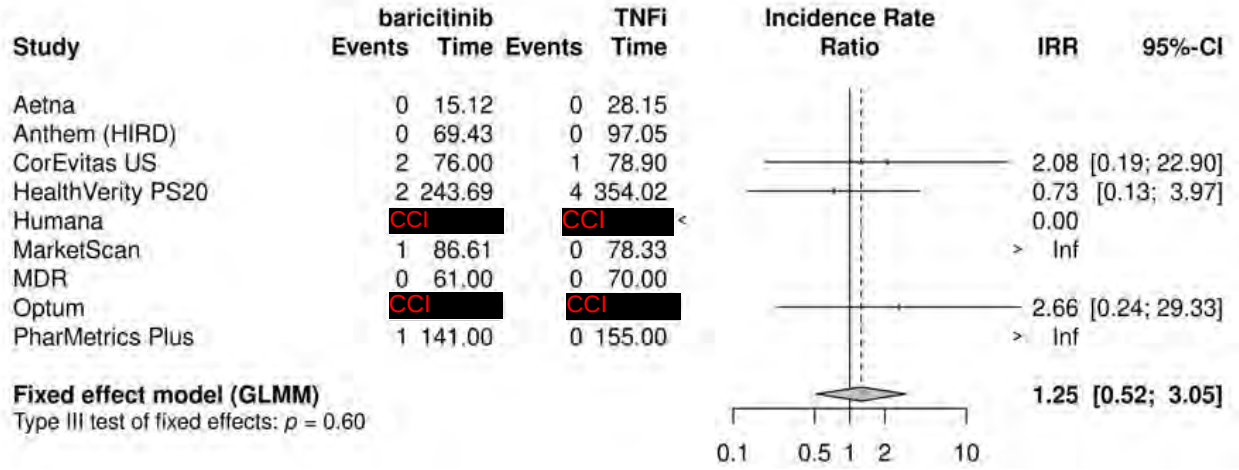
Abbreviations: BKK = Betriebskrankenkasse; CI = confidence interval; JMDC = Japanese Medical Data Center, Inc.'s claims database; JP = Japan; RD = incidence rate difference; PY = person-years; SNDS = Système National des Données de Santé; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Any differences between CIs for the individual incidence rate differences reported here and in Section 10.3 are due to different methods used for the calculation.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\final_ird_vte3_ous.png

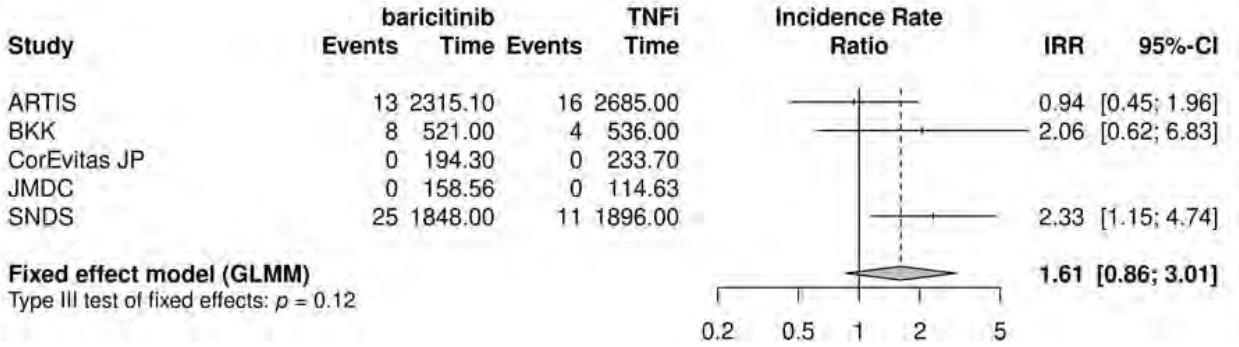
Figure 10.22. Differences in VTE incidence rates between non-US patients treated with baricitinib and TNFi.

10.6.1.2. MACE



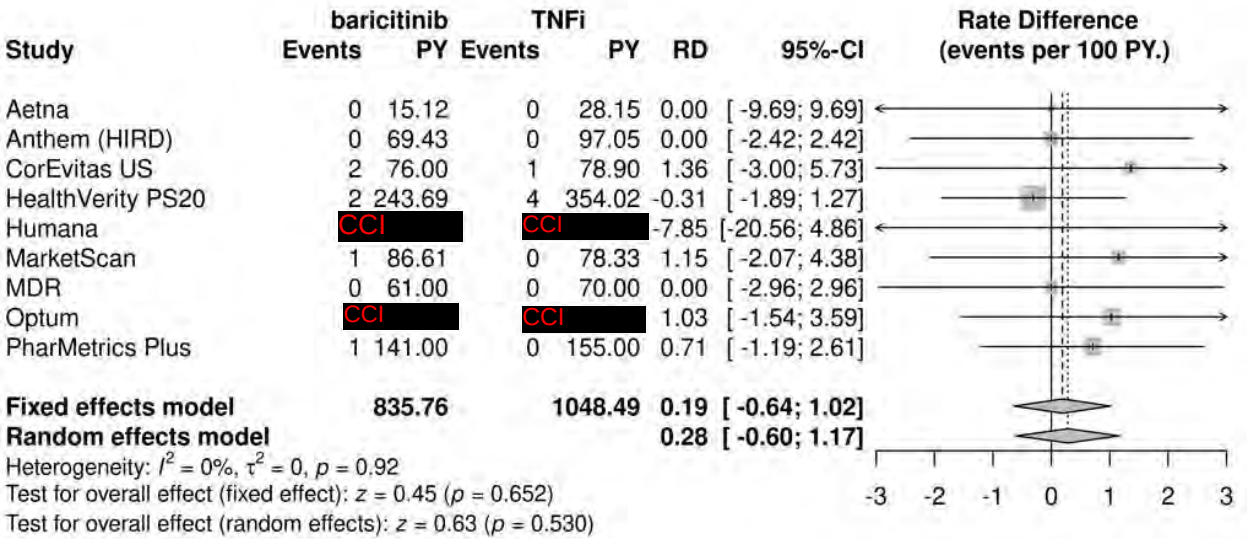
Abbreviations: CI = confidence interval; GLMM = generalised linear mixed model; HIRD = HealthCore Integrated Research Database; Inf = infinity; IRR = incidence rate ratio; MACE = major adverse cardiovascular event; MDR = Military Data Repository; PS20 = Private Source 20; TNFi = tumour necrosis factor inhibitor.
Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\irr_mace_14ds_US.png

Figure 10.23. Incidence rate ratios comparing MACE in US patients treated with baricitinib versus TNFi.



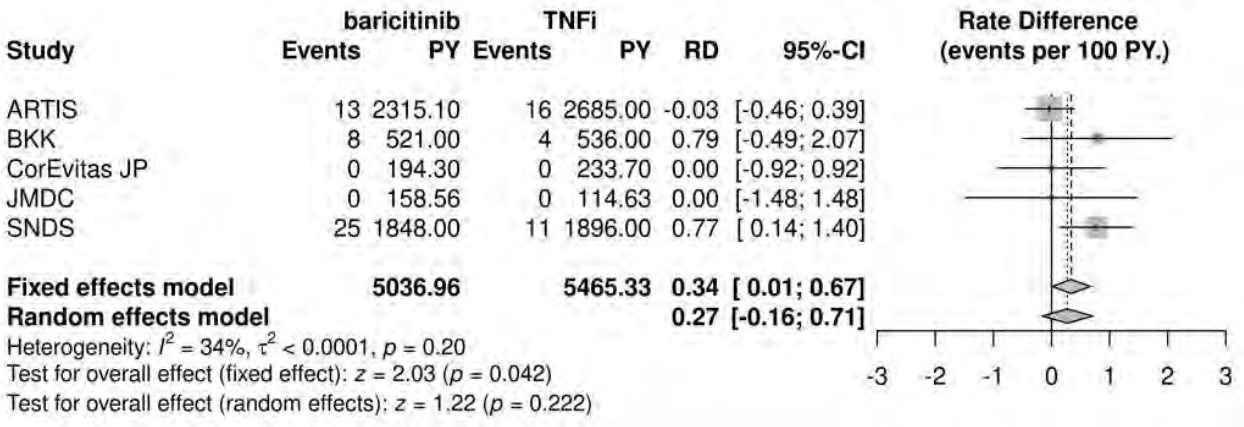
Abbreviations: BKK = Betriebskrankenkasse; CI = confidence interval; GLMM = generalised linear mixed model; IRR = incidence rate ratio; JMDC = Japanese Medical Data Center, Inc.'s claims database; JP = Japan; MACE = major adverse cardiovascular event; SNDS = Système National des Données de Santé; TNFi = tumour necrosis factor inhibitor.
Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\irr_mace_14ds_OUS.png

Figure 10.24. Incidence rate ratios comparing MACE in non-US patients treated with baricitinib versus TNFi.



Abbreviations: CI = confidence interval; HIRD = HealthCore Integrated Research Database; MACE = major adverse cardiovascular event; MDR = Military Health Data Repository; PS20 = Private Source 20; PY = person-years; RD = incidence rate difference; TNFi = tumour necrosis factor inhibitor.
Note: Any differences between CIs for the individual incidence rate differences reported here and in Section 10.3 are due to different methods used for the calculation.
Source:
lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\final_ird_mace3_us.png

Figure 10.25. Differences in MACE incidence rates between US patients treated with baricitinib and TNFi.



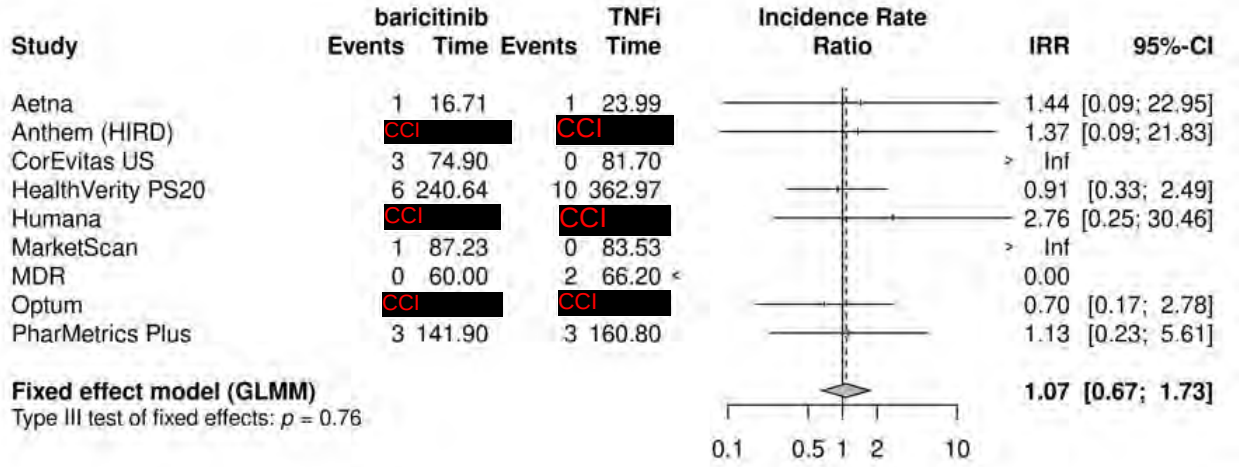
Abbreviations: BKK = Betriebskrankenkasse; CI = confidence interval; JMDC = Japanese Medical Data Center, Inc.'s claims database; JP = Japan; MACE = major adverse cardiovascular event; PY = person-years; RD = incidence rate difference; SNDS = Système National des Données de Santé; TNFi = tumour necrosis factor inhibitor.

Note: Any differences between CIs for the individual incidence rate differences reported here and in Section 10.3 are due to different methods used for the calculation.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\final_ird_mace3_ous.png

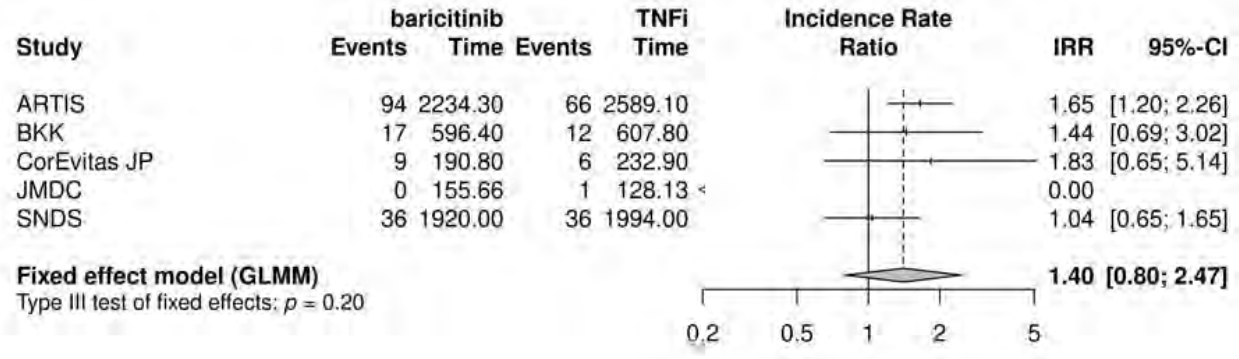
Figure 10.26. Differences in MACE incidence rates between non-US patients treated with baricitinib and TNFi.

10.6.1.3. Serious infection



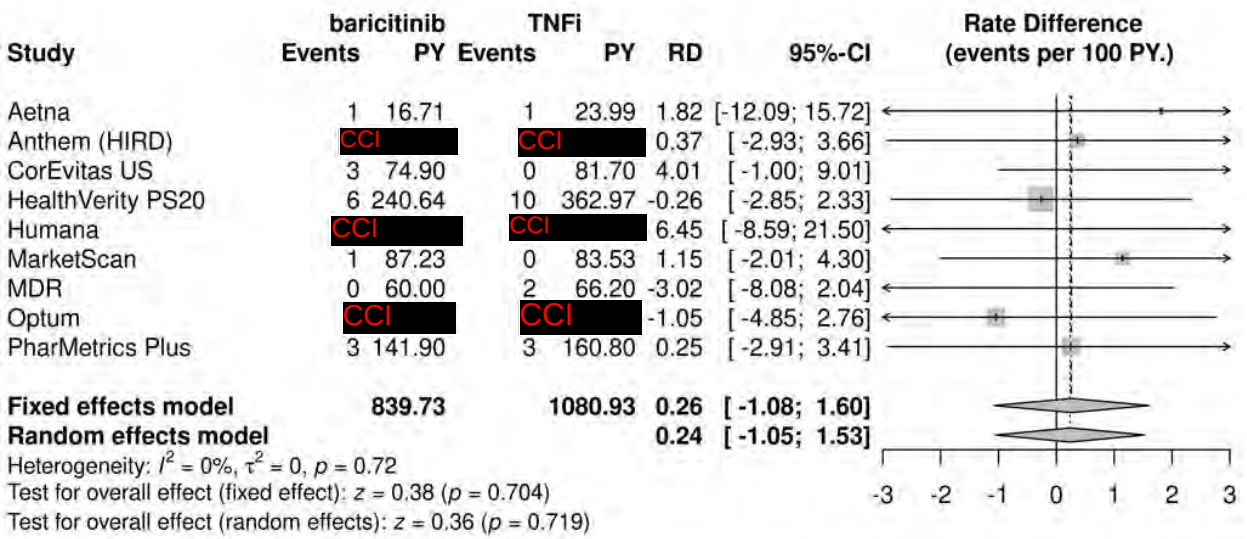
Abbreviations: CI = confidence interval; GLMM = generalized linear mixed model; HIRD = HealthCore Integrated Research Database; IRR = incidence rate ratio; MDR = Military Data Repository; PS20 = Private Source 20; TNFi = tumour necrosis factor inhibitor.
Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\irr_si_14ds_US.png

Figure 10.27 Incidence rate ratios comparing serious infections in US patients treated with baricitinib versus TNFi.



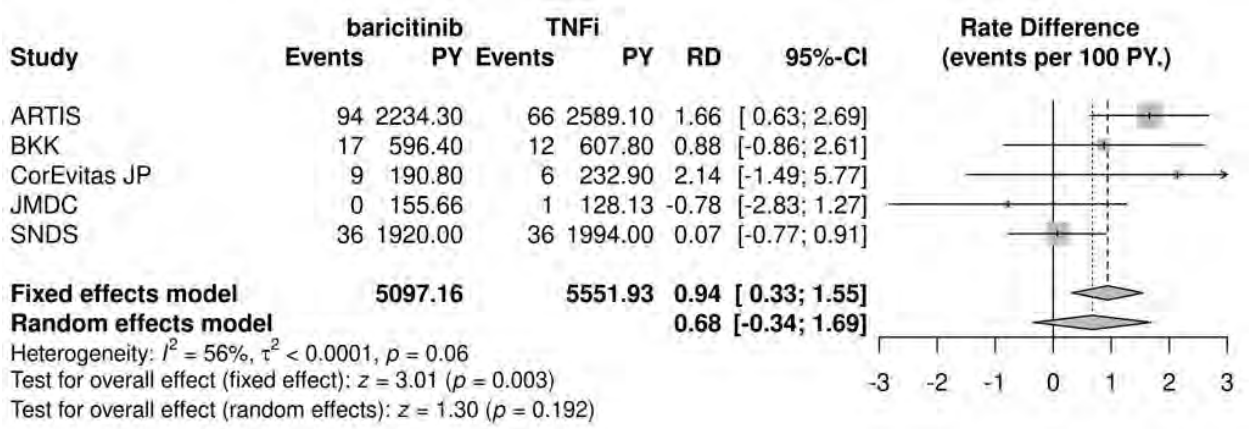
Abbreviations: BKK = Betriebskrankenkasse; CI = confidence interval; GLMM = generalised linear mixed model; IRR = incidence rate ratio; JMDC = Japanese Medical Data Center, Inc.'s claims database; JP = Japan; SNDS = Système National des Données de Santé; TNFi = tumour necrosis factor inhibitor.
Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\irr_si_14ds_OUS.png

Figure 10.28. Incidence rate ratios comparing serious infections in non-US patients treated with baricitinib versus TNFi.



Abbreviations: CI = confidence interval; HIRD = HealthCore Integrated Research Database; MDR = Military Data Repository; PS20 = Private Source 20; PY = person-years; RD = incidence rate difference; TNFi = tumour necrosis factor inhibitor.
Note: Any differences between CIs for the individual incidence rate differences reported here and in Section 10.3 are due to different methods used for the calculation.
Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\final_ird_si3_us.png

Figure 10.29. Differences in serious infection incidence rates between US patients treated with baricitinib and TNFi.



Abbreviations: BKK = Betriebskrankenkasse; CI = confidence interval; JMDC = Japan Medical Data Center, Inc.'s claims database; JP = Japan; PY = person-years; RD = incidence rate difference; SNDS = Système National des Données de Santé; TNFi = tumour necrosis factor inhibitor.
Note: Any differences between CIs for the individual incidence rate differences reported here and in Section 10.3 are due to different methods used for the calculation.
Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\final_ird_si3_ous.png

Figure 10.30. Differences in serious infection incidence rates between non-US patients treated with baricitinib and TNFi.

10.7. Adverse events/adverse reactions

This is a non-interventional study based on secondary data (ie, data previously collected for other purposes) and therefore no individual case safety report collection or reporting of AEs to agencies is required.

The study evaluated VTE, MACE, and serious infection as summarized in this report. No other AEs were evaluated.

11. Discussion

11.1. Key results

Using postmarketing data from 14 data sources across Europe, US, and Japan, this study aimed to evaluate the safety of patients with RA treated with baricitinib in comparison to those treated with TNFi for risk of VTE, MACE, serious infection, addressed by a meta-analysis to combine results across data sources.

Comparing the risk of each event between baricitinib and TNFi-treated cohorts, results are as follows

VTE:

- IRR was significantly elevated overall (IRR=1.51; 95% CI 1.10, 2.08).
    - Risk of VTE was numerically greater but not statistically significant, in the two largest data sources, which contributed approximately two-thirds of exposure to the meta-analysis, (IRR_{ARTIS} = 1.85; 95% CI 0.95, 3.60 and IRR_{SNDS} = 1.59; 95% CI 0.79, 3.21).
- IR was greater among patients treated with baricitinib than with TNFi, the difference was 0.26 (95% CI -0.04, 0.57) per 100 PY. This IRD did not reach statistical significance since the CI includes 0.

MACE:

- IRR was numerically greater for baricitinib compared to TNFi but did not attain statistical significance (IRR = 1.54; 95% CI 0.93, 2.54).
    - A statistically significantly increased risk of MACE was found in SNDS (IRR_{SNDS} =2.33; 95% CI_{SNDS} 1.15, 4.7) and not in the largest data source (IRR_{ARTIS} = 0.94; 95% CI_{ARTIS} 0.5, 1.96)).
- IR was greater among patients treated with baricitinib than with TNFi, the difference was 0.22 (95% CI -0.07, 0.52) per 100 PY. This IRD was not statistically significant since the CI includes 0.

Serious infection:

- IRR was numerically greater for baricitinib compared to TNFi but did not attain statistical significance (IRR= 1.36; 95% CI 0.86, 2.13).
    - A statistically significantly increased risk of serious infection was found in the largest data source (IRR_{ARTIS} = 1.65; 95% CI 1.20, 2.26) and not in the second largest (IRR_{SNDS} = 1.04; 95% CI_{SNDS} 0.65, 1.65).
- IR was greater among patients treated with baricitinib than with TNFi, the difference was 0.57 (95% CI -0.07, 1.21) per 100 PY. This IRD did not reach statistical significance since the CI includes 0.

Hospitalized TB

No comparison was planned to evaluate risk of hospitalized TB, only a description. No events of TB were observed among 9382 eligible unmatched patients with over 6800 PY of exposure to baricitinib.

Potential bias

This study was not able to account for potential differences in the prevalence of BMI, smoking or disease severity in the comparison of treatment groups. Since these are important risk factors for the outcomes evaluated, we cannot exclude the possibility that results may be biased. This would occur if one treatment group had a greater prevalence of risk factors at baseline than the other. One way this could happen is when physicians assign or 'channel' treatment to patients based on certain risk factors for a given outcome, this can result in channelling bias. However, based on quantitative evaluation of the magnitude of potential bias that could have occurred it is unlikely that results were meaningfully impacted by not controlling for these factors. As an example with serious infection in the ARTIS data, an analysis that controlled for DAS28 did not differ to an important extent from the main study result, which did not account for disease severity ($IRR_{ARTIS, adjusted}$ = 1.72, 95% CI 1.24, 2.39 vs. the reported $IRR_{ARTIS, serious\ infection}$ = 1.61, 95% CI 1.15, 2.24) (Section 10.3.2.1.3.1). This sensitivity analysis could not be conducted for VTE or MACE because there were too few events across DAS28 categories.

11.2. Interpretation

This study was designed to address the question of whether baricitinib treatment is a risk for VTE, MACE, or serious infection in patients with RA compared to TNFi. Data from over 7,606 patients (5879.2 PY) treated with baricitinib from 14 data sources across the US, Europe, and Japan, was compared to data from similar patients treated with TNFi (6511.7 PY).

This multi-database multi-country study is the largest investigation of VTE, MACE, and serious infections among patients treated with baricitinib in a real-world setting. However, there are some considerations that should temper interpretation of results, including a small number of observed events and the large contribution to the meta-analysis from two data sources. Almost half of data sources reported zero VTE or MACE events for either baricitinib or TNFi cohorts. The two largest data sources, ARTIS and SNDS were from Europe and together contributed 71% of the total baricitinib exposure time and 72 or 70% of all VTE or MACE evaluated, respectively. Combined, all 9 US data sources contributed 14% of baricitinib exposure, highlighting the limited information available from this region. Exposures contributed to other outcomes were similar.

Overall study findings suggest a statistically significant association between baricitinib and risk of VTE. Overall meta-analysis estimates of MACE and serious infection risk were also elevated with baricitinib treatment.

VTE

Patients with RA are at increased risk of several comorbidities, including VTE. Risk estimates from several studies suggest an approximate doubling of the risk of VTE for people with RA compared to the general population (Choi et al. 2013; Holmqvist et al. 2012; Matta et al. 2009), although a recent Canadian study reported a smaller increase (HR=1.28; Li et al. 2021). The mechanism behind this increased risk is not entirely clear, but systemic inflammation is a hallmark of rheumatoid arthritis and affects at least two components of Virchow's triad required for thrombosis: hypercoagulability and endothelial dysfunction (Reitsma et al. 2012).

The largest analysis assessing VTE risk with baricitinib treatment describes the experience of 3770 patients who contributed 14,744 PY of baricitinib exposure in the baricitinib clinical development trials. In a summary of safety in these patients, Taylor et al. (2022) reported a VTE incidence rate of 0.49 (95% CI 0.38, 0.61) per 100 PY, which is approximately half that observed in the largest Swedish ARTIS and French SNDS baricitinib cohorts in the current study. Since the patient populations included in clinical trials are likely to differ from patients under routine care in the current study, comparisons of the rate reported by Taylor et al and in this study should be made cautiously if at all. While the analysis presented by Taylor et al provides an estimate of absolute risk in the clinical trial population, no comparative measure is reported to inform on the magnitude of risk relative to a similar population untreated with baricitinib. This is because a comparator arm was available for only a fraction of the total follow-up available and different trials had different comparator arms. ORAL Surveillance is a randomized clinical trial of JAKi in patients with RA that was designed to collect and compare information about the CV safety of tofacitinib versus TNFi, including VTE (Ytterberg et al. 2022). In these patients enriched for baseline risk of CV events, the incidence rate of VTE (PE or DVT) among patients treated with tofacitinib 5 mg BID (the standard dose for patients with RA) or TNFi was 0.33 (95% CI 0.19, 0.53) and 0.20 (95% CI 0.10, 0.37) per 100 PY, respectively (Charles-Shoeman et al. 2021; Note: IR and confidence intervals were manually calculated using Fisher's exact formula and event numbers and person-time reported in this reference). An increased but non-significant risk of VTE (HR = 1.66; 95% CI 0.76, 3.63) was seen for patients in the 5 mg BID compared to the TNFi arm, slightly greater than the magnitude of risk observed in patients under routine care in the B023 study. ORAL Surveillance also showed a difference in the magnitude of the effect between doses with a greater and significantly elevated risk of VTE among patients with RA treated with 10 mg BID (HR = 3.52; 95% CI 1.74, 7.12) vs. 5 mg BID. Although both doses of baricitinib used to treat RA were included in the current B023 study, treatment effects by dose were not evaluated separately due to the limited exposure and should not be compared with each other since the baricitinib and TNFi cohorts were propensity-score matched overall and not by dose.

MACE

Inflammation is strongly implicated in atherosclerosis progression and substantial evidence exists showing an increased risk of CV disease in people with RA (Skeoch and Bruce 2015; Roifman et al. 2011) including increased cardiac mortality, which has been recognized for many

decades (Meune et al. 2009). Medications used to treat RA reduce inflammation, but the effects on CV risk differ across drugs. NSAIDs and glucocorticoids appear to increase risk, while some studies have shown a protective effect of treatment with methotrexate and other DMARDs, particularly TNFi (Singh et al. 2020; Roubille et al. 2015). Few studies have evaluated the risk of MACE associated with JAK inhibitors.

Taylor et al reported on the safety of baricitinib using the integrated data from patients receiving any baricitinib dose in the development studies. The incidence rate of MACE was 0.5 (95% CI 0.40, 0.64) per 100 PY based on 14,744 PY of treatment. This is similar to the rate observed in the ARTIS data (IR=0.56 per 100 PY) and approximately one-third the rate observed in the SNDS (IR=1.4, 95% CI 0.9, 2.0 per 100 PY) and BKK (IR = 1.5, 95% CI 0.7, 3.0 per 100 PY) populations. It is important to note that while MACE in clinical trials include CV death, it is not part of the MACE definition in this study due to the absence of vital status in the vast majority of claims data sources. When a subset of the patients described by Taylor et al. was selected based on having at least one CV risk factor (eg, current smoker, hypertension, HDL cholesterol <40 mg/dl, diabetes, or arteriosclerotic CV disease), a MACE rate of 0.77 (95 % CI 0.56, 1.04) per 100 PY was seen in patients aged ≥50 years. Patients from the clinical program may differ from those under routine care with respect to the prevalence of risk factors at baseline so comparisons should be made cautiously, if at all. No relative measure of risk was available for baricitinib (Taylor et al. 2022), due to the lack of a comparator for all but a fraction of the treatment periods.

In the ORAL Surveillance randomized study of tofacitinib, the incidence rates of MACE among patients treated with tofacitinib 5 mg BID and TNFi were 0.91 (95% CI 0.67, 1.21) and 0.73 (95% CI 0.52, 1.01) per 100 PY, respectively. A small increase in risk of MACE (HR_{5mg} = 1.24; 95% 0.81, 1.91) was seen in those treated with tofacitinib compared to TNFi (Ytterberg et al. 2022). This is similar to the increased risk observed in B023 (IRR = 1.54; 95% CI 0.93, 2.54), although the ORAL Surveillance population was enriched for patients at increased risk of MACE and Study B023 is based on patients in routine care. Like patients in Study B023 (see Table 10.2), randomized patients in the ORAL Surveillance noninferiority trial were 50 years of age or older on average. Participants in ORAL Surveillance also had at least one additional CV risk factor (eg, current smoker, hypertension, HDL <40 mg/dL, diabetes mellitus, family history of premature coronary heart disease, extraarticular rheumatoid arthritis, or history of coronary artery disease), many of which are prevalent among patients with RA.

Prompted by the ORAL Surveillance results, an observational study (RA-STAR) by Khosrow-Khavar et al. (2022) compared 12,852 patients treated with tofacitinib to similar patients treated with TNFi. Two comparisons were executed. Designed similarly to B023, the first analysis included patients with RA and data from insurance claims records, specifically Optum Clinformatics 2012-2020, Marketscan 2012-2018, and Medicare 2012-2017. This analysis did not find evidence for an increased risk of CV outcomes (HR=1.01; 95% CI 0.83, 1.23 and IRD = 0.02, 95% CI -0.19, 0.23 per 100 PY). These findings did not differ by age ($HR_{\leq 65\ years}$ = 1.00, 95% CI 0.66, 1.50 vs. $HR_{>65\ years}$ = 1.05, 95% CI 0.84, 1.33) or by subgroups based on sex or previous use of bDMARDs (yes/no). A second analysis aimed to mimic the ORAL Surveillance

trial eligibility using the same claims data. When patients with CV risk factors were evaluated, this second analysis found a non-significant increased risk of MACE (HR = 1.24, 95% CI 0.90, 1.69 and IRD = 0.28, -0.24, 0.80 per 100 PY).

An alternative explanation must also be considered for the observed increased risk of MACE in patients treated with JAKi relative to patients treated with TNFi. TNFi therapy has been associated with a reduction in both C-reactive protein level (Macias et al. 2005; Ridker et al. 2001), a known independent risk factor for the development of CV disease, and CV risk (Singh et al. 2020; Barnabe et al. 2011). The relative risk findings observed in B023, and potentially ORAL Surveillance, are therefore also consistent with a reduction in risk of MACE among patients treated with TNFi relative to baricitinib, and consistent with an increased risk due to baricitinib (or tofacitinib). To exclude this explanation both DMARD classes should be compared with another reference, but this is neither simple nor easily achieved with the available data.

Serious Infections

In addition to other comorbidities, patients with RA experience an increased risk of infection related to their treatments (Taylor et al. 2022). In a meta-analysis of over 40,000 patients with RA from 106 randomized studies, treatment with bDMARDs was associated with a 30 (standard dose) to 90% (high dose) increase in risk of serious infections compared to traditional DMARDs (Singh et al. 2015). This increased burden of infection exists across geographies and even clinical settings, with infection risk increasing by 47% in surgical settings as well (Salt et al. 2017). Patients with RA are also treated with glucocorticosteroids, to manage refractory RA or when starting or stopping bDMARDs, which also increase risk of serious infection, even at low doses (George et al. 2020). In B023, steroid treatment was included in sensitivity analyses as a time-dependent variable, to account for possible differences in use after initiation of index therapy. Unfortunately, there were insufficient events to permit analysis.

Among patients treated with JAKi in phase II and III randomized studies, the incidence rates of serious infection with baricitinib (n = 3520), tofacitinib (n = 5888), and upadacitinib (n = 1736) were 3.16 (95% CI 2.07, 4.63), 1.97 (95% CI 1.41, 2.68) and 3.02 (95% CI 0.98, 7.04) per 100 PY, respectively (Bechman et al. 2019). These rates are lower than the rate observed in baricitinib-treated patients in ARTIS (IR = 4.21 ; 95% CI 3.44, 5.15 per 100 PY) and higher than the rate observed in baricitinib-treated patients in SNDS (IR=1.9; 95% CI 1.3, 2.6 per 100 PY), the two largest data sources in this study by exposure. The definitions used for serious infection in the clinical trials and in B023 are not congruent, however. Clinical trials used adjudicated endpoints and ARTIS and SNDS in B023 relied on validated definitions based on diagnostic codes for infections in hospitalized patients. Interestingly, the IR observed in the placebo groups of these randomized studies also differed (ie, baricitinib: 4.09, tofacitinib: 1.19, and upadacitinib: 1.75 per 100 PY, respectively), highlighting the potential for modest differences in eligibility criteria to impact the frequency of AEs. For this reason, relative measures of risk are likely the most relevant, but comparisons from trials are typically with placebo and are not comparable

with the incidence rate ratios in Study B023, which compared baricitinib to treatment with any TNFi.

Overall

The results calculated in Study B023 are based on patients in routine care and do not lend themselves easily to comparison with information from clinical trials, including the baricitinib trials. The patient populations in observational and randomized clinical studies may be different. Patients in trials may be healthier at baseline, with fewer comorbidities, than patients who are not eligible to participate and may be subject to greater clinical surveillance during a study than patients in routine care. Randomized data provides the highest level of evidence for detecting a treatment effect, when such a design is feasible. Study B023 highlights the challenge of studying uncommon or rare events like VTE and MACE in patients under routine care. Despite the consideration of data from 16 real-world data sources in 6 countries, there were still limited numbers of patients exposed to baricitinib and 0 or low event numbers in most data sources. This suggests that recruitment of sufficient participants willing to be assigned to treatment, rather than reliance on real-world use, may be a critical requirement for understanding the safety profile of baricitinib with respect to rare events. The randomized RA-BRANCH (CT.gov # NCT04086745) and RA-BRIDGE (CT.gov # NCT03915964) studies are designed to together evaluate the safety of baricitinib with respect to VTE, MACE, and serious infection as well as other outcomes. These 2 ongoing studies include randomization, a standard of care comparator, and will have sufficient sample size to evaluate these rare safety endpoints. Thus, completion of these combined studies will provide additional important evidence about the safety of baricitinib treatment in RA.

11.3. Limitations

Several strengths and limitations should be considered when interpreting the results of this study. First, by including information from real-world patients from multiple geographies treated with baricitinib in routine care, this study provides good representation of patients with RA receiving baricitinib. Second, studies to ensure the accuracy of the main VTE outcome were conducted in both US and French claims-based data sources with resulting PPV of 75.5-92%. Third, the study implemented several design and analysis strategies to control for potential confounding including the use of an active comparator, new user study design, implementation of inclusion criteria in US claims-based data to approximate the required indication that baricitinib be used after TNFi, propensity score matching, and further adjustment for variables that were imbalanced after matching. Additional evaluations of potential bias due to unmeasured confounding by smoking, obesity, or disease severity were made. Lastly, the implementation of a common analytic strategy, aligned upon and executed by individual data sources, also reduces sources of heterogeneity that are often seen in published meta-analyses.

There are also limitations that should be considered. First, patients in this study are not randomized to treatment. Rheumatologists and their patients select treatments based on characteristics that are also risk factors for the outcome of interest (eg, age, lifestyle factors, comorbidities, existence of refractory disease, etc). This can create confounding and lead to

biased results if the prevalence of the risk factor differs between the groups being compared. In Study B023, confounding was addressed with elements in the study design (ie, new user active comparator design [Lund et al. 2015]), and the analytic approach (ie, propensity score matching), which were intended to create balance between groups with respect to risk factors for the outcomes. The success of this approach to balance risk factors between the outcomes for available factors can be partially assessed based on the standardised differences reported in the descriptive tables.

Second, claims data present important limitations in the ability of the above methods to control for confounding. Information on some risk factors for the outcomes investigated in this study is not available in administrative claims data. Of the data sources included in the study, 12 data sources (including the French SNDS) do not include direct information on BMI, smoking, or measures of RA disease activity and severity (ie, DAS28, disease duration). Although a proxy measure of disease activity was implemented to classify patients, it may not fully account for missing information on disease activity. Since baricitinib is often used following an inadequate response to TNFi, especially in the US patient population, baricitinib-treated patients may be more likely to have more severe disease. In the presence of confounding by severity, patients treated with baricitinib might appear to have an increased risk of VTE, MACE, or serious infection compared to those treated with TNFi, even though the true risk was lower or not present. Similar impacts to the study findings would be expected to occur if patients treated with baricitinib were more likely to smoke or be obese.

A few approaches were taken to address the possibility of confounding due to the inability to control for smoking, BMI, or disease severity. In the study design, US patients treated with a TNFi were required to have prior treatment with at least one other TNFi (protocol section 9.4.1.1). This mirrors the US Package Insert for baricitinib which restricts the indicated population for baricitinib to patients who have had an inadequate response to a TNFi. Although this requirement made patients in the baricitinib cohort more similar to those in the TNFi cohort with respect to treatment history and, hopefully also disease severity, it may also have tended to make these cohorts less similar with respect to other characteristics, such as disease duration or number of prior DMARDs. This can be assessed through the standardised differences between characteristics that remain after propensity score matching. In the analysis, a proxy for disease activity in claims data, the CIRAS index (Ting et al. 2008), was generally well balanced across treatment cohorts. This is a poor proxy, however, due to the low correlation with clinical measures of disease severity and may not fully account for potential confounding by disease severity. If it were true that the CIRAS index was not able to balance disease severity across treatment groups, residual confounding might be expected to make baricitinib-treated patients appear to have more severe disease than they truly do. Of note, while disease registries and other study designs have direct measures of disease severity (such as DAS28 and CDAI), these may not be available for all patients or at the relevant time, highlighting the complexity of addressing confounding by disease severity in all studies.

Without a way to evaluate the balance of the unmeasured potential confounding factors (ie, smoking, BMI, and disease severity), a post hoc quantitative bias analysis was used to assess the

magnitude of bias that could have been present. This was conducted based on results from the estimated IRR from meta-analysis of US data and IRR_{SNDS} for French patients (Section 10.5). Each analysis considered a range of (a) possible strengths of the risk factor and (b) plausible differences in the prevalence of the confounder between baricitinib and TNFi treatment cohorts. Compared to actual prevalence observed in the US Optum data and the French ESPOIR and CORPUS cohorts, the ranges evaluated were more extreme. In all scenarios, based on quantitative evaluation of the magnitude of potential bias that could have occurred it is unlikely that results were meaningfully impacted by not controlling for these factors.

Third, the duration of the baseline might be another source of potential confounding bias. Baseline risk factors were assessed based on 6 months of data prior to initiation of study drug. This may be too short a period to allow for complete assessment of patient comorbidities and relevant risk factors. We considered this potential limitation of the 6-month baseline using French data by extending the baseline for covariate assessment to two years. This allowed an assessment of the possible misclassification due to using a 6-month baseline. As expected, using a longer baseline increases the prevalence of many risk factors (Annex 16 Table 6S to Table 9S). If the 2-year baseline prevalence reflect the extent of misclassification that may be present in the study, then bias analysis can provide insight about the possible impact to results. Even in the presence of a strong risk factor (eg, RR = 5.5), extreme differences in prevalence between treatment cohorts (ie, 0 vs. 100%), will not meaningfully impact the IRR results reported for patients in SNDS. None of the risk factors in the two-year analysis had differences between baricitinib and TNFi cohorts as extreme as these, nor are any of the risk factors associated with a 5.5-fold or greater increase in the risk of VTE or MACE. This analysis using different baseline periods in SNDS suggest that any differences that may exist between baricitinib and TNFi treatment cohorts which cannot be evaluated using a six-month baseline are unlikely to meaningfully impact the inference made.

A fourth limitation is that claims data are collected for billing purposes, rather than research. Outcomes must be defined based on diagnostic and procedure codes, and medication dispensing records. In most if not all claims data, no information is available about individual healthcare services provided during inpatient stays; instead diagnostic codes reported at discharge from hospital are used. Similarly, exposures must be defined based on claims for medications but because prescription records simply record dispensing, these data do not confirm actual use by the patient (ie, exposure to medication). Consequently, the potential exists for exposure misclassification. Given the serious nature of RA and the cost of these medications, however, misclassification of exposure is unlikely to be a concern. It is also addressed in part by requiring more than 1 dispensing to identify an index exposure to baricitinib or TNFi.

Limitations regarding the outcomes and the potential for outcome misclassification can be addressed through linkage to clinical information to validate the algorithms used to identify events and clarify the ability of the selected case definition to find true cases. Separate evaluations were conducted for VTE case definitions in US and French claims data, with satisfactory PPV estimated for each (75.5% and 92%, respectively). On the basis of these results, there is good certainty that analyses of claims data evaluated true VTE.

Fifth, a priori, it was estimated that to ensure 80% power to detect a difference between treatment cohorts in the case of a true hazard ratio of 1.8, at least 90 patients with events were required, over both baricitinib and TNFi cohorts, based on a 1:1 ratio of baricitinib users to TNFi users and a one-sided Type I error rate of 0.025. There was a total of 97 VTEs identified in this study. However, almost half of data sources reported zero VTE or MACE events for either baricitinib or TNFi cohorts and 70-77% of the total VTE or MACE events for the study came from two European data sources, ARTIS and SNDS. Thus, while a large study with sufficient events to meet a priori power estimates, the distribution of these events across data sources limits interpretation of the meta-analysis.

Lastly, this study has limitations with respect to possible duplication of patients in US data sources. Namely, some patients may be represented in more than one claims database. This occurs because data sources with claims records from multiple health insurers (ie, Marketscan, Optum, Pharmetrics Plus, and PS20) may include some of the same health plans. Among these, the potential for overlap is not expected to be universal; that is, not all sources overlap with each other. Some single-insurer sources may also share some records with the multi-insurer databases (eg, Anthem and Pharmetrics Plus). However, due to the proprietary nature of these large multi-insurer data sources, information about the constituent data sources is not available. The precise extent and magnitude of overlap is therefore not known. Note that patient records *within* a data source are unique. No overlap exists among or within OUS data sources.

CorEvitas RA registries enrol patients without regard to their insurance status, so some registry participants may also be included in administrative claims data. However, CorEvitas sites are selected to be representative of rheumatologists throughout the US, so although the precise overlap cannot be predicted, the extent of overlap with any given US claims database is expected to be small.

11.4. Generalisability

The patients included in this study were identified from large, sometimes national, databases of records generated during the course of routine care. The eligible population is therefore widely representative of those receiving treatment with baricitinib or TNFi for RA across several geographies and healthcare systems. Patients who might not otherwise be available or choose to participate in clinical trials are described.

However, there are differences between patients identified as eligible for this study and those who were ultimately included in analyses. In particular, TNFi patients who are too dissimilar to those treated with baricitinib in each data source are not matched and are excluded from comparative analyses. While this may impact generalisability of the study findings, it does not impact the internal validity of the results. Across data sources, the proportion of baricitinib-treated patients retained in the analytic cohorts ranged from 48% (HIRD) to 97% (ARTIS). Among the 9 US data sources, 3 retained more than 80% of the eligible baricitinib cohort. In general, representation of eligible patients treated with baricitinib was quite good in Europe, where more than 87% of eligible patients were retained for analysis (with the exception of CorEvitas Japan, with 81%).

This suggests that the generalisability of study results may be better for European and Japanese patients than US patients. Interestingly, two doses of baricitinib are available in Europe, with the low 2-mg dose typically reserved for more comorbid, older patients than the 4-mg dose (see for example, Table 11.1). Nonetheless, the cohorts including these sicker patients were more likely to find matches with similar TNFi-treated patients.

Table 11.1. Baricitinib 2Patients in Eligible Versus Matched Cohorts

	Baricitinib		
	Eligible Cohort	Matched Cohort	Retention
Data Source	n	n	%
Aetna	69	37	54
Anthem HIRD	255	123	48
ARTIS	1737	1685	97
BKK	851	765	90
CorEvitas US	118	112	95
CorEvitas JP	210	171	81
HealthVerity PS20	933	748	80
Humana	89	49	55
JMDC	243	213	88
Marketscan	257	185	72
MDR	188	114	61
Optum	348	284	82
Pharmetrics Plus	473	261	55
SNDS	3242	2859	88

Abbreviations: BKK = Betriebskrankenkasse; HIRD = HealthCore Integrated Research Database; JMDC = Japanese Medical Data Center, Inc.'s claims database; JP = Japan; MDR = Military Data Repository; n = number of patients in the specified category; PS20 = Private Source 20; SNDS = Système National des Données de Santé.

Given the large differences between cohorts with respect to the estimated risk associated with exposure to baricitinib, data source-specific results may be most generalisable to specific regions. With only a fraction of the total exposure and events, caution is warranted when considering the generalisability of study results to US patients.

12. Other information

Not applicable.

13. Conclusions

This real-world study analysed data from 11 claims-based and 3 registry sources in Europe, the US, and Japan. Meta-analysis was used to estimate the overall IRR and IRD of VTE, MACE, and serious infection among patients treated with baricitinib compared to those treated with TNFi.

Overall study findings suggest a statistically significant association between baricitinib and risk of VTE. The aggregate IRR from meta-analysis, $IRR_{meta\text{-}analysis}$, is 1.51 (95% CI 1.10, 2.08). IR was greater among patients treated with baricitinib than with TNFi, the difference was 0.26 (95% CI -0.04, 0.57) per 100 PY. Overall meta-analysis estimates of MACE and serious infection risk were also elevated with baricitinib treatment.

For MACE the $IRR_{meta\text{-}analysis}$ is 1.54 (95% CI 0.93, 2.54). The IR was greater among patients treated with baricitinib than with TNFi with a difference of 0.22 (95% CI -0.07, 0.52) per 100 PY. In the largest data sources, there was a statistically significant increase in risk of MACE in one data source (IRR_{SNDS} = 2.33; 95% CI 1.15, 4.74) and not in the other (IRR_{ARTIS} = 0.94, 95% CI 0.45, 1.96)..

Finally, for serious infection the $IRR_{meta\text{-}analysis}$ is 1.36 (95% CI 0.86, 2.13). The IR was greater among patients treated with baricitinib than with TNFi, with a difference of 0.57 (95% CI -0.07, 1.21) per 100 PY. A statistically significant increase in risk of serious infection was seen in the largest data source (IRR_{ARTIS} = 1.65; 95% CI 1.20, 2.26) and not in the second largest source (IRR_{SNDS} = 1.04; 95% CI 0.65, 1.65).

In summary, the findings from this large multi-country study provide additional information about the safety of baricitinib. There is strong evidence of an association between baricitinib and risk of VTE compared to TNFi based on the significant overall meta-analysis result. This agrees with other studies that have found an imbalance of VTE during placebo-controlled periods of randomized studies and the ORAL surveillance study results for tofacitinib, another JAKi. For MACE, the meta-analysis result suggests a modest increase in risk associated with baricitinib compared to TNFi treatment and for serious infection, the overall meta-analysis result suggests a small increase in risk.

Lilly's Assessment of Benefit Risk

Findings from this study reported in comparison to treatment with TNFi should be considered in context with study limitations and evidence from other studies evaluating the safety of baricitinib (Taylor et al. 2022) and other JAK inhibitors (Khosrow-Khavar et al. 2022; Ytterberg et al. 2022). The benefit-risk assessment for baricitinib remains positive as the estimates of the IR difference of VTE, MACE and serious infections between baricitinib and TNFi in B023 are modest and can be further reduced with additional risk-minimizing precautions for individual patients at higher risk of these events.

In response to preliminary analyses from a subset of data sources in B023, the warnings and precautions in the company core data sheet were strengthened. No additional changes to the core

data sheet or risk management plan are warranted. Healthcare professionals should consider information from this and other studies in aggregate and take appropriate precautions in patients with CV risk factors, with risk factors for DVT/PE, and in those with risk factors for serious infection.

14. References

Anand SS. Smoking: a dual pathogen for arterial and venous thrombosis. *Circulation*. 2017;135(1):17-20. https://doi.org/10.1161/CIRCULATIONAHA.116.025024

Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res*. 2011;46(3):399-424. https://doi.org/10.1080/00273171.2011.568786

Aviña-Zubieta JA, Choi HK, Sadatsafavi M, et al. Risk of cardiovascular mortality in patients with rheumatoid arthritis: a meta-analysis of observational studies. *Arthritis Rheum*. 2008;59(12):1690-1697. https://doi.org/10.1002/art.24092

Aviña-Zubieta JA, Thomas J, Sadatsafavi M, et al.. Risk of incident cardiovascular events in patients with rheumatoid arthritis: a meta-analysis of observational studies. *Ann Rheum Dis*. 2012;71(9):1524-1529. https://doi.org/10.1136/annrheumdis-2011-200726

Barnabe C, Martin BJ, Ghali WA. Systematic review and meta-analysis: anti-tumor necrosis factor α therapy and cardiovascular events in rheumatoid arthritis. *Arthritis Care Res (Hoboken)*. 2011;63(4):522-529. https://doi.org/10.1002/acr.20371

Bechman K, Subesinghe S, Norton S, et al. A systematic review and meta-analysis of infection risk with small molecule JAK inhibitors in rheumatoid arthritis. *Rheumatology (Oxford)*. 2019;58(10):1755-1766. https://doi.org/10.1093/rheumatology/kez087

Bezin J, Duong M, Lassalle R, et al. The national healthcare system claims databases in France, SNIIRAM and EGB: powerful tools for pharmacoepidemiology. *Pharmacoepidemiol Drug Saf*. 2017;26(8):954-962. https://doi.org/10.1002/pds.4233

[BMA] British Medical Association. The interface between NHS and private treatment: a practical guide for doctors in England, Wales and Northern Ireland. Guidance from the BMA Medical Ethics Department. 2009. Accessed January 7, 2018. https://www.bma.org.uk/-/media/files/pdfs/practical%20advice%20at%20work/ethics/interfaceguidanceethicsmay2009.pdf.

Charles-Schoeman C, Fleischman R, Mysler E, et al. The risk of venous thromboembolic events in patients with RA aged ≥50 years with ≥1 cardiovascular risk factor: results from a phase 3b/4 randomized safety study of tofacitinib vs TNF inhibitors presented at: ACR Convergence 2021; November 5-9, 2021; virtual conference. Abstract 1941. https://acrabstracts.org/abstract/the-risk-of-venous-thromboembolic-events-in-patients-with-ra-aged-%e2%89%a5-50-years-with-%e2%89%a5-1-cardiovascular-risk-factor-results-from-a-phase-3b-4-randomized-safety-study-of-tofacitinib-vs-tn/

Choi HK, Rho YH, Zhu Y, et al. The risk of pulmonary embolism and deep vein thrombosis in rheumatoid arthritis: a UK population-based outpatient cohort study. *Ann Rheum Dis*. 2013;72(7):1182-1187. https://doi.org/10.1136/annrheumdis-2012-201669

Colling ME, Tourdot BE, Kanthi Y. Inflammation, infection and venous thromboembolism. *Circ Res*. 2021;128(12):2017-2036. https://doi.org/10.1161/circresaha.121.318225

Cornelius ME, Loretan G, Wang TW, Jamal A, Homa DM. Tobacco product use among adults – United States, 2020. Centers for Disease Control and Prevention Morbidity and Mortality Weekly Report, March 18 2022.

Desai RJ, Solomon DH, Shadick N, et al. Identification of smoking using Medicare data--a validation study of claims-based algorithms. *Pharmacoepidemiol Drug Saf*. 2016;25(4):472-475. https://doi.org/10.1002/pds.3953

Doran MF, Crowson CS, Pond GR, et al. Frequency of infection in patients with rheumatoid arthritis compared with controls: a population-based study. *Arthritis Rheum*. 2002;46(9):2287-2293. https://doi.org/10.1002/art.10524

Eichinger S, Hron G, Bialonczyk C, et al. Overweight, obesity, and the risk of recurrent venous thromboembolism. *Arch Intern Med*. 2008;168(15):1678-1683. https://doi.org/10.1001/archinte.168.15.1678

Enga KF, SK Braekkan, IJ Hansen-Krone, S le Cessie, FR Rosendaal, JB Hansen. Cigarette smoking and the risk of venous thromboembolism: the Tromso Study. J Thromb Haemost. 2012;10(10):2068-2074. https://doi.org/ 10.1111/j.1538-7836.2012.04880.x

Fang MC, Fan D, Sung SH, et al. Validity of using inpatient and outpatient administrative codes to identify acute venous thromboembolism: the CVRN VTE study. *Med Care.* 2017;55(12):e137-e143. https://doi.org/10.1097/mlr.0000000000000524

Fralick M, Kesselheim AS, Avorn J, Schneeweiss S. Use of health care databases to support supplemental indications of approved medications. *JAMA Intern Med*. 2018;178(1):55-63. https://doi.org/10.1001/jamainternmed.2017.3919

Franklin JM, Rassen JA, Ackermann D, et al. Metrics for covariate balance in cohort studies of causal effects. *Stat Med*. 2014;33(10):1685-1699. https://doi.org/10.1002/sim.6058

Gabriel SE; Cardiovascular morbidity and mortality in rheumatoid arthritis. *Am J Med*. 2008;121(10 suppl 1):S9-S14. https://doi.org/10.1016/j.amjmed.2008.06.011

George MD, Baker JF, Winthrop K, et al. Risk for serious infection with low-dose glucocorticoids in patients with rheumatoid arthritis: a cohort study. *Ann Intern Med*. 2020;173(11):870-878. https://doi.org/10.7326/m20-1594

Ghosh RE, E Crellin, S Beatty, K Donegan, P Myles, R Williams. How Clinical Practice Research Datalink data are used to support pharmacovigilance. *Ther Adv Drug Saf.* 2019;10:2042098619854010. https://doi.org/ 10.1177/2042098619854010

Gilleron V, Gasnier-Duparc N, Hebbrecht G. Certification des comptes : une incitation à la traçabilité des processus de contrôle [Certification of accounts: an incentive for the traceability of control processes]. *Revue hospitalière de France*. 2018;582:42-46.

Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of obesity and severe obesity among adults: United States, 2017-2018. NCHS Data Brief No. 360 February 2020.

Herrett E, Gallagher AM, Bhaskaran K, et al. Data resource profile: Clinical Practice Research Datalink (CPRD). *Int J Epidemiol.* 2015;44(3):827-836. https://doi.org/10.1093/ije/dyv098

Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557-560. https://doi.org/10.1136/bmj.327.7414.557

Holmqvist ME, Neovius M, Eriksson J, et al. Risk of venous thromboembolism in patients with rheumatoid arthritis and association with disease duration and hospitalization. *JAMA*. 2012;308(13):1350-1356. https://doi.org/10.1001/2012.jama.11741

Khosrow-Khavar F, Kim SC, Lee H, et al. Tofacitinib and risk of cardiovascular outcomes: results from the Safety of TofAcitinib in Routine care patients with Rheumatoid Arthritis (STAR-RA) study. *Ann Rheum Dis*. 2022;81(6):798-804. https://doi.org/10.1136/annrheumdis-2021-221915

Kim SC, Schneeweiss S, Liu J, Solomon DH. Risk of venous thromboembolism in patients with rheumatoid arthritis. *Arthritis Care Res (Hoboken)*. 2013;65(10):1600-1607. https://doi.org/10.1002/acr.22039

Kremer JM, P Emery, HS Camp, A Friedman, L Wang, AA Othman, N Khan, AL Pangan, S Jungerwirth, EC Keystone. A Phase IIb Study of ABT-494, a Selective JAK-1 Inhibitor, in Patients With Rheumatoid Arthritis and an Inadequate Response to Anti-Tumor Necrosis Factor Therapy. Arthritis Rheumatol. 2016;68(12):2867-2877. https://doi.org/10.1002/art.39801

Lash TL, Fox MP, MacLehose RF. Good practices for quantitative bias analysis. *Int J Epidemiol.* 2014;43(6):1969-1985. https://doi.org/10.1093/ije/dyu149

Lau EC, Son MS, Mossad D, et al. The validity of administrative BMI data in total joint arthroplasty. *J Arthroplasty*. 2015;30(10):1683-1687. https://doi.org/10.1016/j.arth.2015.04.029

Lee JJ, Pope JE. A meta-analysis of the risk of venous thromboembolism in inflammatory rheumatic diseases. *Arthritis Res Ther*. 2014;16(5):435. https://doi.org/10.1186/s13075-014-0435-y

Li L, Lu N, Avina-Galindo AM, et al. The risk and trend of pulmonary embolism and deep vein thrombosis in rheumatoid arthritis: a general population-based study. *Rheumatology (Oxford)*. 2021;60(1):188-195. https://doi.org/10.1093/rheumatology/keaa262

Liao KP, DH Solomon. Traditional cardiovascular risk factors, inflammation and cardiovascular risk in rheumatoid arthritis. *Rheumatology (Oxford).* 2013;52(1):45-52. https://doi.org/10.1093/rheumatology/kes243

Lund JL, Richardson DB, Stürmer T. The active comparator, new user study design in pharmacoepidemiology: historical foundations and contemporary application. *Curr Epidemiol Rep.* 2015;2(4):221-228. https://doi.org/10.1007/s40471-015-0053-5

Macías I, García-Pérez S, Ruiz-Tudela M, et al. Modification of pro- and antiinflammatory cytokines and vascular-related molecules by tumor necrosis factor-α blockade in patients with rheumatoid arthritis. J Rheumatol. 2005;32(11):2102-8.

Maini RN, Breedveld FC, Kalden JR, et al.; Sustained improvement over two years in physical function, structural damage, and signs and symptoms among patients with rheumatoid arthritis treated with infliximab and methotrexate. *Arthritis Rheum*. 2004;50(4):1051-1065. https://doi.org/10.1002/art.20159

McCormick N, Bhole V, Lacaille D, Avina-Zubieta JA. Validity of diagnostic codes for acute stroke in administrative databases: a systematic review. *PLoS One*. 2015;10(8):e0135834. https://doi.org/10.1371/journal.pone.0135834

Matta F, R Singala, AY Yaekoub, et al. Risk of venous thromboembolism with rheumatoid arthritis. *Thromb Haemost.* 2009;101(1):134-138. https://doi.org/10.1160/TH08-08-0551

Methotrexate sodium [package insert]. 2022.

Meune C, Touzé E, Trinquart L, Allanore Y. Trends in cardiovascular mortality in patients with rheumatoid arthritis over 50 years: a systematic review and meta-analysis of cohort studies. *Rheumatology (Oxford)*. 2009;48(10):1309-1313. https://doi.org/10.1093/rheumatology/kep252

Molander V, Bower H, Frisell T, Askling J. Risk of venous thromboembolism in rheumatoid arthritis, and its association with disease activity: a nationwide cohort study from Sweden. *Ann Rheum Dis*. 2021;80(2):169-175. https://doi.org/10.1136/annrheumdis-2020-218419

Molander V, Bower H, Askling J. Validation and characterization of venous thromboembolism diagnoses in the Swedish National Patient Register among patients with rheumatoid arthritis. *Scand J Rheumatol*. 2022;1-7. https://doi.org/10.1080/03009742.2021.2001907

Mutru O, Laakso M, Isomäki H, Koota K. Ten year mortality and causes of death in patients with rheumatoid arthritis. *Br Med J (Clin Res Ed.)*. 1985;290(6484):1797-1799. https://doi.org/10.1136/bmj.290.6484.1797

Nagai K, Tanaka T, Kodaira N, et al. Data resource profile: JMDC claims databases sourced from medical institutions. *J Genl Fam Med*. 2020;21(6):211-218. https://doi.org/10.1002/jgf2.367

Nakanishi R, Berman DS, Budoff MJ, et al. Current but not past smoking increases the risk of cardiac events: insights from coronary computed tomographic angiography. *Eur Heart J*. 2015;36(17):1031-1040. https://doi.org/10.1093/eurheartj/ehv013

Ogdie A, Kay McGill N, Shin DB, et al. Risk of venous thromboembolism in patients with psoriatic arthritis, psoriasis and rheumatoid arthritis: a general population-based cohort study. *Eur Heart J*. 2018;39(39):3608-3614. https://doi.org/10.1093/eurheartj/ehx145

Olumiant [package insert]. Indianapolis, IN: Eli Lilly and Company; 2020.

Peng RD, Dominici F, Zeger SL. Reproducible epidemiologic research. *Am J Epidemiol*. 2006;163(9):783-789. https://doi.org/10.1093/aje/kwj093

Picerno V, Ferro F, Adinolfi A, et al. One year in review: the pathogenesis of rheumatoid arthritis. *Clin Exp Rheumatol*. 2015;33(4):551-558.

Rassen JA, Shelat AA, Myers J, et al. One-to-many propensity score matching in cohort studies. *Pharmacoepidemiol Drug Saf*. 2012;21(suppl 2):69-80. https://doi.org/10.1002/pds.3263

Reitsma PH, Versteeg HH, Middeldorp S. Mechanistic view of risk factors for venous thromboembolism. *Arterioscler Thromb Vasc Biol*. 2012;32(3):563-568. https://doi.org/10.1161/atvbaha.111.242818

RFI. French people have stopped giving up smoking, survey shows. Published 31 March 2021. Accessed 27 June 2022. https://www.rfi.fr/en/france/20210531-french-people-have-suddenly-stopped-giving-up-smoking-survey-shows-spf

Ridker PM. High-sensitivity C-reactive protein: potential adjunct for global risk assessment in the primary prevention of cardiovascular disease. *Circulation*. 2001;103(13):1813-1818. https://doi.org/10.1161/01.cir.103.13.1813

Roifman I, Beck PL, Anderson TJ, et al. Chronic inflammatory diseases and cardiovascular risk: a systematic review. *Can J Cardiol*. 2011;27(2):174-182. https://doi.org/10.1016/j.cjca.2010.12.040

Rosenbaum PR, Rubin DB. The Central Role of the Propensity Score in Observational Studies for Causal Effects. *Biometrika*. 1983;70(1):41-55. https://doi.org/10.2307/2335942

Roubille C, Richer V, Starnino T, et al. The effects of tumour necrosis factor inhibitors, methotrexate, non-steroidal anti-inflammatory drugs and corticosteroids on cardiovascular events in rheumatoid arthritis, psoriasis and psoriatic arthritis: a systematic review and meta-analysis. *Ann Rheum Dis*. 2015;74(3):480-489. https://doi.org/10.1136/annrheumdis-2014-206624

Rubin DB. Estimating causal effects from large data sets using propensity scores. Ann Intern Med. 1997;127(8 Pt 2):757-763. https://doi.org/10.7326/0003-4819-127-8_part_2-199710151-00064

Salt E, AT Wiggins, MK Rayens, BJ Morris, D Mannino, A Hoellein, RP Donegan, LJ Crofford. Moderating effects of immunosuppressive medications and risk factors for post-operative joint infection following total joint arthroplasty in patients with rheumatoid arthritis or osteoarthritis. *Semin Arthritis Rheum.* 2017;46(4):423-429. https://doig.org/ 10.1016/j.semarthrit.2016.08.011

Schneeweiss S. Sensitivity analysis and external adjustment for unmeasured confounders in epidemiologic database studies of therapeutics. *Pharmacoepidemiol Drug Saf.* 2006;15(5):291-303. https://doig.org/ 10.1002/pds.1200

Schneeweiss S. Developments in post-marketing comparative effectiveness research. *Clin Pharmacol Ther*. 2007;82(2):143-156. https://doi.org/10.1038/sj.clpt.6100249

Sihvonen S, Korpela M, Laippala P, et al. Death rates and causes of death in patients with rheumatoid arthritis: a population-based study. *Scand J Rheumatol*. 2004;33(4):221-227. https://doi.org/10.1080/03009740410005845

Simon TA, Thompson A, Gandhi KK, et al. Incidence of malignancy in adult patients with rheumatoid arthritis: a meta-analysis. *Arthritis Res Ther*. 2015;17(1):212. https://doi.org/10.1186/s13075-015-0728-9

Singh JA, Cameron C, Noorbaloochi S, et al. Risk of serious infection in biological treatment of patients with rheumatoid arthritis: a systematic review and meta-analysis. *Lancet*. 2015;386(9990):258-265. https://doi.org/10.1016/s0140-6736(14)61704-9

Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis Care Res (Hoboken)*. 2016;68(1):1-25. https://doi.org/10.1002/acr.22783

Singh S, Fumery M, Singh AG, et al. Comparative risk of cardiovascular events with biologic and synthetic disease-modifying antirheumatic drugs in patients with rheumatoid arthritis: a systematic review and meta-analysis. *Arthritis Care Res (Hoboken)*. 2020;72(4):561-576. https://doi.org/10.1002/acr.23875

Skeoch S, Bruce IN. Atherosclerosis in rheumatoid arthritis: is it all about inflammation? *Nat Rev Rheumatol*. 2015;11(7):390-400. https://doi.org/10.1038/nrrheum.2015.40

Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. *Lancet*. 2016;388(10055):2023-2038. https://doi.org/10.1016/s0140-6736(16)30173-8

Smolen JS, Landewé R, Bijlsma J, et al.; EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis*. 2017;76(6):960-977. https://doi.org/10.1136/annrheumdis-2016-210715

Spittal MJ, Pirkis J, Gurrin LC. Meta-analysis of incidence rate data in the presence of zero events. *BMC Med Res Methodol*. 2015;15:42. https://doi.org/10.1186/s12874-015-0031-0

Sweetland S, J Green, B Liu, et al; Million Women Study collaborators. Duration and magnitude of the postoperative risk of venous thromboembolism in middle aged women: prospective cohort study. *BMJ*. 2009;339:b4583. https://doi.org/10.1136/bmj.b4583

Taylor PC, Takeuchi T, Burmester GR, et al. Safety of baricitinib for the treatment of rheumatoid arthritis over a median of 4.6 and up to 9.3 years of treatment: final results from long-term extension study and integrated database. *Ann Rheum Dis.* 2022;81(3):335-343. https://doi.org/10.1136/annrheumdis-2021-221276

Thomsen M, Nordestgaard BG. Myocardial infarction and ischemic heart disease in overweight and obesity with and without metabolic syndrome. *JAMA Intern Med*. 2014;174(1):15-22. https://doi.org/10.1001/jamainternmed.2013.10522

Thurin NH, Bosco-Levy P, Blin P, et al. Intra-database validation of case-identifying algorithms using reconstituted electronic health records from healthcare claims data. BMC Med Res Methodol. 2021;21(1):95. https://doi.org/10.1186/s12874-021-01285-y

Ting G, Schneeweiss S, Scranton R, et al. Development of a health care utilisation data-based index for rheumatoid arthritis severity: a preliminary study. Arthritis Res Ther. 2008;10(4):R95. https://doi.org/10.1186/ar2482

Tuppin P, Rudant J, Constantinou P, et al. Value of a national administrative database to guide public decisions: From the système national d'information interrégimes de l'Assurance Maladie (SNIIRAM) to the système national des données de santé (SNDS) in France. *Rev Epidemiol Sante Publique*. 2017;65 Suppl 4:S149–67. https://doi.org/10.1016/j.respe.2017.05.004

van den Hoek J, Boshuizen HC, Roorda LD, et al. Mortality in patients with rheumatoid arthritis: a 15-year prospective cohort study. Rheumatol Int. 2017;37(4):487-493. https://doi.org/10.1007/s00296-016-3638-5

van Gelder K. Share of individuals who currently smoke cigarettes, cigars, cigarrillos or a pipe in selected European countries in 2020. *Statista*. 2022. Accessed 23 June 2022. https://www.statista.com/statistics/433390/individuals-who-currently-smoke-cigarettes-in-european-countries/#:~:text=In%20fact%2C%20only%2028%20percent,for%20its%20prevalent%20tobacco%20consumption.

Vazquez-Garza E, C Jerjes-Sanchez, A Navarrete, et al. Venous thromboembolism: thrombosis, inflammation, and immunothrombosis for clinicians. *J Thromb Thrombolysis*. 2017;44(3):377-385. https://doi.org/10.1007/s11239-017-1528-7

Wadström H, Eriksson JK, Neovius M, Askling J. ARTIS Study Group. How good is the coverage and how accurate are exposure data in the Swedish Biologics Register (ARTIS)? *Scand J Rheumatol*. 2015;44(1):22-28. https://doi.org/10.3109/03009742.2014.927918

Walker A, Patrick A, Lauer M, et al. A tool for assessing the feasibility of comparative effectiveness research. *Comparative Effectiveness Research*. 2013;3:11-20. http://dx.doi.org/10.2147/CER.S40357

[WHO] World Health Organization. *Nutrition, Physical Activity and Obesity France.* 2013. Accessed 23 June 2022. https://www.euro.who.int/__data/assets/pdf_file/0009/243297/France-WHO-Country-Profile.pdf

Winthrop KL, Baxter R, Liu L, et al. The reliability of diagnostic coding and laboratory data to identify tuberculosis and nontuberculous mycobacterial disease among rheumatoid arthritis patients using anti-tumor necrosis factor therapy. *Pharmacoepidemiol Drug Saf*. 2011;20(3):229-235. https://doi.org/10.1002/pds.2049

WorldOMeters 2019. U.K. Population. Accessed January 7, 2019. http://www.worldometers.info/world-population/uk-population

Yoshida K, Harrold LR, Middaugh N, et al. Time-Varying Association of Rheumatoid Arthritis Disease Activity to Subsequent Cardiovascular Risk. *ACR Open Rheumatol*. 2022;10.1002/acr2.11432. https://doi.org/10.1002/acr2.11432

Ytterberg SR, DL Bhatt, TR Mikuls, et al. OS Investigators. Cardiovascular and Cancer Risk with Tofacitinib in Rheumatoid Arthritis. *N Engl J Med*. 2022;386(4):316-326. https://doi.org/10.1056/nejmoa2109927

Annex 1. List of Standalone Documents

No.	Document Reference No	Date	Title
1.	n/a		Name and affiliation of investigators
2.	7	27 August 2021	statistical analysis plan (SAP)

Annex 2. Aetna – Additional Results

This annex includes information about results for the following analyses:

I. Additional analysis
These additional results were not presented in the body of the report. These results, like those included in the report body, are based on 1:1 baricitinib:TNFi propensity score matching. Specifically, this section of the annex includes:
- Descriptive tables for unmatched eligible patients.
- Descriptive tables for matched patient cohorts for the serious infection analyses

II. Variable Ratio Matching
These results were not presented in the body of this report. They are based on matching baricitinib:TNFi using Variable Ratio matching, i.e., as many matched 1:3 as possible, then the maximum number matched 1:2, then the remaining patients matched 1:1.

I. Additional analysis

Table 1_Aetna. Baseline Demographics, Unmatched [Aetna]

	Baricitinib			TNFi (N=289)	Std. Diff. (Any vs TNFi)
	Any (N=69)	4-mg (N=0)	2-mg (N=69)		
Age [yrs]					
N	69	-	69	289	
Mean (SD)	57.38 (13.03)	-	57.38 (13.03)	55.78 (13.44)	0.12
Median	58.00 [48.00, 68.00]	-	58.00 [48.00, 68.00]	56.00 [47.00, 65.50]	
Min, Max	26.0, 80.0	-	26.0, 80.0	19.0, 82.0	
≥ 65 years	23 (33.3%)	-	23 (33.3%)	77 (26.6%)	0.15
Sex					
Male	7 (10.1%)	-	7 (10.1%)	66 (22.8%)	0.35
Female	62 (89.9%)	-	62 (89.9%)	223 (77.2%)	0.35

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.1. Baseline Demographics, Unmatched Cohorts [Healthagen].docx

Table 4_Aetna. Baseline Demographics Incident Serious Infections, Matched [Aetna]

	Baricitinib			TNFi (N=44)	Std. Diff. (Any vs TNFi)	Total (N=88)
	Any (N=44)	4-mg (N=0)	2-mg (N=44)			
Age [yrs]						
N	44	-	44	44	0.016	88
Mean (SD)	55.05 (13.13)	-	55.05 (13.13)	55.27 (14.86)		55.16 (13.94)
Median	58.00 [44.00, 67.25]	-	58.00 [44.00, 67.25]	56.00 [48.00, 64.00]		57.50 [46.25, 64.75]
Min, Max	26.0, 76.0	-	26.0, 76.0	19.0, 80.0		19.0, 80.0
≥ 65 years	12 (27.3%)	-	12 (27.3%)	10 (22.7%)	0.105	22 (25.0%)
Sex						
Male	5 (11.4%)	-	5 (11.4%)	7 (15.9%)	0.133	12 (13.6%)
Female	39 (88.6%)	-	39 (88.6%)	37 (84.1%)	0.133	76 (86.4%)

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. [Updated 2022.03.15] Table 6.4 - Baseline Demographics Incident Serious Infections, Matched [Healthagen]

Table 6_Aetna. Clinical History at Baseline, Unmatched Cohorts [Aetna]

Characteristic[a,b]	Baricitinib[c] (N=69)	TNFi (N=289)	Std. Diff.
Clinical Conditions during baseline			
Cancer	8 (11.6%)	21 (7.3%)	0.15
NMSC	1 (1.4%)	3 (1.0%)	0.04
Chronic lung disease	13 (18.8%)	44 (15.2%)	0.10
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	3 (4.3%)	9 (3.1%)	0.07
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	-
Congestive heart failure, hospitalized	0 (0.0%)	2 (0.7%)	0.12
Coronary artery disease	3 (4.3%)	19 (6.6%)	0.10
Ischemic heart disease	3 (4.3%)	19 (6.6%)	0.10
Unstable angina	1 (1.4%)	1 (0.3%)	0.12
Ventricular arrhythmia	1 (1.4%)	8 (2.8%)	0.09
Diabetes Mellitus	5 (7.2%)	54 (18.7%)	0.35
Type I	2 (2.9%)	5 (1.7%)	0.08
Type II	5 (7.2%)	54 (18.7%)	0.35
Dyslipidaemia	28 (40.6%)	94 (32.5%)	0.17
Hypertension	31 (44.9%)	120 (41.5%)	0.07
Immune disorders	10 (14.5%)	28 (9.7%)	0.15
AIDS/HIV	0 (0.0%)	0 (0.0%)	-
Antiphospholipid syndrome	1 (1.4%)	0 (0.0%)	0.17
SLE	4 (5.8%)	12 (4.2%)	0.08
Primary Sjögren syndrome	6 (8.7%)	17 (5.9%)	0.11
Liver disorder	3 (4.3%)	5 (1.7%)	0.15
Obesity	15 (21.7%)	78 (27.0%)	0.12
Pregnancy	0 (0.0%)	1 (0.3%)	0.08
RA severity (CIRAS Index), mean (SD)	4.45 (1.34)	4.64 (1.29)	0.14
Smoking	6 (8.7%)	43 (14.9%)	0.19
Surgery, trauma & hospitalization, recent	5 (7.2%)	17 (5.9%)	0.06
TIA	0 (0.0%)	1 (0.3%)	0.08
DMARDs			
cDMARDs, during baseline			
n, total	35 (50.7%)	170 (58.8%)	0.16
Mean (SD)	0.74 (0.74)	0.77 (0.72)	0.04
Median	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-
Min, Max	0.0, 3.0	0.0, 3.0	-
>1 cDMARD concomitantly	10 (14.5%)	39 (13.5%)	0.03
Hydroxychloroquine	6 (8.7%)	45 (15.6%)	0.21
Leflunomide	11 (15.9%)	23 (8.0%)	0.25
Methotrexate	25 (36.2%)	121 (41.9%)	0.12
Minocycline	0 (0.0%)	1 (0.3%)	0.08
Sulfasalazine	2 (2.9%)	17 (5.9%)	0.15
bDMARDs, during baseline[a]			

Characteristic[a,b]	Baricitinib[c] (N=69)	TNFi (N=289)	Std. Diff.
n, total	41 (59.4%)	280 (96.9%)	1.02
Mean (SD)	0.72 (0.68)	1.10 (0.32)	0.71
Median	1.00 [0.00, 1.00]	1.00 [1.00, 1.00]	-
Min, Max	0.0, 2.0	1.0, 3.0	-
cDMARDs, concomitant	17 (24.6%)	138 (47.8%)	0.50
abatacept	6 (8.7%)	8 (2.8%)	0.26
adalimumab[d]	4 (5.8%)	55 (19.0%)	0.41
anakinra	1 (1.4%)	0 (0.0%)	0.17
certolizumab pegol[d]	7 (10.1%)	27 (9.3%)	0.03
etanercept[d]	7 (10.1%)	99 (34.3%)	0.61
golimumab[d]	2 (2.9%)	37 (12.8%)	0.38
infliximab[d]	2 (2.9%)	66 (22.8%)	0.62
rituximab	3 (4.3%)	0 (0.0%)	0.30
sarilumab	8 (11.6%)	2 (0.7%)	0.47
tocilizumab	8 (11.6%)	7 (2.4%)	0.37
Other Prescription Medications			
Antibiotics	32 (46.4%)	145 (50.2%)	0.08
Antidiabetic agents	7 (10.1%)	49 (17.0%)	0.20
Insulins	2 (2.9%)	16 (5.5%)	0.13
Non-insulins	6 (8.7%)	42 (14.5%)	0.18
Aspirin	1 (1.4%)	2 (0.7%)	0.07
Cardiovascular			
Anticoagulant	2 (2.9%)	10 (3.5%)	0.03
Antihypertensives	32 (46.4%)	149 (51.6%)	0.10
Antiplatelet	2 (2.9%)	10 (3.5%)	0.03
Nitrates	1 (1.4%)	6 (2.1%)	0.05
Hormonal			
HRT	6 (8.7%)	9 (3.1%)	0.24
Oral Contraceptives	2 (2.9%)	13 (4.5%)	0.09
SERMs	1 (1.4%)	5 (1.7%)	0.02
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	3 (1.0%)	0.15
Cholesterol absorption inhibitor	1 (1.4%)	2 (0.7%)	0.07
Fibrates	1 (1.4%)	5 (1.7%)	0.02
Niacin	0 (0.0%)	0 (0.0%)	-
Omega-3 fatty acids	0 (0.0%)	4 (1.4%)	0.17
Statins	19 (27.5%)	79 (27.3%)	0.00
Rheumatoid arthritis-related			
Cox-2 Inhibitor	7 (10.1%)	14 (4.8%)	0.20
Glucocorticosteroid	35 (50.7%)	180 (62.3%)	0.24
Vaccinations	16 (23.2%)	81 (28.0%)	0.11

Abbreviations: AIDS = acquired immune deficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drug ; CIRAS = claims-based index for RA severity ; cDMARD = conventional disease-modifying antirheumatic drug; DMARD = disease-modifying antirheumatic drug; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modulator; SLE = systemic lupus erythematosus; Std. Diff = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics, except for bDMARDs, are measured during the 6 months prior to initiation of study medication including the date at which the qualifying exposure of baricitinib or TNFi occurs (index date). bDMARDs are measured from the 6 months prior to the initiation of study medication until the day prior to baricitinib or the index TNFi exposure, excluding the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d TNF inhibitors.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.6. - Clinical History at Baseline, Unmatched Cohorts [Healthagen]_.docx

Table 9_Aetna. Clinical Characteristics Incident Serious Infection Cohorts, Matched [Aetna]

Characteristic[a,b]	Baricitinib[c] (N=44)	TNFi (N=44)	Std. Diff.
Clinical Conditions during baseline			
Cancer	6 (13.6%)	4 (9.1%)	0.14
NMSC	1 (2.3%)	0 (0.0%)	0.22
Chronic lung disease	3 (6.8%)	5 (11.4%)	0.16
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	1 (2.3%)	3 (6.8%)	0.22
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	-
Congestive heart failure, hospitalized	0 (0.0%)	0 (0.0%)	-
Coronary artery disease	0 (0.0%)	1 (2.3%)	0.22
Ischemic heart disease	0 (0.0%)	1 (2.3%)	0.22
Unstable angina	1 (2.3%)	1 (2.3%)	0.0
Ventricular arrhythmia	0 (0.0%)	2 (4.5%)	0.31
Diabetes Mellitus	5 (11.4%)	3 (6.8%)	0.16
Type I	2 (4.5%)	0 (0.0%)	0.31
Type II	5 (11.4%)	3 (6.8%)	0.16
Dyslipidaemia	14 (31.8%)	13 (29.5%)	0.05
Hypertension	19 (43.2%)	15 (34.1%)	0.19
Immune disorders	9 (20.5%)	10 (22.7%)	0.06
AIDS/HIV	0 (0.0%)	0 (0.0%)	-
Antiphospholipid syndrome	2 (4.5%)	0 (0.0%)	0.31
SLE	6 (13.6%)	2 (4.5%)	0.32
Primary Sjögren syndrome	3 (6.8%)	8 (18.2%)	0.35
Liver disorder	0 (0.0%)	0 (0.0%)	-
Obesity	9 (20.5%)	7 (15.9%)	0.12
Pregnancy	0 (0.0%)	0 (0.0%)	-
RA severity (CIRAS Index), mean (SD)	4.53 (1.32)	4.47 (1.26)	0.05
Smoking	4 (9.1%)	3 (6.8%)	0.08
Surgery, trauma & hospitalization, recent	3 (6.8%)	5 (11.4%)	0.16
TIA	0 (0.0%)	0 (0.0%)	-
DMARDs			
cDMARDs, during baseline			
n, total	25 (56.8%)	25 (56.8%)	0.0
Mean (SD)	0.84 (0.81)	0.80 (0.79)	0.06
Median	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-
Min, Max	0.0, 3.0	0.0, 3.0	-
>1 cDMARD concomitantly	9 (20.5%)	8 (18.2%)	0.06
Hydroxychloroquine	7 (15.9%)	5 (11.4%)	0.13
Leflunomide	7 (15.9%)	7 (15.9%)	0.0
Methotrexate	18 (40.9%)	15 (34.1%)	0.14
Minocycline	0 (0.0%)	0 (0.0%)	-
Sulfasalazine	2 (4.5%)	3 (6.8%)	0.10
bDMARDs, during baseline[a]			

Characteristic[a,b]	Baricitinib[c] (N=44)	TNFi (N=44)	Std. Diff.
n, total	15 (34.1%)	44 (100.0%)	1.97
Mean (SD)	0.36 (0.53)	1.32 (0.52)	1.82
Median	0.00 [0.00, 1.00]	1.00 [1.00, 2.00]	-
Min, Max	0.0, 2.0	1.0, 3.0	-
cDMARDs, concomitant	6 (13.6%)	24 (54.5%)	0.96
abatacept	2 (4.5%)	4 (9.1%)	0.18
adalimumab[d]	1 (2.3%)	21 (47.7%)	1.23
anakinra	0 (0.0%)	0 (0.0%)	-
certolizumab pegol[d]	1 (2.3%)	11 (25.0%)	0.70
etanercept[d]	0 (0.0%)	25 (56.8%)	1.62
golimumab[d]	1 (2.3%)	16 (36.4%)	0.96
infliximab[d]	0 (0.0%)	15 (34.1%)	1.02
rituximab	2 (4.5%)	0 (0.0%)	0.31
sarilumab	4 (9.1%)	2 (4.5%)	0.18
tocilizumab	4 (9.1%)	2 (4.5%)	0.18
Other Prescription Medications			
Antibiotics	20 (45.5%)	20 (45.5%)	0.0
Antidiabetic agents	6 (13.6%)	5 (11.4%)	0.07
Insulins	2 (4.5%)	1 (2.3%)	0.13
Non-insulins	5 (11.4%)	5 (11.4%)	0.0
Aspirin	1 (2.3%)	0 (0.0%)	0.22
Cardiovascular			
Anticoagulant	5 (11.4%)	2 (4.5%)	0.25
Antihypertensives	21 (47.7%)	22 (50.0%)	0.05
Antiplatelet	2 (4.5%)	1 (2.3%)	0.13
Nitrates	1 (2.3%)	1 (2.3%)	0.0
Hormonal			
HRT	2 (4.5%)	1 (2.3%)	0.13
Oral Contraceptives	2 (4.5%)	5 (11.4%)	0.25
SERMs	0 (0.0%)	1 (2.3%)	0.22
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	-
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	-
Fibrates	2 (4.5%)	1 (2.3%)	0.13
Niacin	0 (0.0%)	0 (0.0%)	-
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	-
Statins	8 (18.2%)	12 (27.3%)	0.22
Rheumatoid arthritis-related			
Cox-2 Inhibitor	4 (9.1%)	0 (0.0%)	0.45
Glucocorticosteroid	26 (59.1%)	21 (47.7%)	0.23
Vaccinations	8 (18.2%)	11 (25.0%)	0.17

Abbreviations: AIDS = acquired immune deficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drug ; CIRAS = claims-based index for RA severity; cDMARD = conventional disease-modifying antirheumatic drug; DMARD = disease-modifying antirheumatic drug; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modulator; SLE = Systemic lupus erythematosus ; Std. Diff = standardised difference; TIA = Transient ischemic attacks; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics, except for bDMARDs, are measured during the 6 months prior to initiation of study medication including the date at which the qualifying exposure of baricitinib or TNFi occurs (index date). bDMARDs are measured from the 6 months prior to the initiation of study medication until the day prior to baricitinib or the index TNFi exposure, excluding the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d TNF inhibitors.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. [Updated 2022.03.15] Table 6.9. - Clinical Characteristics Incident Serious Infection Cohorts, Matched [Healthagen].docx

Table 11A_Aetna. Baseline Healthcare Resource Utilization, Unmatched [Aetna]

Type of Resource Use	Baricitinib (N=69)	TNFi (N=289)	Std. Diff.
Physician Office Visits			
n, patients	61 (88.4%)	264 (91.3%)	0.1
n, events	771	2826	
Mean (SD)	11.17 (9.48)	9.78 (12.02)	0.13
Median	10.00 [4.00, 16.00]	7.00 [3.00, 13.00]	
Min, Max	0.0, 38.0	0.0, 132.0	
Rheumatologist Visits			
n, patients	56 (81.2%)	237 (82.0%)	0.02
n, events	390	2540	
Mean (SD)	5.65 (6.93)	8.79 (11.55)	0.33
Median	3.00 [2.00, 7.00]	5.00 [1.00, 12.50]	
Min, Max	0.0, 31.0	0.0, 102.0	
Other Outpatient Visits			
n, patients	64 (92.8%)	256 (88.6%)	0.14
n, events	1159	5517	
Mean (SD)	16.80 (17.54)	19.09 (19.52)	0.12
Median	11.00 [4.00, 23.50]	13.00 [5.00, 27.00]	
Min, Max	0.0, 91.0	0.0, 103.0	
Inpatient Visits			
n, patients	8 (11.6%)	27 (9.3%)	0.07
n, events	203	1168	
Mean (SD)	2.94 (11.34)	4.04 (25.93)	0.06
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 68.0	0.0, 401.0	
ED Visits			
n, patients	10 (14.5%)	64 (22.1%)	0.20
n, events	216	876	
Mean (SD)	3.13 (10.72)	3.03 (7.67)	0.01
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 75.0	0.0, 64.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category ; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.11A. Baseline Healthcare Resource Utilization, Unmatched [Healthagen (RA)].docx

Table 11B_Aetna. Baseline Healthcare Resource Utilization, Unmatched [Aetna], count at most one visit per day[1]

Type of Resource Use	Baricitinib (N=69)	TNFi (N=289)	Std. Diff.
Physician Office Visits[1]			
n, patients	61 (88.4%)	264 (91.3%)	0.1
n, events	432	1,402	
Mean (SD)	6.26 (4.86)	4.85 (4.63)	0.30
Median	6.00 [2.50, 9.00]	4.00 [2.00, 7.00]	
Min, Max	0.0, 19.0	0.0, 40.0	
Rheumatologist Visits[1]			
n, patients	56 (81.2%)	237 (82.0%)	0.02
n, events	178	919	
Mean (SD)	2.58 (2.00)	3.18 (3.20)	0.23
Median	2.00 [1.00, 4.00]	3.00 [1.00, 4.00]	
Min, Max	0.0, 8.0	0.0, 24.0	
Other Outpatient Visits[1]			
n, patients	64 (92.8%)	256 (88.6%)	0.14
n, events	329	1,399	
Mean (SD)	4.77 (5.18)	4.84 (5.34)	0.01
Median	3.00 [1.50, 6.00]	3.00 [1.00, 7.00]	
Min, Max	0.0, 31.0	0.0, 46.0	
Inpatient Visits[1]			
n, patients	8 (11.6%)	27 (9.3%)	0.07
n, events	29	220	
Mean (SD)	0.42 (1.44)	0.76 (5.40)	0.09
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 8.0	0.0, 85.0	
ED Visits[1]			
n, patients	10 (14.5%)	64 (22.1%)	0.20
n, events	24	110	
Mean (SD)	0.35 (0.95)	0.38 (0.84)	0.03
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 5.0	0.0, 4.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

[1]In this table, results describe utilization of healthcare where a maximum of one event was allowed per day. In the PS matching analyses, multiple claims on the same day were allowed to capture additional information on the amount of services received in a given visit. These results are presented in table 6.11A.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.11B (count at most one visit per day). Baseline Healthcare Resource Utilization, Unmatched [Healthagen (RA)].docx

Table 12A_Aetna. Baseline Healthcare Resource Utilization Primary VTE Cohorts, Matched [Aetna]

Type of Resource Use	Baricitinib (N=37)	TNFi (N=37)	Std. Diff.
Physician Office Visits			
n, patients	32 (86.5%)	32 (86.5%)	0.00
n, events	359	362	
Mean (SD)	9.70 (8.39)	9.78 (8.74)	0.01
Median	9.00 [4.00, 14.00]	7.00 [2.50, 15.50]	
Min, Max	0.0, 38.0	0.0, 32.0	
Rheumatologist Visits			
n, patients	29 (78.4%)	27 (73.0%)	0.13
n, events	209	215	
Mean (SD)	5.65 (6.91)	5.81 (7.31)	0.02
Median	4.00 [1.00, 7.50]	3.00 [0.00, 8.00]	
Min, Max	0.0, 31.0	0.0, 27.0	
Other Outpatient Visits			
n, patients	34 (91.9%)	31 (83.8%)	0.25
n, events	660	574	
Mean (SD)	17.84 (17.77)	15.51 (19.51)	0.13
Median	10.00 [4.00, 30.50]	11.00 [2.50, 24.00]	
Min, Max	0.0, 64.0	0.0, 103.0	
Inpatient Visits			
n, patients	3 (8.1%)	5 (13.5%)	0.18
n, events	65	131	
Mean (SD)	1.76 (7.63)	3.54 (16.20)	0.14
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 41.0	0.0, 97.0	
ED Visits			
n, patients	4 (10.8%)	6 (16.2%)	0.16
n, events	125	156	
Mean (SD)	3.38 (13.23)	4.22 (12.34)	0.07
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 75.0	0.0, 64.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; RA = rheumatoid arthritis; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.12A. Baseline Healthcare Resource Utilization, Primary VTE Cohorts, Matched [Healthagen (RA)].docx

Table 13A_Aetna. Baseline Healthcare Resource Utilization Primary MACE Cohorts, Matched [Aetna]

Type of Resource Use	Baricitinib (N=43)	TNFi (N=43)	Std. Diff.
Physician Office Visits			
n, patients	38 (88.4%)	38 (88.4%)	0.00
n, events	410	375	
Mean (SD)	9.53 (7.78)	8.72 (8.86)	0.10
Median	9.00 [4.00, 15.00]	6.00 [2.00, 15.00]	
Min, Max	0.0, 37.0	0.0, 40.0	
Rheumatologist Visits			
n, patients	36 (83.7%)	31 (72.1%)	0.28
n, events	274	200	
Mean (SD)	6.37 (7.15)	4.65 (6.11)	0.26
Median	4.00 [2.00, 9.00]	2.00 [0.00, 7.00]	
Min, Max	0.0, 31.0	0.0, 26.0	
Other Outpatient Visits			
n, patients	39 (90.7%)	39 (90.7%)	0.00
n, events	880	809	
Mean (SD)	20.47 (20.39)	18.81 (17.46)	0.09
Median	12.00 [6.00, 34.00]	14.00 [5.00, 30.00]	
Min, Max	0.0, 91.0	0.0, 72.0	
Inpatient Visits			
n, patients	5 (11.6%)	4 (9.3%)	0.08
n, events	89	55	
Mean (SD)	2.07 (7.74)	1.28 (5.25)	0.12
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 41.0	0.0, 30.0	
ED Visits			
n, patients	7 (16.3%)	6 (14.0%)	0.07
n, events	188	86	
Mean (SD)	4.37 (13.21)	2.00 (5.79)	0.23
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 75.0	0.0, 25.0	

Abbreviations: ED = emergency department; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; RA = rheumatoid arthritis; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.13A. Baseline Healthcare Resource Utilization MACE Cohorts, Matched [Healthagen (RA)].docx

Table 14A_Aetna. Baseline Healthcare Resource Utilization Primary Serious Infection Cohorts, Matched [Aetna]

Type of Resource Use	Baricitinib (N=45)	TNFi (N=45)	Std. Diff.
Physician Office Visits			
n, patients	40 (88.9%)	38 (84.4%)	0.13
n, events	456	466	
Mean (SD)	10.13 (7.94)	10.36 (9.48)	0.03
Median	10.00 [4.50, 14.50]	8.00 [3.00, 16.00]	
Min, Max	0.0, 38.0	0.0, 40.0	
Rheumatologist Visits			
n, patients	37 (82.2%)	35 (77.8%)	0.11
n, events	303	255	
Mean (SD)	6.73 (7.64)	5.67 (6.00)	0.16
Median	4.00 [2.00, 9.00]	4.00 [1.00, 8.50]	
Min, Max	0.0, 31.0	0.0, 24.0	
Other Outpatient Visits			
n, patients	41 (91.1%)	42 (93.3%)	0.08
n, events	912	864	
Mean (SD)	20.27 (19.90)	19.20 (17.84)	0.06
Median	14.00 [6.00, 32.50]	10.00 [5.50, 35.50]	
Min, Max	0.0, 91.0	0.0, 66.0	
Inpatient Visits			
n, patients	5 (11.1%)	5 (11.1%)	0.00
n, events	116	42	
Mean (SD)	2.58 (11.02)	0.93 (4.15)	0.20
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 68.0	0.0, 27.0	
ED Visits			
n, patients	7 (15.6%)	11 (24.4%)	0.22
n, events	185	425	
Mean (SD)	4.11 (12.90)	4.38 (9.44)	0.02
Median	0.00 [0.00, 0.00]	0.00 [0.00, 2.50]	
Min, Max	0.0, 75.0	0.0, 39.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; RA = rheumatoid arthritis; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.14A. Baseline Healthcare Resource Utilization Incident Serious Infection Cohorts, Matched [Healthagen (RA)].docx

Table 14B_Aetna. Baseline Healthcare Resource Utilization Serious Infection Cohorts, Matched [Aetna], count at most one visit per day[1]

Type of Resource Use	Baricitinib (N=44)	TNFi (N=44)	Std. Diff.
Physician Office Visits[1]			
n, patients	39 (88.6%)	41 (93.2%)	0.16
n, events	238	228	
Mean (SD)	5.41 (3.97)	5.18 (4.27)	0.06
Median	5.00 [3.00, 8.00]	4.00 [2.25, 6.00]	
Min, Max	0.0, 17.0	0.0, 22.0	
Rheumatologist Visits[1]			
n, patients	34 (77.3%)	35 (79.5%)	0.05
n, events	114	113	
Mean (SD)	2.59 (2.15)	2.57 (2.14)	0.01
Median	2.00 [1.00, 4.00]	2.00 [1.00, 4.00]	
Min, Max	0.0, 8.0	0.0, 8.0	
Other Outpatient Visits[1]			
n, patients	40 (90.9%)	40 (90.9%)	0.00
n, events	201	173	
Mean (SD)	4.57 (5.21)	3.93 (3.19)	0.15
Median	3.00 [2.00, 6.00]	3.00 [2.00, 6.00]	
Min, Max	0.0, 31.0	0.0, 15.0	
Inpatient Visits[1]			
n, patients	4 (9.1%)	5 (11.4%)	0.08
n, events	9	7	
Mean (SD)	0.20 (0.76)	0.16 (0.48)	0.07
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 4.0	0.0, 2.0	
ED Visits[1]			
n, patients	6 (13.6%)	10 (22.7%)	0.24
n, events	17	15	
Mean (SD)	0.39 (1.06)	0.34 (0.71)	0.05
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 5.0	0.0, 3.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; RA = rheumatoid arthritis; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

[1]In this table, results describe utilization of healthcare where a maximum of one event was allowed per day. In the PS matching analyses, multiple claims on the same day were allowed to capture additional information on the amount of services received in a given visit. These results are presented in table 6.14A.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. [Upd. 3.15] Table 6.14B (count at most one visit per day). Baseline HCRU Serious Infection Cohorts, Matched [Healthagen (RA)].docx

Table 16_Aetna. Baseline Prevalence of Outcomes [Aetna]

Outcome in Each Matched Cohort[a,c,d]	Unmatched			Matched			
	Baricitinib[b]	TNFi	Std. Diff	Baricitinib[b]	TNFi	Std. Diff	Total
VTE	N=70	N=289	-	N=41	N=41	-	N=82
Main case definition in baseline	1 (1.4%)	0 (0.0%)	0.17	0 (0.0%)	0 (0.0%)	-	0 (0.0%)
Alternate case definition I in baseline	1 (1.4%)	0 (0.0%)	0.17	0 (0.0%)	0 (0.0%)	-	0 (0.0%)
Alternative case definition II in baseline	1 (1.4%)	5 (5.9%)	0.02	0 (0.0%)	1 (2.4%)	0.22	1 (1.2%)
MACE	N=70	N=289	-	N=43	N=43	-	N=86
MACE in baseline	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)	-	0 (0.0%)
Serious Infection	N=74	N=305	-	N=46	N=46	-	N=92
Serious Infection in baseline	1 (1.4%)	4 (1.3%)	0.00	1 (2.2%)	0 (0.0%)	0.21	1 (1.1%)
Hospitalized Tuberculosis	N=74	N=305	-	N=46	N=46	-	N=92
Hospitalized Tuberculosis in baseline	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)	-	0 (0.0%)

Abbreviations: MACE = major adverse cardiovascular event, defined as hospital primary discharge diagnosis code of acute MI or hospital primary discharge diagnosis code of ischemic or hemorrhagic stroke; N = number of patients in specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism, defined based on the case definitions.

a Baseline prevalence was calculated for each distinct matched cohort for VTE, MACE, serious infection and hospitalized tuberculosis.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c Patients with the prevalent outcomes enumerated in this table are those excluded from the main analyses of each outcome, except for VTE alternative case definitions I and II. Only the VTE main case definition was used as an exclusion criterion in the main analyses.

d In the VTE and MACE analyses, cohorts additionally excluded the use of anticoagulants at the time of cohort entry (see protocol Section 8.7.7), resulting in a different N compared to the Serious Infection and Hospitalized Tuberculosis cohorts.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.16. Baseline Prevalence of Outcomes [Healthagen]_.docx

Table 17_Aetna. Duration of Follow-up Period (Days), Unmatched [Aetna]

	Baricitinib[a] (N=69)	TNFi (N=289)	Std. Diff.
N	69	289	
Mean (SD)	156.62 (149.72)	219.13 (211.75)	0.34
Median	92.00 [59.00, 249.00]	142.00 [80.00, 278.50]	
Min, Max	7.0, 710.0	1.0, 1174.0	

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = standardised difference; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be reported for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.17. Duration of Follow-up Period (Days), Unmatched [Healthagen].docx

Table 18_Aetna. Duration of Follow-up Period (Days) Primary VTE Cohorts, Matched [Aetna]

	Baricitinib[a,b] (N=37)	TNFi (N=37)	Std. Diff.
N	37	37	0
Mean (SD)	126.03 (131.11)	218.76 (166.60)	0.62
Median	59.00 [59.00, 144.00]	143.00 [113.50, 315.50]	
Min, Max	7.0, 594.0	15.0, 660.0	
Reasons for censoring [c]			
Incident event	0	0	-
Medication discontinued	17 (45.9%)	25 (67.6%)	-
Initiated b/tsDMARD	2 (5.4%)	1 (2.7%)	-
End of patient record	17 (45.9%)	10 (27.0%)	-
Death (where available)	0 (0.0%)	0 (0.0%)	-
End of study period (12/31/2020)	0 (0.0%)	0 (0.0%)	-

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = Venous thromboembolism.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be reported for each dose where numbers of patients are sufficient to warrant separate reporting.

b There were 0 patients with a baricitinib dose of 4 mg. Hence, 100% of the patients presented in this column have a baricitinib dose of 2 mg.

c A single patient can be censored on the same day for multiple reasons, e.g., medication discontinued could also be the same day as initiated b/tsDMARD. Further, additional censoring criteria (e.g., switching medication) were specified in the SAP. For these reasons, the total number of reasons for censoring may be less than or greater than the total number of patients.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.18. Duration of Follow-up Period (Days) Primary VTE Cohorts, Matched [Healthagen].docx

Table 21_Aetna. Duration of Follow-up Period (Days) MACE Cohorts, Matched [Aetna]

	Baricitinib[a,b] (N=43)	TNFi (N=43)	Std. Diff.
N	43	43	
Mean (SD)	128.33 (127.33)	238.95 (240.02)	0.58
Median	69.00 [59.00, 146.00]	134.00 [59.00, 382.00]	
Min, Max	7.0, 594.0	15.0, 844.0	
Reasons for censoring			
Incident event	0	0	-
Medication discontinued	20 (46.5%)	16 (37.2%)	-
Initiated b/tsDMARD	3 (7.0%)	3 (7.0%)	-
End of patient record	18 (41.9%)	18 (41.9%)	-
Death (where available)	0 (0.0%)	0 (0.0%)	-
End of study period (12/31/2020)	0 (0.0%)	0 (0.0%)	-

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be reported for each dose where numbers of patients are sufficient to warrant separate reporting.

b There were 0 patients with a baricitinib dose of 4 mg. Hence, 100% of the patients presented in this column have a baricitinib dose of 2 mg.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.21. Duration of Follow-up Period (Days) MACE Cohorts, Matched [Healthagen].docx

Table 22_Aetna. Duration of Follow-up Period (Days) Incident Serious Infection Cohorts, Matched [Aetna]

	Baricitinib[a,b] (N=44)	TNFi (N=44)	Std. Diff.
N	44	44	
Mean (SD)	138.61 (123.54)	198.98 (186.94)	0.38
Median	87.50 [59.00, 183.75]	131.00 [74.75, 244.25]	
Min, Max	7.0, 594.0	1.0, 804.0	
Reasons for censoring[c]			
Incident event	1	1	-
Medication discontinued	22 (50.0%)	24 (54.5%)	-
Initiated b/tsDMARD	2 (4.5%)	1 (2.3%)	-
End of patient record	19 (43.2%)	14 (31.8%)	-
Death (where available)	0 (0.0%)	0 (0.0%)	-
End of study period (07/05/2021)	0 (0.0%)	0 (0.0%)	-

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b There were 0 patients with a baricitinib dose of 4 mg. Hence, 100% of the patients presented in this column have a baricitinib dose of 2 mg.

c A single patient can be censored on the same day for multiple reasons, e.g., medication discontinued could also be the same day as initiated b/tsDMARD. Further, additional censoring criteria (e.g., switching medication) were specified in the SAP. For these reasons, the total number of reasons for censoring may be less than or greater than the total number of patients.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. [Updated 2022.03.15] Table 6.22. Duration of Follow-up Period (Days) Incident Serious Infection Cohorts, Matched [Healthagen].docx

Table 39_Aetna. Pattern of VTE and Related Diagnostic Codes in Patients with RA [Aetna]

Code	Total Patients (N=2)
Pulmonary Embolism	
I26.0 - Pulmonary embolism with acute cor pulmonale	0 (0.0%)
I26.02 - Saddle embolus of pulmonary artery with acute cor pulmonale	0 (0.0%)
I26.09 - Other pulmonary embolism with acute cor pulmonale	0 (0.0%)
I26.9 - Pulmonary embolism without acute cor pulmonale	0 (0.0%)
I26.92 - Saddle embolus of pulmonary artery without acute cor pulmonale	0 (0.0%)
I26.99 - Other pulmonary embolism without acute cor pulmonale	1 (50.0%)
Deep Vein Thrombosis, lower	
I80.10 - Phlebitis and thrombophlebitis of unspecified femoral vein	0 (0.0%)
I80.11 - Phlebitis and thrombophlebitis of right femoral vein	0 (0.0%)
I80.13 - Phlebitis and thrombophlebitis of femoral vein, bilateral	0 (0.0%)
I80.211 - Phlebitis and thrombophlebitis of right iliac vein	0 (0.0%)
I80.221 - Phlebitis and thrombophlebitis of right popliteal vein	0 (0.0%)
I80.223 - Phlebitis and thrombophlebitis of popliteal vein, bilateral	0 (0.0%)
I80.232 - Phlebitis and thrombophlebitis of left tibial vein	0 (0.0%)
I80.233 - Phlebitis and thrombophlebitis of tibial vein, bilateral	0 (0.0%)
I80.292 - Phlebitis and thrombophlebitis of other deep vessels of left lower extremity	0 (0.0%)
I80.293 - Phlebitis and thrombophlebitis of other deep vessels of lower extremity, bilateral	0 (0.0%)
I80.3 - Phlebitis and thrombophlebitis of lower extremities, unspecified	0 (0.0%)
I82.419 - Acute embolism and thrombosis of unspecified femoral vein	0 (0.0%)
I82.423 - Acute embolism and thrombosis of iliac vein, bilateral	0 (0.0%)
I82.431 - Acute embolism and thrombosis of right popliteal vein	0 (0.0%)
I82.432 - Acute embolism and thrombosis of left popliteal vein	0 (0.0%)
I82.433 - Acute embolism and thrombosis of popliteal vein, bilateral	0 (0.0%)
I82.441 - Acute embolism and thrombosis of right tibial vein	0 (0.0%)
I82.442 - Acute embolism and thrombosis of left tibial vein	0 (0.0%)
I82.443 - Acute embolism and thrombosis of tibial vein, bilateral	0 (0.0%)
I82.449 - Acute embolism and thrombosis of unspecified tibial vein	0 (0.0%)
I82.491 - Acute embolism and thrombosis of other specified deep vein of right lower extremity	0 (0.0%)
I82.4Y1 - Acute embolism and thrombosis of unspecified deep veins of right proximal lower extremity	0 (0.0%)
I82.4Y3 - Acute embolism and thrombosis of unspecified deep veins of proximal lower extremity, bilateral	0 (0.0%)
I82.4Y9 - Acute embolism and thrombosis of unspecified deep veins of unspecified proximal lower extremity	0 (0.0%)

Code	Total Patients (N=2)
I82.4Z1 - Acute embolism and thrombosis of unspecified deep veins of right distal lower extremity	0 (0.0%)
I82.4Z2 - Acute embolism and thrombosis of unspecified deep veins of left distal lower extremity	0 (0.0%)
I82.4Z3 - Acute embolism and thrombosis of unspecified deep veins of distal lower extremity, bilateral	0 (0.0%)
I80.12 - Phlebitis and thrombophlebitis of left femoral vein	0 (0.0%)
I80.201 - Phlebitis and thrombophlebitis of unspecified deep vessels of right lower extremity	0 (0.0%)
I80.202 - Phlebitis and thrombophlebitis of unspecified deep vessels of left lower extremity	0 (0.0%)
I80.203 - Phlebitis and thrombophlebitis of unspecified deep vessels of lower extremities, bilateral	0 (0.0%)
I80.209 - Phlebitis and thrombophlebitis of unspecified deep vessels of unspecified lower extremity	0 (0.0%)
I80.212 - Phlebitis and thrombophlebitis of left iliac vein	0 (0.0%)
I80.213 - Phlebitis and thrombophlebitis of iliac vein, bilateral	0 (0.0%)
I80.219 - Phlebitis and thrombophlebitis of unspecified iliac vein	0 (0.0%)
I80.222 - Phlebitis and thrombophlebitis of left popliteal vein	0 (0.0%)
I80.229 - Phlebitis and thrombophlebitis of unspecified popliteal vein	0 (0.0%)
I80.231 - Phlebitis and thrombophlebitis of right tibial vein	0 (0.0%)
I80.291 - Phlebitis and thrombophlebitis of other deep vessels of right lower extremity	0 (0.0%)
I80.299 - Phlebitis and thrombophlebitis of other deep vessels of unspecified lower extremity	0 (0.0%)
I82.401 - Acute embolism and thrombosis of unspecified deep veins of right lower extremity	0 (0.0%)
I82.402 - Acute embolism and thrombosis of unspecified deep veins of left lower extremity	0 (0.0%)
I82.403 - Acute embolism and thrombosis of unspecified deep veins of lower extremity, bilateral	0 (0.0%)
I82.409 - Acute embolism and thrombosis of unspecified deep veins of unspecified lower extremity	0 (0.0%)
I82.411 - Acute embolism and thrombosis of right femoral vein	0 (0.0%)
I82.412 - Acute embolism and thrombosis of left femoral vein	1 (50.0%)
I82.413 - Acute embolism and thrombosis of femoral vein, bilateral	0 (0.0%)
I82.421 - Acute embolism and thrombosis of right iliac vein	0 (0.0%)
I82.422 - Acute embolism and thrombosis of left iliac vein	0 (0.0%)
I82.429 - Acute embolism and thrombosis of unspecified iliac vein	0 (0.0%)
I82.439 - Acute embolism and thrombosis of unspecified popliteal vein	0 (0.0%)
I82.492 - Acute embolism and thrombosis of other specified deep vein of left lower extremity	0 (0.0%)

Code	Total Patients (N=2)
I82.493 - Acute embolism and thrombosis of other specified deep vein of lower extremity, bilateral	0 (0.0%)
I82.499 - Acute embolism and thrombosis of other specified deep vein of unspecified lower extremity	0 (0.0%)
I82.4Y2 - Acute embolism and thrombosis of unspecified deep veins of left proximal lower extremity	0 (0.0%)
Deep Vein Thrombosis, upper	
I82.210 - Acute embolism and thrombosis of superior vena cava	0 (0.0%)
I82.601 - Acute embolism and thrombosis of unspecified veins of right upper extremity	0 (0.0%)
I82.621 - Acute embolism and thrombosis of deep veins of right upper extremity	0 (0.0%)
I82.622 - Acute embolism and thrombosis of deep veins of left upper extremity	0 (0.0%)
I82.623 - Acute embolism and thrombosis of deep veins of upper extremity, bilateral	0 (0.0%)
I82.A12 - Acute embolism and thrombosis of left axillary vein	0 (0.0%)
I82.C11 - Acute embolism and thrombosis of right internal jugular vein	0 (0.0%)
I82.C13 - Acute embolism and thrombosis of internal jugular vein, bilateral	0 (0.0%)
I82.C19 - Acute embolism and thrombosis of unspecified internal jugular vein	0 (0.0%)
I82.602 - Acute embolism and thrombosis of unspecified veins of left upper extremity	0 (0.0%)
I82.603 - Acute embolism and thrombosis of unspecified veins of upper extremity, bilateral	0 (0.0%)
I82.609 - Acute embolism and thrombosis of unspecified veins of unspecified upper extremity	0 (0.0%)
I82.629 - Acute embolism and thrombosis of deep veins of unspecified upper extremity	0 (0.0%)
I82.A11 - Acute embolism and thrombosis of right axillary vein	0 (0.0%)
I82.A13 - Acute embolism and thrombosis of axillary vein, bilateral	0 (0.0%)
I82.A19 - Acute embolism and thrombosis of unspecified axillary vein	0 (0.0%)
I82.C12 - Acute embolism and thrombosis of left internal jugular vein	0 (0.0%)
Other Venous Thrombosis	
I81 - Portal vein thrombosis	0 (0.0%)
I82.0 - Budd-Chiari syndrome	0 (0.0%)
I82.1 - Thrombophlebitis migrans	0 (0.0%)
I82.3 - Embolism and thrombosis of renal vein	0 (0.0%)
I82.90 - Acute embolism and thrombosis of unspecified vein	0 (0.0%)
I82.B13 - Acute embolism and thrombosis of subclavian vein, bilateral	0 (0.0%)
I80.8 - Phlebitis and thrombophlebitis of other sites	0 (0.0%)
I80.9 - Phlebitis and thrombophlebitis of unspecified site	0 (0.0%)
I82.220 - Acute embolism and thrombosis of inferior vena cava	0 (0.0%)
I82.890 - Acute embolism and thrombosis of other specified veins	0 (0.0%)
I82.B11 - Acute embolism and thrombosis of right subclavian vein	0 (0.0%)

Code	Total Patients (N=2)
I82.B12 - Acute embolism and thrombosis of left subclavian vein	0 (0.0%)

Abbreviations: ICD-10 = International Classification of Disease, 10th Revision; N = Number of patients in the specified category; RA = rheumatoid arthritis;
VTE = venous thromboembolism.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.39. Pattern of VTE and Related Diagnostic Codes in Patients with RA [Healthagen].docx

Table 40_Aetna. Clinical Characteristics of RA Patients with VTE, Primary Definition [Aetna]

Characteristic[a,b]	Baricitinibc (N=0)	TNFi (N=0)	Total (N=0)
Age (mean) [SD]	- (-)	- (-)	- (-)
Sex			
Female	0 (0.0%)	0 (0.0%)	0 (0.0%)
Male	0 (0.0%)	0 (0.0%)	0 (0.0%)
Clinical Conditions during baseline			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic Lung disease Disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular conditions			
Atrial arrhythmia/ fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dyslipidaemia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertension	0 (0.0%)	0 (0.0%)	0 (0.0%)
Immune disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Primary Sjögren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	- (-)	- (-)	- (-)
Smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)
Surgery, trauma, & hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medication			
Antibiotics	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antidiabetic agents	0 (0.0%)	0 (0.0%)	0 (0.0%)
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			
Antihypertensives	0 (0.0%)	0 (0.0%)	0 (0.0%)

Characteristic[a,b]	**Baricitinibc (N=0)**	**TNFi (N=0)**	**Total (N=0)**
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anticoagulant	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiplatelet	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			
Oral contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERM	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucocorticosteroid	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vaccinations	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post index Occurrence[d]			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hospitalization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Surgery	0 (0.0%)	0 (0.0%)	0 (0.0%)
Trauma	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modifier; TNFi = tumour necrosis factor inhibitor; VTE = Venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d Except for cancer diagnosed within 90 days of VTE diagnosis, events in this category must have occurred in the 4 weeks immediately prior to VTE (Kline et al. 2017).

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.40. - Clinical Characteristics of RA Patients with VTE, Primary Definition [Healthagen].docx

Table 41_Aetna. Pattern of RA Medication Use in Patients with VTE, Primary Definition [Aetna]

Characteristic[a]	Unmatched		Matched		
	Baricitinib[b] (N=0)	TNFi (N=2)	Baricitinib[b] (N=0)	TNFi (N=0)	Total (N=0)
Baseline Medication					
cDMARDs, during baseline					
n, total	0 (0.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	- (-)	1.00 (1.41)	- (-)	- (-)	- (-)
Median	- [-, -]	1.00 [0.00, 2.00]	- [-, -]	- [-, -]	- [-, -]
Min, Max	-, -	0.0, 2.0	-, -	-, -	-, -
>1 cDMARD concomitantly	0 (0.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hydroxychloroquine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Leflunomide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate	0 (0.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
bDMARDs, during baseline					
n, total	0 (0.0%)	2 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	- (-)	1.50 (0.71)	- (-)	- (-)	- (-)
Median	- [-, -]	1.50 [1.00, 2.00]	- [-, -]	- [-, -]	- [-, -]
Min, Max	-, -	1.0, 2.0	-, -	-, -	-, -
cDMARDs, concomitant	0 (0.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abatacept	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adalimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Etanercept[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Golimumab[c]	0 (0.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infliximab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	0 (0.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Medication[d]					
Methotrexate, concomitant	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Concomitant cDMARD	0 (0.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dose change, baricitinib	NA[d]	0 (0.0%)	NA[d]	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c TNF inhibitors

d Only baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked 'NA' as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.41. - Pattern of RA Medication Use in Patients with VTE, Primary Definition [Healthagen].docx

Table 42_Aetna. Time to First Event Outcome (days) - VTE, Primary Definition [Aetna]

Time	Unmatched		Matched		
	Baricitinib[a,b] (N=69)	TNFi (N=289)	Baricitinib[a,b] (N=37)	TNFi (N=37)	Total (N=74)
n	69	289	37	37	74
Mean (SD)	- (-)	133.50 (143.54))	- (-)	- (-)	- (-)
Median	- [-, -]	133.50 [32.00, 235.00]	- [-, -]	- [-, -]	- [-, -]
Min, Max	-,-	32.0, 235.0	-,-	-,-	-,-

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category SD = standard deviation; VTE = venous thromboembolism.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Only baricitinib 2-mg dose is available in the US

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.42. Time to First Event Outcome (days) - VTE, Primary Definition [Healthagen].docx

Table 48_Aetna. Comparative Risk of Incident VTE, Primary Definition [Aetna]

	TNFi	Baricitinib HR	95%CI	p-value
Base Model[1,2]	Ref	-	-	-

Abbreviations: cDMARD = conventional disease-modifying antirheumatic drug; CI = confidence interval; HR = Cox proportional hazard ratio; Ref = referent group; VTE = venous thromboembolism.

1 Base model = propensity score-matched model with confounders, outcome and baricitinib exposure.

2 Zero events in both the baricitinib exposure and TNFi referent groups preclude analyzing models with additional parameters. The model did not converge.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.48. Comparative Risk of Incident VTE, Primary Definition [Healthagen (RA)], updated base model = PS matched.docx

Table 51_Aetna. Clinical Characteristics of RA Patients with MACE, Primary Definition [Aetna]

Characteristic[a,b]	Baricitinibc (N=0)	TNFi (N=0)	Total (N=0)
Age (mean) [SD]	- (-)	- (-)	- (-)
Sex			
Female	0 (0.0%)	0 (0.0%)	0 (0.0%)
Male	0 (0.0%)	0 (0.0%)	0 (0.0%)
Clinical Conditions during baseline			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic lung disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dyslipidaemia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertension	0 (0.0%)	0 (0.0%)	0 (0.0%)
Immune disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Primary Sjögren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	- (-)	- (-)	- (-)
Smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)
Surgery, Trauma, & Hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medications			
Antibiotics	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antidiabetic agents	0 (0.0%)	0 (0.0%)	0 (0.0%)
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			
Anticoagulant	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antihypertensives	0 (0.0%)	0 (0.0%)	0 (0.0%)

Characteristic[a,b]	**Baricitinibc (N=0)**	**TNFi (N=0)**	**Total (N=0)**
Antiplatelet	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			
Oral contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERM	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol absorption Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucocorticosteroid	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vaccinations	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Occurrence[d]			
Methotrexate, concomitant	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; HRT = hormone replacement therapy; SD = standard deviation; RA = rheumatoid arthritis; SERM = selective estrogen receptor modifier; SLE = systemic lupus erythematosus; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d Events in this category must have occurred in the 7 days immediately prior to MACE.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.51. - Clinical Characteristics of RA Patients with MACE [Healthagen]_.docx

Table 52_Aetna. Pattern of RA Medication Use in Patients with MACE, Primary Definition [Aetna]

Characteristic[a]	Unmatched		Matched		
	Baricitinib[b] (N=0)	TNFi (N=1)	Baricitinib[b] (N=0)	TNFi (N=0)	Total (N=0)
Baseline Medication					
cDMARDs, during baseline					
n, total	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	- (-)	0.00 (0.00)	- (-)	- (-)	- (-)
Median	- [-, -]	0.00 [0.00, 0.00]	- [-, -]	- [-, -]	- [-, -]
Min, Max	-, -		-, -	-, -	-, -
>1 cDMARD concomitantly	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hydroxychloroquine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Leflunomide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
bDMARDs, during baseline					
n, total	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	- (-)	1.00 (0.00)	- (-)	- (-)	- (-)
Median	- [-, -]	1.00 [1.00, 1.00]	- [-, -]	- [-, -]	- [-, -]
Min, Max	-, -		-, -	-, -	-, -
cDMARDs, concomitant	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abatacept	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adalimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Etanercept[c]	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Golimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infliximab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Medication[d]					
Methotrexate, concomitant	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Concomitant cDMARD	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dose change, baricitinib	NA[d]	0 (0.0%)	NA[d]	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c TNF inhibitors.

d Only baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked 'NA' as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.52. - Pattern of RA Medication Use in Patients with MACE [Healthagen].docx

Table 53_Aetna. Time to First MACE Event (Days), Primary Definition [Aetna]

	Unmatched		Matched		
	Baricitiniba,b (N=70)	TNFi (N=289)	Baricitiniba,b (N=43)	TNFi (N=43)	Total (N=86)
n	70	289	43	43	86
Mean (SD)	- (-)	37.00 (0.00)	- (-)	- (-)	- (-)
Median	- [-, -]	37.00 [37.00, 37.00]	- [-, -]	- [-, -]	- [-, -]
Min, Max	-,-	37.0, 37.0	-,-	-,-	-,-

Abbreviations: MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis code of acute myocardial infarction or ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Only baricitinib 2-mg dose is available in the US

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.53. - Time to First MACE (Days) [Healthagen].docx

Table 55_Aetna. Comparative Risk of MACE [Aetna]

	TNFi	Baricitinib		p-value
		HR	95%CI	
Base Model[1,2]	Ref	-	-	-

Abbreviations: CI = confidence interval; HR = Cox proportional hazard ratio; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis code of acute myocardial infarction or ischemic or hemorrhagic stroke; Ref = referent group; TNFi = tumour necrosis factor inhibitor.

1 Base model = propensity score-matched model with confounders, outcome and baricitinib exposure.

2 Zero events in the TNFi group preclude analysing models with additional parameters. The model did not converge.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.55. - Comparative Risk of MACE [Healthagen (RA)].docx

Table 56_Aetna. Clinical Characteristics of RA Patients with Incident Serious Infections [Aetna]

Characteristics[a,b]	Baricitinib[c] (N=1)	TNFi (N=1)	Total (N=2)
Age (mean) [SD]	50.00 (0.00)	53.00 (0.00)	51.50 (2.12)
Sex			
Female	1 (100.0%)	1 (100.0%)	2 (100.0%)
Male	0 (0.0%)	0 (0.0%)	0 (0.0%)
Clinical Conditions during baseline			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic Lung disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive Heart Failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dyslipidaemia	1 (100.0%)	0 (0.0%)	1 (50.0%)
Hypertension	1 (100.0%)	0 (0.0%)	1 (50.0%)
Immune disorders	1 (100.0%)	0 (0.0%)	1 (50.0%)
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	1 (100.0%)	0 (0.0%)	1 (50.0%)
Primary Sjögren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	4.32 (0.00)	4.36 (0.00)	4.34 (0.03)
Smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)
Surgery, Trauma, & Hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medications			
Antibiotics	1 (100.0%)	0 (0.0%)	1 (50.0%)
Antidiabetic agents	0 (0.0%)	0 (0.0%)	0 (0.0%)
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			
Anticoagulant	1 (100.0%)	0 (0.0%)	1 (50.0%)

Characteristics[a,b]	Baricitinib[c] (N=1)	TNFi (N=1)	Total (N=2)
Antihypertensives	1 (100.0%)	1 (100.0%)	2 (100.0%)
Antiplatelet	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oral Contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERMs	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucocorticosteroid	1 (100.0%)	1 (100.0%)	2 (100.0%)
Vaccinations	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: AIDS = acquired immune deficiency syndrome; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; N = number of patients in the analysis in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modifier; SLE = systemic lupus erythematosus; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = Venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. [Updated 2022.03.15] Table 6.56. Clinical Characteristics of RA Patients with Incident Serious Infections [Healthagen].docx

Table 57_Aetna. Pattern of RA Medication Use in Patients with Serious Infection Event [Aetna]

Characteristic[a]	Unmatched		Matched		
	Baricitinib[b] (N=1)	TNFi (N=4)	Baricitinib[b] (N=1)	TNFi (N=1)	Total (N=2)
Baseline Medication DMARDS					
cDMARDs, during baseline					
n, total	1 (100.0%)	2 (50.0%)	1 (100.0%)	1 (100.0%)	2 (100.0%)
Mean (SD)	1.00 (0.00)	0.75 (0.50)	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)
Median	1.00 [1.00, 1.00]	1.00 [0.25, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
Min, Max	1.0, 1.0	0.0, 1.0	1.0, 1.0	1.0, 1.0	1.0, 1.0
>1 cDMARD concomitantly	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hydroxychloroquine	1 (100.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	1 (50.0%)
Leflunomide	0 (0.0%)	1 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate	0 (0.0%)	1 (25.0%)	0 (0.0%)	1 (100.0%)	1 (50.0%)
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
bDMARDs, during baseline					
n, total	0 (0.0%)	4 (100.0%)	0 (0.0%)	1 (100.0%)	1 (50.0%)
Mean (SD)	0.00 (0.00)	1.00 (0.00)	0.00 (0.00)	1.00 (0.00)	0.50 (0.71)
Median	0.00 [0.00, 0.00]	1.00 [1.00, 1.00]	0.00 [0.00, 0.00]	1.00 [1.00, 1.00]	0.50 [0.00, 1.00]
Min, Max	0.0, 0.0	1.0, 1.0	0.0, 0.0	1.0, 1.0	0.0, 1.0
cDMARDs, concomitant	0 (0.0%)	2 (50.0%)	0 (0.0%)	1 (100.0%)	1 (50.0%)
Abatacept	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adalimumab[c]	0 (0.0%)	3 (75.0%)	0 (0.0%)	1 (100.0%)	1 (50.0%)
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	1 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Etanercept[c]	0 (0.0%)	2 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Golimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infliximab[c]	0 (0.0%)	2 (50.0%)	0 (0.0%)	1 (100.0%)	1 (50.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Medication					
Methotrexate, concomitant	0 (0.0%)	2 (50.0%)	0 (0.0%)	1 (100.0%)	1 (50.0%)
Other Concomitant cDMARD	1 (100.0%)	2 (50.0%)	1 (100.0%)	0 (0.0%)	1 (50.0%)
Dose change, baricitinib	NA	0 (0.0%)	NA	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; DMARD = disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c TNF inhibitors.

d Only baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked 'NA' as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.57. Pattern of RA Medication Use in Patients with Serious Infection Event [Healthagen].docx

Table 58_Aetna. Time to First Serious Infection (Days) [Aetna]

	Unmatched		Matched		
	Baricitinib[a,b] (N=73)	**TNFi (N=301)**	**Baricitinib[a,b] (N=44)**	**TNFi (N=44)**	**Total (N=88)**
n	73	301	44	44	88
Mean (SD)	26.00 (0.00)	352.00 (343.72)	26.00 (0.00)	562.00 (0.00)	294.00 (379.01)
Median	26.00 [26.00, 26.00]	329.50 [43.00, 683.50]	26.00 [26.00, 26.00]	562.00 [562.00, 562.00]	294.00 [26.00, 562.00]
Min, Max	26.0, 26.0	25.0, 724.0	26.0, 26.0	562.0, 562.0	26.0, 562.0

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Only baricitinib 2-mg dose is available in the US

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. [Updated 2022.03.15] Table 6.58. Time to First Seroius Infection (Days) [Healthagen (RA)].docx

Table 60_Aetna. Serious Infection Events Per Patient During All Available Follow-up [Aetna]

Number of Infections per Person	Unmatched		Matched		
	Baricitinib (N=73)	TNFi (N=301)	Baricitinib (N=44)	TNFi (N=44)	Total (N=88)
0	71 (97.3%)	288 (95.7%)	42 (95.5%)	43 (97.7%)	85 (96.6%)
1	0 (0.0%)	2 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
4	0 (0.0%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
5	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
6	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
>6	2 (2.7%)	10 (3.3%)	2 (4.5%)	1 (2.3%)	3 (3.4%)

Abbreviations: N = number of patients in the specified category; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.60. Serious Infection Events Per Patient During All Available Follow-up [Healthagen].docx

Table 64_Aetna. Incidence Rate of Hospitalized TB Event [Aetna]

	Unmatched		Matched		
	Baricitinib (N=74)	**TNFi (N=305)**	**Baricitinib (N=46)**	**TNFi (N=46)**	**Total (N=92)**
Overall					
Person-Years	31.57	180.95	16.73	22.12	38.84[a]
TB Events	0.0	0.0	0.0	0.0	0.0
TB Events/100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 11.69	0.00, 2.04	0.00, 22.06	0.00, 16.68	0.00, 9.50

Abbreviations: CI = confidence interval; N = number of patients in the specified category; PY = person-years; TB = tuberculosis; TNFi = tumour necrosis factor inhibitor.

a The person-years in the matched groups do not sum to the total due to rounding.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.64. Incidence Rate of Hospitalized TB Event [Healthagen].docx

II. Variable Ratio Matching

All prior tables presented in this annex were based on propensity score matched baricitinib:TNFi cohorts using a 1:1 matching strategy. In this section of the annex, the tables include results that are based on a variable ratio matching (VRM) approach as described in Section 9.9.6.1 of the final study report.

The main analysis was modified to use 1:1 matching, as this allows the results in the meta-analysis to be directly proportional to the amount of baricitinib exposure in each data source. For transparency, comparative results generated using VRM prior to the adoption of the 1:1 matching are included here.

Table 45_Aetna_VRM. Incidence Rate of Event - VTE, Primary Definition [Aetna]

	Unmatched		Matched		
	Baricitinib[a] (N=69)	**TNFi (N=289)**	**Baricitinib[a] (N=39)**	**TNFi (N=92)**	**Total (N=131)**
Overall					
Person-Years	29.61	173.51	10.41	51.98	62.39
VTE Events	0	2	0	0	0
VTE Events/100 PY	0.00	1.15	0.00	0.00	0.00
95% CI	0.00, 12.46	0.14, 4.16	0.00, 35.42	0.00, 7.10	0.00, 5.91
Concomitant MTX Use[b]					
Total, n	13 (18.8%)	81 (28.0%)	5 (12.8%)	31 (33.7%)	36 (27.5%)
Person-Years	8.04	67.58	2.28	24.98	27.27
VTE Events	0	0	0	0	0
VTE Events/100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 45.89	0.00, 5.46	0.00, 161.44	0.00, 14.77	0.00, 13.53
No Concomitant MTX Use[b]					
Total, n	56 (81.2%)	208 (72.0%)	34 (87.2%)	61 (66.3%)	95 (72.5%)
Person-Years	21.57	105.93	8.13	27.00	35.13
VTE Events	0	2	0	0	0
VTE Events/100 PY	0.00	1.89	0.00	0.00	0.00
95% CI	0.00, 17.10	0.23, 6.82	0.00, 45.38	0.00, 13.66	0.00, 10.50

Abbreviations: CI = confidence intervals; MTX = methotrexate; N = number of patients in the specified category; PY = person-year; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available.

b Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period

c N (%) of subgroups may not always sum precisely to total group N (%) due to rounding

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.45. Incidence Rate of Event - VTE, Primary Definition [Healthagen (RA)]_vrm.docx

Table 48_Aetna_VRM. Comparative Risk of Incident VTE, Primary Definition [Aetna]

	TNFi	Baricitinib		p-value
		HR	95%CI	
Base Model[1]	Ref	<0.001	<0.001, >999.999	0.90

Abbreviations: CI = confidence interval; HR = Cox proportional hazard ratio; Ref = referent group; VTE = venous thromboembolism.

1 Overall, rare outcome events in the exposed and/or referent groups preclude the interpretability of the HR
Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.48. Comparative Risk of Incident VTE, Primary Definition [Healthagen (RA)]_vrm.docx

Table 54_Aetna_VRM. Incidence Rate of Event - MACE [Aetna]

Model	Unmatched		Matched		
	Baricitinib[a] (N=70)	TNFi (N=289)	Baricitinib[a] (N=39)	TNFi (N=93)	Total (N=132)
Overall					
Person-Years	29.77	173.27	13.81	52.48	66.29
MACE	0	1	0	0	0
MACE/100 PY	0.00	0.58	0.00	0.00	0.00
95% CI	0.00, 12.39	0.02, 3.22	0.00, 26.71	0.00, 7.03	0.00, 5.57
MI					
MI	0	0	0	0	0
Person-Years	29.77	173.75	13.81	52.48	66.29
IR per100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 12.39	0.00, 2.12	0.00, 26.71	0.00, 7.03	0.00, 5.57
Stroke, any					
Stroke	0	1	0	0	0
Person-Years	29.77	173.27	13.81	52.48	66.29
IR per 100 PY	0.00	0.58	0.00	0.00	0.00
95% CI	0.00, 12.39	0.02, 3.22	0.00, 26.71	0.00, 7.03	0.00, 5.57
Concomitant MTX Use[b]					
MACE	0	0	0	0	0
Person-Years	8.04	67.58	4.10	20.22	24.32

IR per 100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 45.89	0.00, 5.46	0.00, 89.94	0.00, 18.25	0.00, 15.17
No Concomitant MTX Use[b]					
MACE	0	1	0	0	0
Person-Years	21.73	105.68	9.71	32.26	41.97
IR per 100 PY	0.00	0.95	0.00	0.00	0.00
95% CI	0.00, 16.98	0.02, 5.27	0.00, 37.99	0.00, 11.44	0.00, 8.79

Abbreviations: CI = confidence interval; IR = incidence rate; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; MI = myocardial infarction; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

c N in subgroups may not always sum precisely to total group N due to rounding.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.54. Incidence Rate of Event - MACE [Healthagen (RA)]_vrm.docx

Table 59_Aetna_VRM. Incidence Rate of Event - First Serious Infection [Aetna]

	Unmatched		**Matched**		
	Baricitinib (N=73)	**TNFi (N=301)**	**Baricitinib (N=42)**	**TNFi (N=102)**	**Total (N=144)**
SI Events	1	4	1	0	1
Person-years	31.32	177.83	15.92	57.02	72.94
IR per 100 PY	3.19	2.25	6.28	0.00	1.37
95% CI	0.08, 17.79	0.61, 5.76	0.16, 35.00	0.00, 6.47	0.04, 7.64

Abbreviations: CI = confidence interval; IR = incidence rate; N = number of patients in the specified category; PY = person-years; SI = serious infection; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\AETNA\7. Table 6.59. Incidence Rate of Event - First Serious Infection [Healthagen RA]_vrm.docx

Annex 3. Anthem – Additional Results

This annex includes information about results for the following analyses:

I. Additional analysis

These are the additional results that were not presented in the body of this report. Like the results in the body, they are based on 1:1 baricitinib:TNFi propensity-score matching. Specifically, this includes the following:

a. Descriptive tables for unmatched eligible patients.
b. Descriptive tables for matched patient cohorts for the VTE, MACE and serious infection analyses

II. 1:3 Ratio Matching

These results were not presented in the body of this report. They are based on matching baricitinib:TNFi using 1:3 matching.

To maintain privacy for this data source counts are reported as ≤ 10 when counts are between 1 and 10. When no events have occurred, '0' is recorded.

I. Additional Analyses

Table 1_HIRD. Baseline Demographics, Unmatched [HIRD]

	Baricitinib (N=255)	TNFi (N=1,304)	Std. Diff. (Baricitinib vs. TNFi)
Age [yrs]			
N	255	1,304	
Mean (SD)	55.0 (11.8)	53.9 (13.4)	0.08
Median	56.0	55.0	
Min, Max	21.0, 88.0	18.0, 92.0	
≥65 years	39 (15.3%)	260 (19.9%)	-0.12
Sex			
Male	42 (16.5%)	308 (23.6%)	-0.18
Female	213 (83.5%)	996 (76.4%)	

Abbreviations: HIRD = HealthCore Integrated Research Database; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthcore_HC\Table6.1_sv1.docx

Table 4_HIRD. Baseline Demographics Incident Serious Infections Cohorts, Matched [HIRD]

	Baricitinib (N=130)	TNFi (N=130)	Std. Diff. (Any vs. TNFi)	Total (N=260)
Age [yrs]				
N	130	130		260
Mean (SD)	56.5 (11.2)	55.6 (12.7)	0.08	56.0 (12.0)
Median	57.0	57.0		57.0
Min, Max	21.0, 88.0	19.0, 91.0		19.0, 91.0
≥65 years	21 (16.2%)	28 (21.5%)	-0.14	49 (18.9%)
Sex				
Male	25 (19.2%)	25 (19.2%)	0.00	50 (19.2%)
Female	105 (80.8%)	105 (80.8%)		210 (80.8%)

Abbreviations: N = number of patients in the specified category; HIRD = HealthCore Integrated Research Database; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus; yrs = years.
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Table 6_HIRD. Clinical History at Baseline, Unmatched Cohorts [HIRD]

Characteristic[a,b]	Baricitinib[c] (N=255)	TNFi (N=1,304)	Std. Diff.
Clinical Conditions during Baseline			
Cancer	21 (8.2%)	99 (7.6%)	0.02
NMSC	≤ 10	15 (1.2%)	0.00
Chronic lung disease	47 (18.4%)	184 (14.1%)	0.12
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	≤ 10	18 (1.4%)	-0.11
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	NA
Congestive heart failure, hospitalized	≤ 10	≤ 10	0.17
Coronary artery disease	18 (7.1%)	66 (5.1%)	0.08
Ischemic heart disease	18 (7.1%)	76 (5.8%)	0.05
Unstable angina	0 (0.0%)	≤ 10	NA
Ventricular arrhythmia	≤ 10	37 (2.8%)	0.02
Diabetes Mellitus	36 (14.1%)	190 (14.6%)	-0.01
Type I	≤ 10	20 (1.5%)	-0.03
Type II	34 (13.3%)	182 (14.0%)	-0.02
Dyslipidaemia	75 (29.4%)	384 (29.4%)	-0.00
Hypertension	82 (32.2%)	505 (38.7%)	-0.14
Immune disorders	42 (16.5%)	111 (8.5%)	0.24
AIDS/HIV	≤ 10	≤ 10	0.07
Antiphospholipid syndrome	≤ 10	≤ 10	0.01
SLE	18 (7.1%)	30 (2.3%)	0.23
Primary Sjögren syndrome	26 (10.2%)	84 (6.4%)	0.14
Liver disorder	≤ 10	17 (1.3%)	-0.05
Obesity	59 (23.1%)	314 (24.1%)	-0.02
Pregnancy	≤ 10	15 (1.2%)	-0.09
RA Severity (CIRAS Index), mean (SD)	3.8 (1.5)	3.7 (1.4)	0.03

Characteristic[a,b]	Baricitinib[c] (N=255)	TNFi (N=1,304)	Std. Diff.
Smoking	31 (12.2%)	171 (13.1%)	-0.03
Surgery, trauma & hospitalization, recent	12 (4.7%)	40 (3.1%)	0.08
TIA	≤ 10	11 (0.8%)	-0.06
DMARDs			
cDMARDs, during baseline			
n, total	131 (51.4%)	761 (58.4%)	-0.14
Mean (SD)	0.7 (0.7)	0.7 (0.7)	-0.09
Median	1.0	1.0	NA
Min, Max	0.0, 3.0	0.0, 4.0	NA
>1 cDMARD concomitantly	17 (6.7%)	89 (6.8%)	-0.01
Hydroxychloroquine	43 (16.9%)	176 (13.5%)	0.09
Leflunomide	36 (14.1%)	141 (10.8%)	0.10
Methotrexate	65 (25.5%)	479 (36.7%)	-0.24
Minocycline	0 (0.0%)	0 (0.0%)	NA
Sulfasalazine	≤ 10	89 (6.8%)	-0.13
bDMARDs, during baseline			
n, total	124 (48.6%)	1,304 (100.0%)	-1.45
Mean (SD)	0.5 (0.6)	1.0 (0.2)	-1.16
Median	0.0	1.0	NA
Min, Max	0.0, 3.0	1.0, 3.0	NA
cDMARDs, concomitant	36 (14.1%)	485 (37.2%)	-0.55
abatacept	28 (11.0%)	28 (2.1%)	0.36
adalimumab[d]	18 (7.1%)	474 (36.3%)	-0.76
anakinra	≤ 10	≤ 10	0.11
certolizumab pegol[d]	12 (4.7%)	128 (9.8%)	-0.20
etanercept[d]	12 (4.7%)	345 (26.5%)	-0.63
golimumab[d]	13 (5.1%)	141 (10.8%)	-0.21
infliximab[d]	≤ 10	227 (17.4%)	-0.52
rituximab	≤ 10	≤ 10	0.28
sarilumab	20 (7.8%)	≤ 10	0.38
tocilizumab	14 (5.5%)	≤ 10	0.29
Other Prescription Medications			
Antibiotics	≤ 10	47 (3.6%)	-0.03
Antidiabetic agents	25 (9.8%)	128 (9.8%)	-0.00
Insulins	≤ 10	39 (3.0%)	0.01
Non-insulins	21 (8.2%)	108 (8.3%)	-0.00
Aspirin	≤ 10	≤ 10	0.06
Cardiovascular			
Anticoagulant	≤ 10	18 (1.4%)	-0.02
Antihypertensives	110 (43.1%)	595 (45.6%)	-0.05
Antiplatelet	≤ 10	19 (1.5%)	0.04
Nitrates	≤ 10	19 (1.5%)	-0.02
Hormonal			
HRT	≤ 10	54 (4.1%)	-0.05
Oral Contraceptives	16 (6.3%)	77 (5.9%)	0.02

Characteristic[a,b]	Baricitinib[c] (N=255)	TNFi (N=1,304)	Std. Diff.
SERMs	≤ 10	≤ 10	0.06
Lipid-lowering agents			
Bile acid binding	≤ 10	21 (1.6%)	-0.12
Cholesterol absorption inhibitor	0 (0.0%)	12 (0.9%)	NA
Fibrates	≤ 10	18 (1.4%)	-0.06
Niacin	0 (0.0%)	0 (0.0%)	NA
Omega-3 fatty acids	≤ 10	≤ 10	0.05
Statins	60 (23.5%)	290 (22.2%)	0.03
Rheumatoid arthritis-related			
Cox-2 Inhibitor	14 (5.5%)	100 (7.7%)	-0.09
Glucocorticosteroid	175 (68.6%)	832 (63.8%)	0.10
Vaccinations	61 (23.9%)	320 (24.5%)	-0.01

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; cDMARD = conventional disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; HIRD = HealthCore Integrated Research Database; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff. = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day of cohort entry, with the exception of baseline bDMARDs.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4 mg baricitinib doses are included when the 4 mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d TNF inhibitors. Unless otherwise noted, characteristics in this table and similar tables are measured during baseline, including on the index day.

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Table 9_HIRD. Clinical Characteristics Incident Serious Infection Cohorts, Matched [HIRD]

Characteristic[a,b]	Baricitinib[c] (N=130)	TNFi[d] (N=130)	Std. Diff.
Clinical Conditions during Baseline			
Cancer	≤ 10	15 (11.5%)	-0.13
NMSC	≤ 10	≤ 10	0.06
Chronic lung disease	23 (17.7%)	25 (19.2%)	-0.04
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	≤ 10	≤ 10	0.09
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	NA
Congestive heart failure, hospitalized	≤ 10	≤ 10	0.13
Coronary artery disease	≤ 10	≤ 10	0.06

Characteristic[a,b]	Baricitinib[c] (N=130)	TNFi[d] (N=130)	Std. Diff.
Ischemic heart disease	11 (8.5%)	≤ 10	0.03
Unstable angina	0 (0.0%)	0 (0.0%)	NA
Ventricular arrhythmia	≤ 10	≤ 10	-0.04
Diabetes Mellitus	19 (14.6%)	23 (17.7%)	-0.08
Type I	≤ 10	≤ 10	-0.13
Type II	18 (13.8%)	22 (16.9%)	-0.09
Dyslipidaemia	44 (33.8%)	42 (32.3%)	0.03
Hypertension	41 (31.5%)	51 (39.2%)	-0.16
Immune disorders	16 (12.3%)	20 (15.4%)	-0.09
AIDS/HIV	0 (0.0%)	0 (0.0%)	NA
Antiphospholipid syndrome	≤ 10	0 (0.0%)	NA
SLE	≤ 10	≤ 10	-0.14
Primary Sjögren syndrome	11 (8.5%)	13 (10.0%)	-0.05
Liver disorder	≤ 10	≤ 10	0.00
Obesity	25 (19.2%)	34 (26.2%)	-0.17
Pregnancy	≤ 10	≤ 10	-0.13
RA Severity (CIRAS Index), mean (SD)	3.7 (1.4)	3.6 (1.3)	0.07
Smoking	16 (12.3%)	18 (13.8%)	-0.05
Surgery, trauma & hospitalization, recent	≤ 10	0 (0.0%)	NA
TIA	0 (0.0%)	0 (0.0%)	NA
DMARDs			
cDMARDs, during baseline			
n, total	64 (49.2%)	87 (66.9%)	-0.36
Mean (SD)	0.6 (0.7)	0.8 (0.7)	-0.23
Median	0.0	1.0	NA
Min, Max	0.0, 2.0	0.0, 3.0	NA
>1 cDMARD concomitantly	≤ 10	≤ 10	0.00
Hydroxychloroquine	16 (12.3%)	15 (11.5%)	0.02
Leflunomide	19 (14.6%)	21 (16.2%)	-0.04
Methotrexate	35 (26.9%)	52 (40.0%)	-0.28
Minocycline	0 (0.0%)	0 (0.0%)	NA
Sulfasalazine	≤ 10	≤ 10	-0.03
bDMARDs, during baseline			
n, total	130 (100.0%)	130 (100.0%)	NA
Mean (SD)	1.1 (0.3)	1.1 (0.3)	0.03
Median	1.0	1.0	NA
Min, Max	1.0, 3.0	1.0, 2.0	NA
cDMARDs, concomitant	40 (30.8%)	57 (43.8%)	-0.27
abatacept	29 (22.3%)	≤ 10	0.54
adalimumab[d]	20 (15.4%)	44 (33.8%)	-0.44
anakinra	≤ 10	0 (0.0%)	NA
certolizumab pegol[d]	12 (9.2%)	18 (13.8%)	-0.14
etanercept[d]	13 (10.0%)	36 (27.7%)	-0.46
golimumab[d]	13 (10.0%)	16 (12.3%)	-0.07
infliximab[d]	≤ 10	18 (13.8%)	-0.32

Characteristic[a,b]	Baricitinib[c] (N=130)	TNFi[d] (N=130)	Std. Diff.
rituximab	≤ 10	0 (0.0%)	NA
sarilumab	20 (15.4%)	≤ 10	0.47
tocilizumab	17 (13.1%)	0 (0.0%)	NA
Other Prescription Medications			
Antibiotics	≤ 10	≤ 10	0.17
Antidiabetic agents	11 (8.5%)	12 (9.2%)	-0.03
Insulins	≤ 10	≤ 10	0.00
Non-insulins	≤ 10	≤ 10	0.03
Aspirin	≤ 10	0 (0.0%)	NA
Cardiovascular			
Anticoagulant	≤ 10	≤ 10	0.03
Antihypertensives	55 (42.3%)	59 (45.4%)	-0.06
Antiplatelet	≤ 10	≤ 10	0.00
Nitrates	≤ 10	≤ 10	0.13
Hormonal			
HRT	≤ 10	≤ 10	-0.04
Oral Contraceptives	≤ 10	≤ 10	0.04
SERMs	≤ 10	≤ 10	0.07
Lipid-lowering agents			
Bile acid binding	≤ 10	≤ 10	-0.21
Cholesterol absorption inhibitor	0 (0.0%)	≤ 10	NA
Fibrates	0 (0.0%)	≤ 10	NA
Niacin	0 (0.0%)	0 (0.0%)	NA
Omega-3 fatty acids	≤ 10	≤ 10	-0.07
Statins	33 (25.4%)	35 (26.9%)	-0.04
Rheumatoid arthritis-related			
Cox-2 Inhibitor	≤ 10	≤ 10	0.03
Glucocorticosteroid	97 (74.6%)	107 (82.3%)	-0.19
Vaccinations	32 (24.6%)	37 (28.5%)	-0.09

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; cDMARD = conventional disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; HIRD = HealthCore Integrated Research Database; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff. = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day of cohort entry, with the exception of baseline bDMARDs.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4 mg baricitinib doses are included when the 4 mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d TNF inhibitors.

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Table 11_HIRD. Baseline Healthcare Resource Utilization, Unmatched [HIRD]

Type of Resource Use	Baricitinib (N=255)	TNFi (N=1,304)	Std. Diff.
Physician Office Visits			
n, patient	230 (90.2%)	1,199 (91.9%)	-0.06
n, events			
Mean (SD)	6.1 (5.1)	5.7 (4.4)	0.08
Median	5.0	5.0	
Min, Max	1.0, 37.0	1.0, 34.0	
Rheumatologist Visits			
n, patient	224 (87.8%)	1,128 (86.5%)	0.04
n, events			
Mean (SD)	2.5 (1.4)	2.5 (1.6)	0.03
Median	2.0	2.0	
Min, Max	1.0, 10.0	1.0, 15.0	
Other Outpatient Visits			
n, patient	247 (96.9%)	1,274 (97.7%)	-0.05
n, events			
Mean (SD)	13.6 (13.3)	13.4 (12.3)	0.02
Median	9.0	10.0	
Min, Max	1.0, 84.0	1.0, 108.0	
Inpatient Visits			
n, patient	24 (9.4%)	81 (6.2%)	0.12
n, events			
Mean (SD)	1.1 (0.3)	1.1 (0.4)	0.04
Median	1.0	1.0	
Min, Max	1.0, 2.0	1.0, 3.0	
ED Visits			
n, patient	33 (12.9%)	205 (15.7%)	-0.08
n, events			
Mean (SD)	1.4 (0.8)	1.3 (0.8)	0.09
Median	1.0	1.0	
Min, Max	1.0, 4.0	1.0, 9.0	

Abbreviations: ED = emergency department; HIRD = HealthCore Integrated Research Database; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits. Other outpatient visits do not include physician office visits or rheumatologist visits.

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Table 14_HIRD. Baseline Healthcare Resource Utilization Incident Serious Infection Cohorts, Matched [HIRD]

Type of Resource Use	Baricitinib (N=130)	TNFi (N=130)	Std. Diff.
Physician Office Visits			
n, patient	114 (87.7%)	118 (90.8%)	-0.10
n, events			
Mean (SD)	6.2 (5.6)	5.7 (4.3)	0.10
Median	4.5	5.0	NA
Min, Max	1.0, 37.0	1.0, 26.0	NA
Rheumatologist Visits			
n, patient	119 (91.5%)	114 (87.7%)	0.13
n, events			
Mean (SD)	2.5 (1.3)	2.3 (1.4)	0.12
Median	2.0	2.0	NA
Min, Max	1.0, 7.0	1.0, 11.0	NA
Other Outpatient Visits			
n, patient	128 (98.5%)	127 (97.7%)	0.06
n, events			
Mean (SD)	14.5 (14.9)	15.1 (13.9)	-0.05
Median	9.5	13.0	NA
Min, Max	1.0, 84.0	1.0, 108.0	NA
Inpatient Visits			
n, patient	11 (8.5%)	≤ 10	0.19
n, events			
Mean (SD)	1.1 (0.3)	1.2 (0.4)	-0.29
Median	1.0	1.0	NA
Min, Max	1.0, 2.0	1.0, 2.0	NA
ED Visits			
n, patient	19 (14.6%)	24 (18.5%)	-0.10
n, events			
Mean (SD)	1.2 (0.5)	1.4 (1.0)	-0.25
Median	1.0	1.0	NA
Min, Max	1.0, 3.0	1.0, 5.0	NA

Abbreviations: ED = emergency department; HIRD = HealthCore Integrated Research Database; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

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Table 17_HIRD. Duration of Follow-up Period (Days), Unmatched [HIRD]

	Baricitinib[a] (N=255)	TNFi (N=1,304)	Std. Diff.
N	255	1,304	
Mean (SD)	187.8 (171.2)	288.8 (226.2)	-0.50
Median	127.0	215.0	
Min, Max	3.0, 881.0	1.0, 972.0	

Abbreviations: HIRD = HealthCore Integrated Research Database; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

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Table 18_HIRD. Duration of Follow-up Period (Days) Primary VTE Cohorts, Matched [HIRD]

	Baricitinib[a] (N=123)	TNFi (N=123)	Std. Diff.
N	123	123	.
Mean (SD)	206.2 (188.1)	294.0 (250.9)	-0.40
Median	146.0	189.0	
Min, Max	4.0, 881.0	5.0, 958.0	
Reasons for censoring			
Incident event	0 (0.0%)	0 (0.0%)	
Medication discontinued	86 (69.9%)	38 (30.9%)	0.85
Initiated b/tsDMARD	14 (11.4%)	31 (25.2%)	-0.36
End of patient record	≤ 10	20 (16.3%)	-0.25
Death (where available)	0 (0.0%)	0 (0.0%)	
End of study period (02/28/2021)	13 (10.6%)	34 (27.6%)	-0.44

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; HIRD = HealthCore Integrated Research Database; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thrombotic event

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

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Table 21_HIRD. Duration of Follow-up Period (Days) MACE Cohorts, Matched [HIRD]

	Baricitinib[a] (N=123)	TNFi (N=123)	Std. Diff.
N	123	123	.
Mean (SD)	206.2 (188.1)	288.2 (223.2)	-0.40
Median	146.0	219.0	
Min, Max	4.0, 881.0	3.0, 894.0	
Reasons for censoring			
Incident event	0 (0.0%)	0 (0.0%)	
Medication discontinued	86 (69.9%)	44 (35.8%)	0.73
Initiated b/tsDMARD	14 (11.4%)	35 (28.5%)	-0.44
End of patient record	≤ 10	15 (12.2%)	-0.13
Death (where available)	0 (0.0%)	≤ 10	
End of study period (02/28/2021)	13 (10.6%)	28 (22.8%)	-0.33

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; HIRD = HealthCore Integrated Research Database; MACE =major adverse cardiovascular event; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mgbaricitinib doses are included when the 4-mgdose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

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Table 22_HIRD. Duration of Follow-up Period (Days) Incident Serious Infection Cohorts, Matched [HIRD]

	Baricitinib[a] (N=130)	TNFi (N=130)	Std. Diff.
N	130	130	
Mean (SD)	205.9 (185.2)	281.2 (213.8)	-0.38
Median	149.5	203.0	
Min, Max	4.0, 881.0	4.0, 940.0	
Reasons for censoring			
Incident event	≤ 10	≤ 10	0.00
Medication discontinued	91 (70.0%)	38 (29.2%)	0.89
Initiated b/tsDMARD	15 (11.5%)	34 (26.2%)	-0.38
End of patient record	11 (8.5%)	19 (14.6%)	-0.19
Death (where available)	0 (0.0%)	0 (0.0%)	
End of study period (02/28/2022)	12 (9.2%)	38 (29.2%)	-0.52

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; HIRD = HealthCore Integrated Research Database; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional

columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.
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Table 40_HIRD. Clinical Characteristics of RA Patients with VTE, Primary Definition [HIRD]

Characteristic[a,b]	Baricitinib[c] (N=0)	TNFi (N=0)	Total (N=0)
Age (mean) [SD]	NA	NA	NA
Sex			
Female	0 (0.0%)	0 (0.0%)	0 (0.0%)
Male	0 (0.0%)	0 (0.0%)	0 (0.0%)
Clinical Conditions during baseline			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic Lung disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular conditions			
Atrial arrhythmia/ fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dyslipidaemia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertension	0 (0.0%)	0 (0.0%)	0 (0.0%)
Immune disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Primary Sjögren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	NA	NA	NA
Smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)
Surgery, trauma, & hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medication			
Antibiotics	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antidiabetic agents	0 (0.0%)	0 (0.0%)	0 (0.0%)
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			

Characteristic[a,b]	Baricitinib[c] (N=0)	TNFi (N=0)	Total (N=0)
Antihypertensives	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anticoagulant	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiplatelet	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			
Oral contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERM	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucocorticosteroid	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vaccinations	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post index Occurrence[d]			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hospitalization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Surgery	0 (0.0%)	0 (0.0%)	0 (0.0%)
Trauma	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: AIDS = ; CIRAS = claims-based index for RA severity; HIRD = HealthCore Integrated Research Database; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modifier; SLE = systemic lupus erythematosus; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = Venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day of cohort entry, with the exception of baseline bDMARDs.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d Except for cancer diagnosed within 90 days of VTE diagnosis, events in this category must have occurred in the 4 weeks immediately prior to VTE (Kline et al. 2017).

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Table 41_HIRD. Pattern of RA Medication Use in Patients with VTE, Primary Definition [HIRD]

	Unmatched		Matched		
Characteristic[a]	**Baricitinib[b] (N ≤ 10)**	**TNFi (N ≤ 10)**	**Baricitinib[b] (N=0)**	**TNFi (N=0)**	**Total (N=0)**
Baseline Medication					
cDMARDs, during baseline					
n, total	≤ 10	≤ 10	0 (0%)	0 (0%)	0 (0%)
Mean (SD)	1.0 (NA)	1.0 (1.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Median	1.0	1.0	0.0	0.0	0.0
Min, Max	1.0, 1.0	0.0, 2.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
>1 cDMARD concomitantly	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hydroxychloroquine	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Leflunomide	≤ 10	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
bDMARDs, during baseline					
n, total	0 (0.0%)	≤ 10	0 (0%)	0 (0%)	0 (0%)
Mean (SD)	0.0 (NA)	1.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Median	0.0	1.0	0.0	0.0	0.0
Min, Max	0.0, 0.0	1.0, 1.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
cDMARDs, concomitant	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abatacept	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adalimumab[c]	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Etanercept[c]	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Golimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infliximab[c]	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sarilumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Medication[d]					
Methotrexate, concomitant	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Concomitant cDMARD	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dose change, baricitinib	NA	NA	NA	NA	NA

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; HIRD = HealthCore Integrated Research Database; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day of cohort entry, with the exception of baseline bDMARDs.

b Both 2- and 4 mg baricitinib doses are included when the 4 mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.
c TNF inhibitors.
d Only baricitinib 2 mg dose is available in the US, so the baricitinib cells should be marked 'NA' as necessary
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Table 42_HIRD. Time to First VTE Event (Days), Primary Definition [HIRD]

	Unmatched		Matched		
	Baricitinib[a] (N ≤ 10)	**TNFi (N ≤ 10)**	**Baricitinib[a] (N=0)**	**TNFi (N=0)**	**Total (N=0)**
n	≤ 10	≤ 10	0	0	0
Mean (SD)	≤ 10	≤ 10	NA (NA)	NA (NA)	NA (NA)
Median	49.0	100.0	NA	NA	NA
Min, Max	49.0, 49.0	34.0, 682.0	NA, NA	NA, NA	NA, NA

Abbreviations: HIRD = HealthCore Integrated Research Database; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; SD = standard deviation; VTE = venous thromboembolism.
a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.
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Table 48_HIRD. Comparative Risk of Incident VTE, Primary Definition [HIRD]

	TNFi	Baricitinib		p-value
Base Model	Ref	NA	NA, NA	NA

Abbreviations: HIRD = HealthCore Integrated Research Database; NA = not applicable; Ref = referent group; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.
HealthCore was unable to perform any of the models in this table due to there being zero VTE events in both of the matched treatment groups.
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Table 51_HIRD. Clinical Characteristics of RA Patients with MACE [HIRD]

Characteristic[a,b]	**Baricitinib[c] (N=0)**	**TNFi (N=0)**	**Total (N=0)**
Age (mean) [SD]	NA (NA)	NA (NA)	NA (NA)
Sex			
Female	0 (0.0%)	0 (0.0%)	0 (0.0%)
Male	0 (0.0%)	0 (0.0%)	0 (0.0%)
Clinical Conditions during Baseline			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic lung disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)

Characteristic[a,b]	Baricitinib[c] (N=0)	TNFi (N=0)	Total (N=0)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dyslipidaemia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertension	0 (0.0%)	0 (0.0%)	0 (0.0%)
Immune disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Primary Sjögren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)
Surgery, Trauma, & Hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medications			
Antibiotics	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antidiabetic agents	0 (0.0%)	0 (0.0%)	0 (0.0%)
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			
Anticoagulant	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antihypertensives	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiplatelet	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			
Oral contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERM	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			

Characteristic[a,b]	Baricitinib[c] (N=0)	TNFi (N=0)	Total (N=0)
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol absorption Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucocorticosteroid	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vaccinations	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Occurrence[d]			
Methotrexate, concomitant	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: HIRD = HealthCore Integrated Research Database; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; HRT = hormone replacement therapy; SD = standard deviation; RA = rheumatoid arthritis; SERM = selective estrogen receptor modifier; TB = tuberculosis; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day of cohort entry, with the exception of baseline bDMARDs.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4 mg baricitinib doses are included when the 4 mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d Events in this category must have occurred in the 7 days immediately prior to MACE

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Table 52_HIRD. Pattern of RA Medication Use in Patients with MACE [HIRD]

	Unmatched		Matched		
Characteristic[a]	**Baricitinib[b] (N=0)**	**TNFi (N ≤ 10)**	**Baricitinib[b] (N=0)**	**TNFi (N=0)**	**Total (N=0)**
Baseline Medication					
cDMARDs, during baseline					
n, total	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	0.0 (NA)	0.4 (0.8)	0.0 (NA)	0 (NA)	0 (NA)
Median	0.0	0.0	0.0	0.0	0.0
Min, Max	0.0, 0.0	0.0, 2.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
>1 cDMARD concomitant	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hydroxychloroquine	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Leflunomide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Characteristic[a]	Unmatched		Matched		
	Baricitinib[b] (N=0)	TNFi (N ≤ 10)	Baricitinib[b] (N=0)	TNFi (N=0)	Total (N=0)
Methotrexate	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
bDMARDs, during baseline					
n, total	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	0.0 (NA)	1.0 (0.0)	0.0 (NA)	0.0 (NA)	0.0 (NA)
Median	0.0	1.0	0.0	0.0	0.0
Min, Max	0.0, 0.0	0.0, 1.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
cDMARDs, concomitant	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abatacept	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adalimumab[c]	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Etanercept[c]	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Golimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infliximab[c]	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sarilumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Medication					
Concomitant Methotrexate	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Concomitant cDMARD	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dose change, baricitinib	NA	NA	NA	NA	NA

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day of cohort entry, with the exception of baseline bDMARDs.

b Both 2- and 4 mg baricitinib doses are included when the 4 mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c TNF inhibitors.

d Only baricitinib 2-mg dose is available in the US, so the baricitinib dose change should be marked 'NA' in US data

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Table 53_HIRD. Time to First MACE (Days) [HIRD]

	Unmatched		Matched		
	Baricitinib[a] (N=0)	TNFi (N ≤ 10)	Baricitinib[a] (N=0)	TNFi (N=0)	Total (N=0)
n	0	≤ 10	0	0	0
Mean (SD)	NA (NA)	307.9 (260.0)	NA (NA)	NA (NA)	NA (NA)
Median	NA	265.0	NA	NA	NA
Min, Max	NA, NA	23.0, 767.0	NA, NA	NA, NA	NA, NA

Abbreviations: HIRD = HealthCore Integrated Research Database; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis code of acute myocardial infarction or ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category;NA = not applicable; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4 mg baricitinib doses are included when the 4 mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

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Table 56_HIRD. Clinical Characteristics of RA Patients with Incident Serious Infections [HIRD]

Characteristic[a,b]	Baricitinib[c] (N ≤ 10)	TNFi (N ≤ 10)	Total (N ≤ 10)
Age (mean) [SD]	≤ 10	≤ 10	57.0 (11.3)
Sex			
Female	≤ 10	≤ 10	≤ 10
Male	0 (0.0%)	0 (0.0%)	0 (0.0%)
Clinical Conditions during Baseline			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic Lung disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive Heart Failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	0 (0.0%)	≤ 10	≤ 10
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	0 (0.0%)	≤ 10	≤ 10
Dyslipidaemia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertension	0 (0.0%)	0 (0.0%)	0 (0.0%)
Immune disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)

Characteristic[a,b]	Baricitinib[c] (N ≤ 10)	TNFi (N ≤ 10)	Total (N ≤ 10)
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Primary Sjögren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	≤ 10	≤ 10	3.3 (1.0)
Smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)
Surgery, Trauma, & Hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medications			
Antibiotics	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antidiabetic agents	0 (0.0%)	≤ 10	≤ 10
Insulins	0 (0.0%)	≤ 10	≤ 10
Non-insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			
Anticoagulant	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antihypertensives	≤ 10	0 (0.0%)	≤ 10
Antiplatelet	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oral Contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERMs	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	≤ 10	≤ 10
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucocorticosteroid	≤ 10	≤ 10	≤ 10
Vaccinations	0 (0.0%)	≤ 10	≤ 10

Abbreviations: AIDS = acquired immunodeficiency syndrome; CIRAS = claims-based index for RA severity; HIRD = HealthCore Integrated Research Database; HIV = human immunodeficiency virus; HRT = hormone

replacement therapy; N = number of patients in the analysis in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modifier; SLE = systemic lupus erythematosus; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day of cohort entry, with the exception of baseline bDMARDs.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

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Table 57_HIRD. Pattern of RA Medication Use in Patients with Serious Infection, Primary Definition [HIRD]

	Unmatched		Matched		
Characteristic[a]	**Baricitinib[b] (N ≤ 10)**	**TNFi (N=19)**	**Baricitinib[b] (N ≤ 10)**	**TNFi (N ≤ 10)**	**Total (N ≤ 10)**
Baseline Medication					
DMARDS					
cDMARDs, during baseline					
n, total	≤ 10	11 (57.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	0.3 (0.6)	0.7 (0.7)	NA (NA)	NA (NA)	0.0 (0.0)
Median	0.0	1.0	NA	NA	NA
Min, Max	0.0, 1.0	0.0, 2.0	NA, NA	NA, NA	NA, NA
>1 cDMARD, concomitantly	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hydroxychloroquine	≤ 10	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Leflunomide	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
bDMARDs, during baseline					
n, total	≤ 10	19 (100.0%)	≤ 10	≤ 10	≤ 10
Mean (SD)	0.7 (1.2)	1.0 (0.0)	≤ 10	≤ 10	1.5 (0.7)
Median	0.0	1.0	2.0	1.0	1.5
Min, Max	0.0, 2.0	1.0, 1.0	2.0, 2.0	1.0, 1.0	1.0, 2.0
Concomitant cDMARDs	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abatacept	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adalimumab[c]	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	≤ 10	≤ 10	≤ 10	0 (0.0%)	≤ 10

Characteristic[a]	Unmatched		Matched		
	Baricitinib[b] (N ≤ 10)	TNFi (N=19)	Baricitinib[b] (N ≤ 10)	TNFi (N ≤ 10)	Total (N ≤ 10)
Etanercept[c]	0 (0.0%)	≤ 10	0 (0.0%)	≤ 10	≤ 10
Golimumab[c]	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infliximab[c]	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sarilumab	≤ 10	0 (0.0%)	≤ 10	0 (0.0%)	≤ 10
Tocilizumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Medication					
Methotrexate, concomitant	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Concomitant cDMARD	0 (0.0%)	≤ 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dose change, baricitinib	NA	NA	NA	NA	NA

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; HIRD = HealthCore Integrated Research Database; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day of cohort entry, with the exception of baseline bDMARDs.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c TNF inhibitors.

d Only baricitinib 2-mg dose is available in the US, so the baricitinib dose change should be marked 'NA' in US data.

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Table 58_HIRD. Time to First Serious Infection Event (Days) [HIRD]

	Unmatched		Matched		
	Baricitinib (N ≤ 10)	TNFi (N=19)	Baricitinib (N ≤ 10)	TNFi (N ≤ 10)	Total (N ≤ 10)
n	≤ 10	19	≤ 10	≤ 10	≤ 10
Mean (SD)	51.3 (44.2)	212.2 (141.2)	≤ 10	≤ 10	68.0 (48.1)
Median	31.0	200.0	102.0	34.0	68.0
Min, Max	21.0, 102.0	6.0, 546.0	102.0, 102.0	34.0, 34.0	34.0, 102.0

Abbreviations: HIRD = HealthCore Integrated Research Database; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

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II. 1:3 Matching

All prior tables presented in this annex were based on propensity score matched baricitinib:TNFi cohorts using 1:1 propensity score matching. In this section of the annex, the tables include results based on 1:3 baricitinib:TNFi matching as described in Section 9.9.6.1 of the final study report.

The main analysis was modified to use 1:1 matching, as this allows the meta-analysis result to be directly proportional to the amount of baricitinib exposure in each data source. For transparency, comparative results generated using 1:3 matching prior to the adoption of the 1:1 matching are included here.

Table 45_HIRD_1to3. Incidence rate of VTE, Primary Definition [HIRD]

	Unmatched		Matched		
	Baricitinib[a] (N=255)	**TNFi (N=1304)**	**Baricitinib[a] (N=121)**	**TNFi (N=363)**	**Total (N=484)**
Overall					
Person-Years	NA	NA	68.83	296.07	364.90
VTE Events	≤ 10	≤ 10	0	0	0
VTE Events/100 PY	0.76	0.68	0.00	0.00	0.00
95% CI	0.02, 4.25	0.27, 1.40	0.00, 5.40	0.00, 1.25	0.00, 1.01
Concomitant MTX Use					
Total, n	≤ 10	355 (22.77%)	≤ 10	83 (17.15%)	86 (17.77%)
Person-Years	NA	NA	NA	90.32	91.30
VTE Events	0	≤ 10	0	0	0
VTE Events/100 PY	0.00	0.87	0.00	0.00	0.00
95% CI	0.00, 341.10	0.18, 2.53	0.00, 374.28	0.00, 4.08	0.00, 4.04
No Concomitant MTX Use					
Total, n	251 (16.10%)	949 (60.87%)	118 (24.38%)	280 (57.85%)	398 (82.23%)
Person-Years	NA	NA	67.84	205.75	273.59
VTE Events	≤ 10	≤ 10	0	0	0
VTE Events/100 PY	0.77	0.58	0.00	0.00	0.00
95% CI	0.02, 4.28	0.16, 1.49	0.00, 5.44	0.00, 1.79	0.00, 1.35

Abbreviations: CI = confidence intervals; HIRD = HealthCore Integrated Research Database; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

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Table 48_HIRD_1to3. Comparative Risk of Incident VTE, Primary Definition [HIRD]

	TNFi	Baricitinib		p-value
Base Model	Ref	NA	NA, NA	NA

Abbreviations: HIRD = HealthCore Integrated Research Database; NA = not applicable; Ref = referent group; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

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HealthCore was unable to perform any of the models in this table due to there being zero VTE events in both of the matched treatment groups.

Table 54_HIRD_1to3. Incidence Rate of MACE [HIRD]

Model	Unmatched		Matched		
	Baricitinib[a] (N=255)	TNFi (N=1308)	Baricitinib[a] (N=123)	TNFi (N=369)	Total (N=492)
Overall					
Person-Years	131.16	NA	69.43	NA	NA
MACE	0	≤ 10	0	≤ 10	≤ 10
MACE/100 PY	0.00	0.67	0.00	0.38	0.30
95% CI	0.00, 2.81	0.27, 1.39	0.00, 5.31	0.01, 2.09	0.01, 1.66
MI					
MI	0	≤ 10	0	0	0
Person-Years	131.16	NA	69.43	266.37	335.80
IR per 100 PY	0.00	0.19	0.00	0.00	0.00
95% CI	0.00, 2.81	0.02, 0.70	0.00, 5.31	0.00, 1.38	0.00, 1.10
Stroke, any					
Stroke	0	≤ 10	0	≤ 10	≤ 10
Person-Years	131.16	NA	69.43	NA	NA
IR per 100 PY	0.00	0.48	0.00	0.38	0.30
95% CI	0.00, 2.81	0.16, 1.13	0.00, 5.31	0.01, 2.09	0.01, 1.66
Concomitant MTX Use					
MACE	0	≤ 10	0	0	0
Person-Years	1.08	NA	0.99	86.41	87.39
IR per 100 PY	0.00	0.29	0.00	0.00	0.00
95% CI	0.00, 341.10	0.01, 1.60	0.00, 374.28	0.00, 4.27	0.00, 4.22
No Concomitant MTX Use					
MACE	0	≤ 10	0	≤ 10	≤ 10
Person-Years	130.08	NA	68.44	NA	NA
IR per 100 PY	0.00	0.87	0.00	0.56	0.40
95% CI	0.00, 2.84	0.32, 1.90	0.00, 5.39	0.01, 3.10	0.01, 2.24

Abbreviations: CI = confidence interval; HIRD = HealthCore Integrated Research Database; IR = Incidence Rate; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; MI = myocardial infarction; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

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Table 59_HIRD_1to3. Incidence Rate of First Serious Infection [HIRD]

	Unmatched		Matched		
	Baricitinib (N=263)	TNFi (N=1342)	Baricitinib (N=130)	TNFi (N=390)	Total (N=520)
SI Events	≤ 10	19	≤ 10	≤ 10	≤ 10
Person-years	NA	1052.66	NA	NA	NA
IR per 100 PY	2.23	1.80	1.36	1.55	1.52
95% CI	0.46, 6.51	1.09, 2.82	0.03, 7.60	0.50, 3.62	0.56, 3.30

Abbreviations: CI = confidence interval; HIRD = HealthCore Integrated Research Database; IR = Incidence Rate; N = number of patients in the specified category; NA = not applicable; PY = person-years; SI = serious infection; TNFi = tumour necrosis factor inhibitor.

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Annex 4. CorEvitas US – Additional Results

This annex includes information about results for the following analyses:

I. Additional analysis
These additional results were not presented in the body of the report. These results, like those included in the report body, are based on 1:1 baricitinib:TNFi propensity score matching. Specifically, this section in the annex includes:
- Descriptive tables for unmatched eligible patients.
- Descriptive tables for matched patient cohorts for the serious infection analyses

II. Variable Ratio Matching
These results were not presented in the body of this report. They are based on matching baricitinib:TNFi using Variable Ratio matching, i.e., as many matched 1:3 as possible, then the maximum number matched 1:2, then the remaining patients matched 1:1.

I. Additional analysis

Table 1_Cor_US. Baseline Demographics, Unmatched [COR_US]

	Baricitinib (N=118)	TNFi (N=1897)	Std. Diff.
Age [yrs]			
n	118	1897	0.094
Mean ± SD	60.2 ± 11.4	59.0 ± 13.0	
Median	61.0	60.0	
Min, Max	27.0, 81.0	18.0, 90.0	
≥ 65 years	43 (36.4%)	716 (37.7%)	0.027
Gender			
Male	29 (24.6%)	396 (20.9%)	0.088
Female	89 (75.4%)	1501 (79.1%)	
BMI			
n	116	1860	0.069
Mean ± SD	30.0 ± 7.5	30.5 ± 7.4	
Median	28.8	29.5	
Min, Max	16.1, 50.9	15.2, 64.0	
Smoking (current or former)	66 (55.9%)	882 (47.1%)	0.177
Alcohol use	42 (35.6%)	870 (45.9%)	0.212
Education			
College/university	56 (50.0%)	1123 (62.0%)	0.244

Abbreviations: BMI = body-mass index; Max = maximum; Min = minimum; N = number of patients in a category; SD = standard deviation; Std Diff = absolute value of the standardised difference; TNFi = tumour necrosis factor inhibitor.

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Table 4_Cor_US. Baseline Demographics, Incident Serious infection, Matched [COR_US]

	Baricitinib (N=114)	TNFi (N=114)	Std. Diff.	Total (N=228)
Age [yrs]				
n	114	114	0.084	228
Mean ± SD	60.2 ±11.4	61.3 ±12.7		60.8 ±12.0
Median	61.0	61.5		61.0
Min, Max	27.0, 81.0	23.0, 84.0		23.0, 84.0
≥ 65 years	42 (36.8%)	49 (43.0%)	0.126	91 (39.9%)
Gender				
Male	27 (23.7%)	28 (24.6%)	0.021	55 (24.1%)
Female	87 (76.3%)	86 (75.4%)		173 (75.9%)
BMI				
n	112	110	0.109	222
Mean ± SD	29.8 ± 7.3	29.0 ± 6.3		29.4 ± 6.8
Median	28.8	27.8		28.4
Min, Max	16.1, 50.9	17.7, 56.8		16.1, 56.8
Smoking (current or former)	63 (55.3%)	60 (52.6%)	0.053	123 (53.9%)
Alcohol use	39 (34.2%)	48 (42.1%)	0.163	87 (38.2%)
Education				
College/university	54 (50.0%)	68 (61.8%)	0.240	122 (56.0%)

Abbreviations: BMI = body-mass index; Cor_US = CorEvitas United States; Max = maximum; Min = minimum; N = count of patients in a category; SD = standard deviation; Std Diff = absolute value of the standardised difference; TNFi = tumour necrosis factor inhibitor.

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Table 6_Cor_US. Clinical history at baseline, Unmatched Cohorts [COR_US]

	Baricitinib (N=118)	TNFi (N=1897)	Std. Diff.
History of MD-reported comorbidities (ever experienced)			
Cancer, Non-NMSC	7 (5.9%)	138 (7.3%)	0.054
Cancer, NMSC only	13 (11.0%)	107 (5.6%)	0.196
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	12 (10.2%)	196 (10.3%)	0.005
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	5 (4.2%)	58 (3.1%)	0.063
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	10 (8.5%)	123 (6.5%)	0.076
Cardiovascular revascularization	2 (1.7%)	44 (2.3%)	0.045
Congestive heart failure (hospitalized & non-hospitalized)	4 (3.4%)	24 (1.3%)	0.141
Coronary artery disease	6 (5.1%)	68 (3.6%)	0.074
Ischemic heart disease	7 (5.9%)	92 (4.8%)	0.048
TIA	1 (0.8%)	22 (1.2%)	0.031
Unstable angina	0 (0.0%)	11 (0.6%)	0.108
Ventricular arrhythmia	1 (0.8%)	13 (0.7%)	0.019
Diabetes mellitus	13 (11.0%)	220 (11.6%)	0.018
Hyperlipidemia	27 (22.9%)	331 (17.4%)	0.136
Hypertension (hospitalized & non-hospitalized)	48 (40.7%)	673 (35.5%)	0.107
Immune disorders	31 (26.3%)	352 (18.8%)	0.180
Secondary Sjogren Syndrome	31 (26.3%)	352 (18.8%)	0.180
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	5 (4.2%)	54 (2.8%)	0.075
Obesity, current	42 (36.2%)	875 (47.0%)	0.221
Pregnancy, recent (current or since last visit)	0 (0.0%)	11 (0.6%)	0.111
RA severity (CDAI)			
n	118	1897	0.188
Mean ± SD	19.0 ±11.7	16.7 ±13.0	

	Baricitinib (N=118)	TNFi (N=1897)	Std. Diff.
Median	17.4	14.0	
25th percentile, 75th percentile	11.0, 25.0	6.5, 24.0	
Min, Max	0.8, 51.2	0.0, 72.5	
Prevalent outcomes			
VTE (at any time in the past)	6 (5.1%)	34 (1.8%)	0.181
MACE (at any time in the past)	3 (2.5%)	65 (3.4%)	0.052
Myocardial infarction	3 (2.5%)	33 (1.7%)	0.055
Stroke	0 (0.0%)	34 (1.8%)	0.191
Serious infection (at any time in the past)	10 (8.5%)	174 (9.2%)	0.025
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)	
DMARD history			
Number of cDMARDs used (ever)			
0	3 (2.5%)	73 (3.8%)	0.074
1	40 (33.9%)	843 (44.4%)	0.217
2+	75 (63.6%)	981 (51.7%)	0.241
Methotrexate (prior use)	108 (91.5%)	1653 (87.1%)	0.142
Number of bDMARDs used (ever)			
0	15 (12.7%)	908 (47.9%)	0.828
1	19 (16.1%)	550 (29.0%)	0.312
2+	84 (71.2%)	439 (23.1%)	1.098
Prior bDMARD use[a]	103 (87.3%)	989 (52.1%)	0.828
Prior TNFi bDMARD use	100 (84.7%)	906 (47.8%)	0.850
Prior non-TNFi bDMARD use	72 (61.0%)	404 (21.3%)	0.882
DMARD, current (baseline)			
cDMARD, concomitant use at baseline	73 (61.9%)	1346 (71.0%)	0.193
Methotrexate, concomitant use at baseline	53 (44.9%)	980 (51.7%)	0.135
Prescription medication use, current (baseline)			
Other prescription medications			
Cardiovascular medications			
Anticoagulant (coumadin/warfarin; patient-reported)	3 (2.5%)	30 (1.6%)	0.068
Antihypertensives (blood pressure lowering medication(s); patient-reported)	55 (46.6%)	768 (40.5%)	0.124

	Baricitinib (N=118)	TNFi (N=1897)	Std. Diff.
Antiplatelet (Plavix; patient-reported)	2 (1.7%)	41 (2.2%)	0.034
Nitrates (angina/nitrate medications; patient-reported)	2 (1.7%)	17 (0.9%)	0.071
Hormonal Medication HRT (in RA US only)	1 (0.8%)	17 (0.9%)	0.005
Lipid-lowering agents (cholesterol medication; patient-reported)	31 (26.3%)	395 (20.8%)	0.129
RA-related			
Aspirin (includes non-prescription)	19 (16.1%)	253 (13.3%)	0.078
Celebrex (in RA US only)	12 (10.2%)	107 (5.6%)	0.168
Prednisone	43 (36.4%)	526 (27.7%)	0.187
Vaccinations			
Influenza (baseline) (in RA US only	45 (45.0%)	702 (41.4%)	0.072
Pneumonia (ever) (in RA US only)	27 (26.2%)	442 (25.3%)	0.021
Shingles (ever)	23 (21.7%)	386 (21.5%)	0.005

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; CDAI = clinical disease activity index; cDMARD = conventional disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; HRT = hormone replacement therapy ; MACE = major adverse cardiovascular event; Max = maximum; MD = medical doctor; Min = minimum; N = count of patients in the category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; Std Diff = absolute value of the standardised difference; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\CorEvitas_us_COR_US\ RA US Formatted Tables_V2_20210910.docx – Page(s) 7 - 9

Table 9_Cor_US. Clinical Characteristics Incident Serious Infection Cohorts, Matched [COR_US]

	Baricitinib (N=114)	TNFi (N=114)	Std. Diff.	Total (N=228)
History of MD-reported comorbidities (ever experienced)				
Cancer, Non-NMSC	6 (5.3%)	7 (6.1%)	0.038	13 (5.7%)
Cancer, NMSC only	12 (10.5%)	5 (4.4%)	0.235	17 (7.5%)
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	11 (9.6%)	15 (13.2%)	0.111	26 (11.4%)
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	5 (4.4%)	5 (4.4%)	0.000	10 (4.4%)
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	9 (7.9%)	11 (9.6%)	0.062	20 (8.8%)
Cardiovascular revascularization	2 (1.8%)	5 (4.4%)	0.153	7 (3.1%)
Congestive heart failure (hospitalized & non-hospitalized)	3 (2.6%)	4 (3.5%)	0.051	7 (3.1%)
Coronary artery disease	5 (4.4%)	7 (6.1%)	0.079	12 (5.3%)
Ischemic heart disease	6 (5.3%)	9 (7.9%)	0.106	15 (6.6%)
TIA	1 (0.9%)	1 (0.9%)	0.000	2 (0.9%)
Unstable angina	0 (0.0%)	2 (1.8%)	0.189	2 (0.9%)
Ventricular arrhythmia	1 (0.9%)	1 (0.9%)	0.000	2 (0.9%)
Diabetes mellitus	12 (10.5%)	13 (11.4%)	0.028	25 (11.0%)
Hyperlipidaemia	25 (21.9%)	21 (18.4%)	0.088	46 (20.2%)
Hypertension (hospitalized & non-hospitalized)	45 (39.5%)	37 (32.5%)	0.147	82 (36.0%)
Immune disorders	30 (26.3%)	31 (27.2%)	0.020	61 (26.8%)
Secondary Sjogren Syndrome	30 (26.3%)	31 (27.2%)	0.020	61 (26.8%)
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	5 (4.4%)	4 (3.5%)	0.045	9 (3.9%)
Obesity, current	40 (35.7%)	39 (35.5%)	0.005	79 (35.6%)
Pregnancy, recent (current or since last visit)	0 (0.0%)	0 (0.0%)		0 (0.0%)
RA severity (CDAI)				
n	114	114	0.135	228
Mean ± SD	19.2 ±11.8	17.6 ±13.1		18.4 ±12.5
Median	17.9	14.0		16.5
25^{th} percentile, 75^{th} percentile	11.0, 25.0	6.6, 26.5		8.2, 25.5
Min, Max	0.8, 51.2	0.0, 55.0		0.0, 55.0
Prevalent outcomes				
VTE (at any time in the past)	6 (5.3%)	2 (1.8%)	0.192	8 (3.5%)
MACE (at any time in the past)	3 (2.6%)	4 (3.5%)	0.051	7 (3.1%)
Myocardial infarction	3 (2.6%)	1 (0.9%)	0.134	4 (1.8%)
Stroke	0 (0.0%)	3 (2.6%)	0.232	3 (1.3%)
Serious infection (at any time in the past)	7 (6.1%)	6 (5.3%)	0.038	13 (5.7%)

	Baricitinib (N=114)	TNFi (N=114)	Std. Diff.	Total (N=228)
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)		0 (0.0%)
DMARD history				
Number of cDMARDs used (ever)				
0	3 (2.6%)	2 (1.8%)	0.060	5 (2.2%)
1	39 (34.2%)	38 (33.3%)	0.019	77 (33.8%)
2+	72 (63.2%)	74 (64.9%)	0.037	146 (64.0%)
Methotrexate (prior use)	104 (91.2%)	102 (89.5%)	0.059	206 (90.4%)
Number of bDMARDs used (ever)				
0	15 (13.2%)	18 (15.8%)	0.075	33 (14.5%)
1	19 (16.7%)	14 (12.3%)	0.125	33 (14.5%)
2+	80 (70.2%)	82 (71.9%)	0.039	162 (71.1%)
Prior bDMARD use [a]	99 (86.8%)	96 (84.2%)	0.075	195 (85.5%)
Prior TNF bDMARD use	96 (84.2%)	90 (78.9%)	0.136	186 (81.6%)
Prior non-TNF bDMARD use	68 (59.6%)	63 (55.3%)	0.089	131 (57.5%)
DMARD, current (baseline)				
cDMARD, concomitant use at baseline	71 (62.3%)	80 (70.2%)	0.168	151 (66.2%)
Methotrexate, concomitant use at baseline	52 (45.6%)	53 (46.5%)	0.018	105 (46.1%)
Prescription medication use, current (baseline)				
Other prescription medications				
Cardiovascular medications				
Anticoagulant (coumadin/warfarin; patient-reported)	2 (1.8%)	3 (2.6%)	0.060	5 (2.2%)
Antihypertensives (blood pressure lowering medication(s); patient-reported)	52 (45.6%)	48 (42.1%)	0.071	100 (43.9%)
Antiplatelet (Plavix; patient-reported)	2 (1.8%)	5 (4.4%)	0.153	7 (3.1%)
Nitrates (angina/nitrate medications; patient-reported)	2 (1.8%)	2 (1.8%)	0.000	4 (1.8%)
Hormonal Medication HRT (in RA US only)	1 (0.9%)	0 (0.0%)	0.133	1 (0.4%)
Lipid-lowering agents (cholesterol medication; patient-reported)	28 (24.6%)	33 (28.9%)	0.099	61 (26.8%)
RA-related				
Aspirin (includes non-prescription)	19 (16.7%)	19 (16.7%)	0.000	38 (16.7%)
Celebrex (in RA US only)	12 (10.5%)	9 (7.9%)	0.091	21 (9.2%)
Prednisone	42 (36.8%)	39 (34.2%)	0.055	81 (35.5%)
Vaccinations				
Influenza (baseline) (in RA US only)	44 (45.8%)	50 (48.1%)	0.045	94 (47.0%)
Pneumonia (ever) (in RA US only)	26 (26.3%)	26 (24.3%)	0.045	52 (25.2%)
Shingles (ever)	22 (21.6%)	29 (27.1%)	0.129	51 (24.4%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; CDAI = clinical disease activity index; cDMARD = conventional disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; HRT = hormone replacement therapy; MACE = major adverse cardiovascular event; Max = maximum; Min = minimum; MD = medical doctor; N = count of patients in a category ; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; Std Diff = absolute value of the standardised difference; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Many characteristics of the cohort are included in this table but propensity score matching is only expected to balance those risk factors listed in Table 66 for each outcome e.g. congestive heart failure for VTE. Other factors are included for descriptive purposes only and may not be balanced across treatment groups but do not contribute to confounding bias e.g. diabetes for VTE.

a Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

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Table 16_Cor_US. Baseline Prevalence of Outcomes [CorEvitas US]

	Pre-matched			Matched*			
	Baricitinib (N=118)	**TNFi (N=1,897)**	**Std. Diff.**	**Baricitinib**	**TNFi**	**Std. Diff.**	**Total**
VTE	6 (5.1%)	34 (1.8%)	0.181	N=112 3 (2.7%)	N=112 2 (1.8%)	0.060	N=224 5 (2.2%)
MACE	3 (2.5%)	65 (3.4%)	0.052	N=114 2 (1.8%)	N=114 4 (3.5%)	0.110	N=228 6 (2.6%)
Serious Infection	10 (8.5%)	174 (9.2%)	0.025	N=114 7 (6.1%)	N=114 6 (5.3%)	0.038	N=228 13 (5.7%)
Hospitalized Tuberculosis	0 (0.0%)	0 (0.0%)		N=117 0 (0.0%)	N=117 0 (0.0%)		N=234 0 (0.0%)

Abbreviations: MACE = Major Adverse Cardiovascular Event; N = number of patients in the specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

* matched refers to the outcome-specific matched population

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Table 17_Cor_US. Duration of Exposure (Months*), in Pre-matched Population - exposure ends at discontinuation/last follow-up visit [COR_US]

	Baricitinib (N=118)	TNFi (N=1897)	Std. Diff.
N	118	1897	
Mean ± SD	8.1 ± 6.4	9.2 ± 6.4	0.173
Median	6.0	7.0	
Min, Max	1.0, 27.0	1.0, 30.0	

Abbreviations: Max = maximum; Min = minimum; N = count of patients in a category; RA = rheumatoid arthritis; SD = standard deviation; Std Diff = absolute value of standardised difference; TNFi = tumour necrosis factor inhibitor

* CorEvitas' RA US Registry collects drug information at the month-level so time is reported in months. A rough conversion to days can be made by multiplying the values in this table by a factor of 30.4375 (the average number of days in a month)

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Table 18_Cor_US. Duration of Exposure (Months*), in VTE-matched Population - exposure ends at discontinuation/last follow-up visit; excludes patients with VTE within 6 months prior to index date or currently taking anticoagulant [COR_US]

	Baricitinib (N=112)	TNFi (N=112)	Std. Diff.
N	112	112	
Mean ± SD	8.2 ± 6.4	9.1 ± 6.6	0.142
Median	6.0	7.0	
Min, Max	1.0, 27.0	1.0, 26.0	
Reason for censoring			
Discontinue index medication (and did not start another b/tsDMARD within 30 days)	20 (17.9%)	33 (29.5%)	
Discontinue index medication (and started another b/tsDMARD within 30 days)	34 (30.4%)	23 (20.5%)	
End of follow-up for that patient	58 (51.8%)	55 (49.1%)	
Death	n/a	n/a	
Incident event (VTE)	0 (0.0%)	1 (0.9%)	

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; RA = rheumatoid arthritis; SD = standard deviation; Std Diff = absolute value of standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

* CorEvitas RA US registry collects drug information at the month-level so time is reported in months. A rough conversion to days can be made by multiplying the values in this table by a factor of 30.4375 (the average number of days in a month)

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Table 21_Cor_US. Duration of Exposure (Months*), in MACE-matched Population - exposure ends at discontinuation/last follow-up visit; excludes patients with MACE within 6 months prior to index date or taking anticoagulant [COR_US]

	Baricitinib (N=114)	TNFi (N=114)	Std. Diff.
N	114	114	
Mean ± SD	8.1 ± 6.4	8.4 ± 5.5	0.043
Median	6.0	6.0	
Min, Max	1.0, 27.0	1.0, 25.0	
Reason for censoring			
Discontinue index medication (and did not start another b/tsDMARD within 30 days)	21 (18.4%)	33 (28.9%)	
Discontinue index medication (and started another b/tsDMARD within 30 days)	34 (29.8%)	24 (21.1%)	
End of follow-up for that patient	57 (50.0%)	56 (49.1%)	
Death	n/a	n/a	
Incident event (MACE)	2 (1.8%)	1 (0.9%)	

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; MACE = major adverse cardiovascular event; Max = maximum; Min = minimum; n/a = not available; N = number of patients in the specified category; RA = rheumatoid arthritis; SD = standard deviation; Std Diff = absolute value of standardised difference; TNFi = tumour necrosis factor inhibitor

* CorEvitas RA US registry collects drug information at the month-level so time is reported in months. A rough conversion to days can be made by multiplying the values in this table by a factor of 30.4375 (the average number of days in a month)

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Table 22_Cor_US. Duration of Exposure (Months*), in Serious Infection-matched Population - exposure ends at discontinuation/last follow-up visit; excludes patients with serious infection within 6 months prior to index date [COR_US]

	Baricitinib (N=114)	TNFi (N=114)	Std. Diff.
N	114	114	
Mean ± SD	8.3 ± 6.5	8.6 ± 5.9	0.057
Median	6.0	7.0	
Min, Max	1.0, 27.0	1.0, 30.0	
Reason for censoring			
Discontinue index medication (and did not start another b/tsDMARD within 30 days)	21 (18.4%)	29 (25.4%)	
Discontinue index medication (and started another b/tsDMARD within 30 days)	32 (28.1%)	22 (19.3%)	
End of follow-up for that patient	58 (50.9%)	63 (55.3%)	
Death	n/a	n/a	
Incident event (serious infection)	3 (2.6%)	0 (0.0%)	

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; n/a = not available; RA = rheumatoid arthritis; SD = standard deviation; Std Diff = absolute value of standardised difference; TNFi = tumour necrosis factor inhibitor.

* CorEvitas RA US registry collects drug information at the month-level so time is reported in months. A rough conversion to days can be made by multiplying the values in this table by a factor of 30.4375 (the average number of days in a month)

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Table 24_Cor_US. Baseline Clinical Characteristics by Exposure Duration, Pre-matched Population - exposure ends at discontinuation/last follow-up visit. [COR_US]

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N=55)	TNFi (N=684)	Std. Diff.	Baricitinib (N=34)	TNFi (N=619)	Std. Diff.	Baricitinib (N=25)	TNFi (N=536)	Std. Diff.	Baricitinib (N=4)	TNFi (N=58)	Std. Diff.
Age [yrs]												
n	55	684	0.04	34	619	0.14	25	536	0.61	4	58	0.47
Mean ± SD	59.2 ± 12.0	58.7 ± 13.4		56.7 ± 11.2	58.5 ± 13.4		65.8 ± 7.8	59.7 ± 12.1		67.5 ± 11.6	62.5 ± 9.7	
Median	61.0	60.0		57.0	59.0		66.0	61.0		68.0	64.0	
Min, Max	27.0, 79.0	19.0, 90.0		31.0, 81.0	18.0, 90.0		53.0, 79.0	20.0, 87.0		56.0, 78.0	37.0, 82.0	
≥ 65 years	17 (30.9%)	246 (36.0%)	0.11	8 (23.5%)	226 (36.5%)	0.29	16 (64.0%)	218 (40.7%)	0.48	2 (50.0%)	26 (44.8%)	0.10
Gender												
Male	13 (23.6%)	140 (20.5%)	0.08	7 (20.6%)	124 (20.0%)	0.01	5 (20.0%)	118 (22.0%)	0.05	4 (100.0%)	14 (24.1%)	2.51
Female	42 (76.4%)	544 (79.5%)		27 (79.4%)	495 (80.0%)		20 (80.0%)	418 (78.0%)		0 (0.0%)	44 (75.9%)	
History of MD-reported comorbidities (ever experienced)												
Cancer, Non-NMSC	4 (7.3%)	44 (6.4%)	0.03	1 (2.9%)	39 (6.3%)	0.16	2 (8.0%)	48 (9.0%)	0.03	0 (0.0%)	7 (12.1%)	0.52
Cancer, NMSC only	4 (7.3%)	38 (5.6%)	0.07	3 (8.8%)	38 (6.1%)	0.10	5 (20.0%)	29 (5.4%)	0.45	1 (25.0%)	2 (3.4%)	0.65
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	4 (7.3%)	57 (8.3%)	0.04	6 (17.6%)	79 (12.8%)	0.14	2 (8.0%)	56 (10.4%)	0.08	0 (0.0%)	4 (6.9%)	0.38
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	3 (5.5%)	22 (3.2%)	0.11	1 (2.9%)	17 (2.7%)	0.01	0 (0.0%)	18 (3.4%)	0.26	1 (25.0%)	1 (1.7%)	0.73
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	7 (12.7%)	48 (7.0%)	0.19	1 (2.9%)	38 (6.1%)	0.15	1 (4.0%)	34 (6.3%)	0.11	1 (25.0%)	3 (5.2%)	0.58

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N=55)	TNFi (N=684)	Std. Diff.	Baricitinib (N=34)	TNFi (N=619)	Std. Diff.	Baricitinib (N=25)	TNFi (N=536)	Std. Diff.	Baricitinib (N=4)	TNFi (N=58)	Std. Diff.
Cardiovascular revascularization	2 (3.6%)	22 (3.2%)	0.02	0 (0.0%)	11 (1.8%)	0.19	0 (0.0%)	11 (2.1%)	0.20	0 (0.0%)	0 (0.0%)	
Congestive heart failure (hospitalized & non-hospitalized)	4 (7.3%)	4 (0.6%)	0.35	0 (0.0%)	9 (1.5%)	0.17	0 (0.0%)	10 (1.9%)	0.19	0 (0.0%)	1 (1.7%)	0.19
Coronary artery disease	3 (5.5%)	30 (4.4%)	0.05	1 (2.9%)	20 (3.2%)	0.02	1 (4.0%)	18 (3.4%)	0.03	1 (25.0%)	0 (0.0%)	0.82
Ischemic heart disease	4 (7.3%)	37 (5.4%)	0.08	1 (2.9%)	31 (5.0%)	0.11	1 (4.0%)	24 (4.5%)	0.02	1 (25.0%)	0 (0.0%)	0.82
TIA	1 (1.8%)	9 (1.3%)	0.04	0 (0.0%)	8 (1.3%)	0.16	0 (0.0%)	3 (0.6%)	0.11	0 (0.0%)	2 (3.4%)	0.27
Unstable angina	0 (0.0%)	1 (0.1%)	0.05	0 (0.0%)	4 (0.6%)	0.11	0 (0.0%)	6 (1.1%)	0.15	0 (0.0%)	0 (0.0%)	
Ventricular arrhythmia	1 (1.8%)	8 (1.2%)	0.05	0 (0.0%)	1 (0.2%)	0.06	0 (0.0%)	4 (0.7%)	0.12	0 (0.0%)	0 (0.0%)	
Diabetes mellitus	11 (20.0%)	86 (12.6%)	0.20	1 (2.9%)	70 (11.3%)	0.33	1 (4.0%)	59 (11.0%)	0.27	0 (0.0%)	5 (8.6%)	0.43
Hyperlipidemia	11 (20.0%)	129 (18.9%)	0.03	10 (29.4%)	104 (16.8%)	0.30	6 (24.0%)	88 (16.4%)	0.19	0 (0.0%)	10 (17.2%)	0.65
Hypertension (hospitalized & non-hospitalized)	21 (38.2%)	254 (37.1%)	0.02	18 (52.9%)	218 (35.2%)	0.36	7 (28.0%)	178 (33.2%)	0.11	2 (50.0%)	23 (39.7%)	0.21
Immune disorders	13 (23.6%)	127 (19.0%)	0.11	10 (29.4%)	124 (20.2%)	0.22	8 (32.0%)	93 (17.4%)	0.34	0 (0.0%)	8 (13.8%)	0.57
Secondary Sjogren Syndrome	13 (23.6%)	127 (19.0%)	0.11	10 (29.4%)	124 (20.2%)	0.22	8 (32.0%)	93 (17.4%)	0.34	0 (0.0%)	8 (13.8%)	0.57
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	1 (1.8%)	21 (3.1%)	0.08	1 (2.9%)	21 (3.4%)	0.03	3 (12.0%)	10 (1.9%)	0.41	0 (0.0%)	2 (3.4%)	0.27
Obesity, current	17 (31.5%)	315 (47.2%)	0.33	14 (42.4%)	280 (46.4%)	0.08	10 (40.0%)	259 (48.8%)	0.18	1 (25.0%)	21 (36.8%)	0.26
Pregnancy, recent (current or since last visit)	0 (0.0%)	4 (0.6%)	0.11	0 (0.0%)	2 (0.3%)	0.08	0 (0.0%)	5 (1.0%)	0.14	0 (0.0%)	0 (0.0%)	
Smoking (current or former)	32 (58.2%)	307 (45.4%)	0.26	15 (44.1%)	297 (48.8%)	0.09	17 (68.0%)	250 (47.1%)	0.43	2 (50.0%)	28 (49.1%)	0.02
RA severity (CDAI)												
n	55	684	0.17	34	619	0.17	25	536	0.26	4	58	0.10

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N=55)	TNFi (N=684)	Std. Diff.	Baricitinib (N=34)	TNFi (N=619)	Std. Diff.	Baricitinib (N=25)	TNFi (N=536)	Std. Diff.	Baricitinib (N=4)	TNFi (N=58)	Std. Diff.
Mean ± SD	18.9 ± 10.8	16.9 ± 13.3		19.3 ± 12.8	17.2 ± 12.9		19.3 ± 12.5	16.1 ± 12.8		15.5 ± 11.8	14.3 ± 12.2	
Median	15.8	14.0		20.4	14.7		18.0	13.0		16.3	11.3	
Min, Max	4.0, 51.2	0.0, 70.2		1.0, 49.0	0.0, 66.0		2.1, 48.5	0.0, 72.5		0.8, 28.6	0.0, 48.0	
Prevalent outcomes												
VTE (at any time in the past)	4 (7.3%)	14 (2.0%)	0.25	1 (2.9%)	9 (1.5%)	0.10	1 (4.0%)	11 (2.1%)	0.11	0 (0.0%)	0 (0.0%)	
MACE (at any time in the past)	1 (1.8%)	29 (4.2%)	0.14	0 (0.0%)	17 (2.7%)	0.24	2 (8.0%)	16 (3.0%)	0.22	0 (0.0%)	3 (5.2%)	0.33
Myocardial infarction	1 (1.8%)	16 (2.3%)	0.04	0 (0.0%)	11 (1.8%)	0.19	2 (8.0%)	6 (1.1%)	0.33	0 (0.0%)	0 (0.0%)	
Stroke	0 (0.0%)	14 (2.0%)	0.20	0 (0.0%)	6 (1.0%)	0.14	0 (0.0%)	11 (2.1%)	0.20	0 (0.0%)	3 (5.2%)	0.33
Serious infection (at any time in the past)	5 (9.1%)	66 (9.6%)	0.02	3 (8.8%)	54 (8.7%)	0.00	2 (8.0%)	44 (8.2%)	0.01	0 (0.0%)	10 (17.2%)	0.65
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
DMARD history												
Number of cDMARDs used (ever)												
0	0 (0.0%)	25 (3.7%)	0.28	1 (2.9%)	28 (4.5%)	0.08	1 (4.0%)	17 (3.2%)	0.04	1 (25.0%)	3 (5.2%)	0.58
1	19 (34.5%)	302 (44.2%)	0.20	10 (29.4%)	264 (42.6%)	0.28	9 (36.0%)	248 (46.3%)	0.21	2 (50.0%)	29 (50.0%)	0.00
2+	36 (65.5%)	357 (52.2%)	0.27	23 (67.6%)	327 (52.8%)	0.31	15 (60.0%)	271 (50.6%)	0.19	1 (25.0%)	26 (44.8%)	0.43
Methotrexate (prior use)	51 (92.7%)	598 (87.4%)	0.18	32 (94.1%)	540 (87.2%)	0.24	22 (88.0%)	462 (86.2%)	0.05	3 (75.0%)	53 (91.4%)	0.45
Number of bDMARDs used (ever)												
0	5 (9.1%)	300 (43.9%)	0.86	5 (14.7%)	324 (52.3%)	0.87	4 (16.0%)	254 (47.4%)	0.72	1 (25.0%)	30 (51.7%)	0.57
1	8 (14.5%)	206 (30.1%)	0.38	5 (14.7%)	167 (27.0%)	0.31	6 (24.0%)	157 (29.3%)	0.12	0 (0.0%)	20 (34.5%)	1.03

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N=55)	TNFi (N=684)	Std. Diff.	Baricitinib (N=34)	TNFi (N=619)	Std. Diff.	Baricitinib (N=25)	TNFi (N=536)	Std. Diff.	Baricitinib (N=4)	TNFi (N=58)	Std. Diff.
2+	42 (76.4%)	178 (26.0%)	1.17	24 (70.6%)	128 (20.7%)	1.16	15 (60.0%)	125 (23.3%)	0.80	3 (75.0%)	8 (13.8%)	1.56
Prior bDMARD use[a]	50 (90.9%)	384 (56.1%)	0.86	29 (85.3%)	295 (47.7%)	0.87	21 (84.0%)	282 (52.6%)	0.72	3 (75.0%)	28 (48.3%)	0.57
Prior TNFi bDMARD use	49 (89.1%)	349 (51.0%)	0.91	27 (79.4%)	271 (43.8%)	0.79	21 (84.0%)	262 (48.9%)	0.80	3 (75.0%)	24 (41.4%)	0.73
Prior non-TNFi bDMARD use	39 (70.9%)	163 (23.8%)	1.07	21 (61.8%)	125 (20.2%)	0.93	10 (40.0%)	105 (19.6%)	0.46	2 (50.0%)	11 (19.0%)	0.69
DMARD, current (baseline)												
cDMARD, concomitant use at baseline	33 (60.0%)	476 (69.6%)	0.20	22 (64.7%)	447 (72.2%)	0.16	17 (68.0%)	386 (72.0%)	0.09	1 (25.0%)	37 (63.8%)	0.85
Methotrexate, concomitant use at baseline	21 (38.2%)	343 (50.1%)	0.24	17 (50.0%)	322 (52.0%)	0.04	14 (56.0%)	283 (52.8%)	0.06	1 (25.0%)	32 (55.2%)	0.65
Prescription medication use, current (baseline)												
Other prescription medications												
Cardiovascular medications												
Anticoagulant (coumadin/warfarin; patient-reported)	3 (5.5%)	15 (2.2%)	0.17	0 (0.0%)	8 (1.3%)	0.16	0 (0.0%)	7 (1.3%)	0.16	0 (0.0%)	0 (0.0%)	
Antihypertensives (blood pressure lowering medication(s); patient-reported)	24 (43.6%)	278 (40.6%)	0.06	19 (55.9%)	249 (40.2%)	0.32	12 (48.0%)	218 (40.7%)	0.15	0 (0.0%)	23 (39.7%)	1.15
Antiplatelet (Plavix; patient-reported)	1 (1.8%)	13 (1.9%)	0.01	1 (2.9%)	10 (1.6%)	0.09	0 (0.0%)	17 (3.2%)	0.26	0 (0.0%)	1 (1.7%)	0.19
Nitrates (angina/nitrate medications; patient-reported)	0 (0.0%)	10 (1.5%)	0.17	2 (5.9%)	5 (0.8%)	0.29	0 (0.0%)	2 (0.4%)	0.09	0 (0.0%)	0 (0.0%)	
Hormonal Medication HRT (in RA US only)	1 (1.8%)	6 (0.9%)	0.08	0 (0.0%)	8 (1.3%)	0.16	0 (0.0%)	3 (0.6%)	0.11	0 (0.0%)	0 (0.0%)	
Lipid-lowering agents (cholesterol medication; patient-reported)	15 (27.3%)	149 (21.8%)	0.13	8 (23.5%)	127 (20.5%)	0.07	8 (32.0%)	108 (20.1%)	0.27	0 (0.0%)	11 (19.0%)	0.68
RA-related												
Aspirin (includes non-prescription)	6 (10.9%)	87 (12.7%)	0.06	5 (14.7%)	69 (11.1%)	0.11	6 (24.0%)	92 (17.2%)	0.17	2 (50.0%)	5 (8.6%)	1.02

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N=55)	TNFi (N=684)	Std. Diff.	Baricitinib (N=34)	TNFi (N=619)	Std. Diff.	Baricitinib (N=25)	TNFi (N=536)	Std. Diff.	Baricitinib (N=4)	TNFi (N=58)	Std. Diff.
Celebrex (in RA US only)	7 (12.7%)	42 (6.1%)	0.23	3 (8.8%)	39 (6.3%)	0.10	2 (8.0%)	23 (4.3%)	0.15	0 (0.0%)	3 (5.2%)	0.33
Prednisone	20 (36.4%)	205 (30.0%)	0.14	15 (44.1%)	172 (27.8%)	0.35	8 (32.0%)	139 (25.9%)	0.13	0 (0.0%)	10 (17.2%)	0.65
Vaccinations												
Influenza (baseline) (in RA US only)	24 (50.0%)	259 (42.3%)	0.15	10 (33.3%)	229 (40.9%)	0.16	11 (52.4%)	192 (40.9%)	0.23	0 (0.0%)	22 (41.5%)	1.19
Pneumonia (ever) (in RA US only)	13 (25.0%)	157 (25.1%)	0.00	9 (30.0%)	161 (27.9%)	0.05	5 (25.0%)	113 (23.1%)	0.04	0 (0.0%)	11 (20.4%)	0.72
Shingles (ever)	11 (20.8%)	136 (21.2%)	0.01	4 (13.3%)	132 (22.4%)	0.24	8 (38.1%)	107 (21.1%)	0.38	0 (0.0%)	11 (19.3%)	0.69

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; CDAI = clinical disease activity index; cDMARD = conventional disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; HRT = hormone replacement therapy; MACE = major adverse cardiovascular event (MI (myocardial infarction) and stroke); Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; Std Diff = absolute value of the standardised difference; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

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Table 40_Cor_US. Baseline Clinical Characteristics of RA Patients with VTE, VTE-matched Population - excludes patients with a VTE within 6 months prior to index date or on anticoagulant [COR_US]

	Baricitinib (N=0)	TNFi (N=1)	Total (N=1)
Age [yrs]			
n	0	1	1
Mean ± SD	0.0 ±0.0	44.0 ±.	44.0 ±.
Median	0.0	44.0	44.0
Min, Max	0.0, 0.0	44.0, 44.0	44.0, 44.0
Gender			
Male	0 (0.0%)	1 (100.0%)	1 (100.0%)
Female	0 (0.0%)	0 (0.0%)	0 (0.0%)
History of MD-reported comorbidities (ever experienced)			
Cancer, Non-NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cancer, NMSC only	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure (hospitalized & non-hospitalized)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyperlipidemia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertension (hospitalized & non-hospitalized)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Immune disorders	0 (0.0%)	1 (100.0%)	1 (100.0%)
Secondary Sjogren Syndrome	0 (0.0%)	1 (100.0%)	1 (100.0%)
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity, current	0 (0.0%)	1 (100.0%)	1 (100.0%)
Pregnancy, recent (current or since last visit)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Smoking (current or former)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA severity (CDAI)			
n	0	1	1

	Baricitinib (N=0)	TNFi (N=1)	Total (N=1)
Mean ± SD	0.0 ±0.0	19.3 ±.	19.3 ±.
Median	0.0	19.3	19.3
Min, Max	0.0, 0.0	19.3, 19.3	19.3, 19.3
Prevalent outcomes			
VTE (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MACE (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Myocardial infarction	0 (0.0%)	0 (0.0%)	0 (0.0%)
Stroke	0 (0.0%)	0 (0.0%)	0 (0.0%)
Serious infection (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prescription medication use, current (baseline)			
Other prescription medications			
Cardiovascular medications			
Anticoagulant (coumadin/warfarin; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antihypertensives (blood pressure lowering medication(s); patient-reported)	0 (0.0%)	1 (100.0%)	1 (100.0%)
Antiplatelet (Plavix; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nitrates (angina/nitrate medications; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal Medication HRT (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents (cholesterol medication; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA-related			
Aspirin (includes non-prescription)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Celebrex (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prednisone	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vaccinations			
Influenza (baseline) (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pneumonia (ever) (in RA US only)	0 (0.0%)	1 (100.0%)	1 (0.0%)
Shingles (ever)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Occurrence			
Cancer diagnosis within 90 days after VTE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Concomitant Methotrexate in 1 month prior to VTE	0 (0.0%)	1 (100.0%)	1 (100.0%)

Abbreviations: COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; HRT = hormone replacement therapy; MACE = major adverse cardiovascular event; Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

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Table 41_Cor_US. Pattern of RA Medication Use in Patients with VTE – excludes patients with a VTE within 6 months prior to index date or on anticoagulant [Cor_US]

	Pre-matched		Matched		
	Baricitinib (N=0)	TNFi (N=7)	Baricitinib (N=0)	TNFi (N=1)	Total (N=1)
Baseline Medication					
DMARD history					
Number of cDMARDs used (ever)					
0	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
1	0 (0.0%)	3 (42.9%)	0 (0.0%)	1 (100.0%)	1 (100.0%)
2+	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate (prior use)	0 (0.0%)	5 (71.4%)	0 (0.0%)	1 (100.0%)	1 (100.0%)
Number of bDMARDs used (ever)					
0	0 (0.0%)	4 (57.1%)	0 (0.0%)	1 (100.0%)	1 (100.0%)
1	0 (0.0%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2+	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prior bDMARD use[a]	0 (0.0%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prior TNF bDMARD use	0 (0.0%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prior non-TNF bDMARD use	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DMARD, current (baseline)					
Concomitant non-methotrexate cDMARD use at baseline	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate, concomitant use at baseline	0 (0.0%)	3 (42.9%)	0 (0.0%)	1 (100.0%)	1 (100.0%)
Post-index Medication (Prior to VTE)					
Concomitant methotrexate use during exposure (regardless of use at index date)	0 (0.0%)	4 (57.1%)	0 (0.0%)	1 (100.0%)	1 (100.0%)
Concomitant non-methotrexate cDMARD during exposure (regardless of use at index date)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = conventional disease-modifying antirheumatic drugs; N = count of patients in category; RA = rheumatoid arthritis; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

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Table 42_Cor_US. Time to First VTE Event (Months*) – excludes patients with a VTE within 6 months prior to index date or on anticoagulant [COR_US]

	Pre-matched		Matched		
	Baricitinib (N=0)	**TNFi (N=7)**	**Baricitinib (N=0)**	**TNFi (N=1)**	**Total (N=1)**
n	0	7	0	1	1
Mean ± SD	0.0 ± 0.0	1.5 ± 1.2	0.0 ± 0.0	0.5 ±.	0.5 ±.
Median	0.0	1.0	0.0	0.5	0.5
Min, Max	0.0, 0.0	0.5, 3.0	0.0, 0.0	0.5, 0.5	0.5, 0.5
25th percentile, 75th percentile	0.0, 0.0	0.5, 3.0	0.0, 0.0	0.5, 0.5	0.5, 0.5

Abbreviations: Min = minimum; Max = maximum; RA = rheumatoid arthritis; SD = standard deviation; VTE = venous thromboembolism; TNFi = tumour necrosis factor inhibitor.

* CorEvitas RA US registry collects drug information at the month-level so time is reported in months. A rough conversion to days can be made by multiplying the values in this table by a factor of 30.4375 (the average number of days in a month)

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Table 51_Cor_US. Baseline Clinical Characteristics of RA Patients with MACE, MACE-matched Population -excludes patients with a MACE within 6 months prior to index date or on anticoagulant [COR_US]

	Baricitinib (N=2)	**TNFi (N=1)**	**Total (N=3)**
Age [yrs]			
n	2	1	3
Mean ± SD	62.5 ±20.5	74.0 ±.	66.3 ±15.9
Median	62.5	74.0	74.0
Min, Max	48.0, 77.0	74.0, 74.0	48.0, 77.0
Gender			
Male	2 (100.0%)	1 (100.0%)	3 (100.0%)
Female	0 (0.0%)	0 (0.0%)	0 (0.0%)
History of MD-reported comorbidities (ever experienced)			
Cancer, Non-NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cancer, NMSC only	1 (50.0%)	0 (0.0%)	1 (33.3%)
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	0 (0.0%)	1 (100.0%)	1 (33.3%)
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	1 (50.0%)	0 (0.0%)	1 (33.3%)
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	1 (50.0%)	0 (0.0%)	1 (33.3%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure (hospitalized & non-hospitalized)	0 (0.0%)	0 (0.0%)	0 (0.0%)

	Baricitinib (N=2)	TNFi (N=1)	Total (N=3)
Coronary artery disease	1 (50.0%)	0 (0.0%)	1 (33.3%)
Ischemic heart disease	1 (50.0%)	0 (0.0%)	1 (33.3%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyperlipidemia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertension (hospitalized & non-hospitalized)	1 (50.0%)	1 (100.0%)	2 (66.7%)
Immune disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)
Secondary Sjogren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity, current	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pregnancy, recent (current or since last visit)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Smoking (current or former)	1 (50.0%)	1 (100.0%)	2 (66.7%)
RA severity (CDAI)			
n	2	1	3
Mean ± SD	13.0 ± 0.7	10.0 ±.	12.0 ± 1.8
Median	13.0	10.0	12.5
Min, Max	12.5, 13.5	10.0, 10.0	10.0, 13.5
Prevalent outcomes			
VTE (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MACE (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Myocardial infarction	0 (0.0%)	0 (0.0%)	0 (0.0%)
Stroke	0 (0.0%)	0 (0.0%)	0 (0.0%)
Serious infection (at any time in the past)	0 (0.0%)	1 (100.0%)	1 (33.3%)
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prescription medication use, current (baseline)			
Other prescription medications			
Cardiovascular medications			
Anticoagulant (coumadin/warfarin; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antihypertensives (blood pressure lowering medication(s); patient-reported)	0 (0.0%)	1 (100.0%)	1 (33.3%)
Antiplatelet (Plavix; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nitrates (angina/nitrate medications; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal Medication HRT (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents (cholesterol medication; patient-reported)	0 (0.0%)	1 (100.0%)	1 (33.3%)
RA-related			
Aspirin (includes non-prescription)	1 (50.0%)	1 (100.0%)	2 (66.7%)
Celebrex (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prednisone	0 (0.0%)	0 (0.0%)	0 (0.0%)

	Baricitinib (N=2)	TNFi (N=1)	Total (N=3)
Vaccinations			
Influenza (baseline) (in RA US only)	1 (100.0%)	1 (100.0%)	2 (100.0%)
Pneumonia (ever) (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Shingles (ever)	1 (100.0%)	0 (0.0%)	1 (50.0%)
Post-index Occurrence			
Concomitant Methotrexate in 1** month prior to MACE	1 (50.0%)	1 (100.0%)	2 (66.7%)

Abbreviations: COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event (MI [myocardial infarction] and stroke); Max = maximum; Min = minimum; N = number of patients in a category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

** CorEvitas drug use information collected at the month-level so "in 7 days prior to MACE" is replaced with "in 1 month prior to MACE.

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Table 52_Cor_US. Pattern of RA Medication Use in Patients with MACE – excludes patients with a MACE within 6 months prior to index date or on anticoagulant. [Cor_US]

	Pre-matched		Matched		
	Baricitinib (N=2)	TNFi (N=4)	Baricitinib (N=2)	TNFi (N=1)	Total (N=3)
Baseline Medication					
DMARD history					
Number of cDMARDs used (ever)					
0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
1	0 (0.0%)	1 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2+	2 (100.0%)	3 (75.0%)	2 (100.0%)	1 (100.0%)	3 (100.0%)
Methotrexate (prior use)	2 (100.0%)	4 (100.0%)	2 (100.0%)	1 (100.0%)	3 (100.0%)
Number of bDMARDs used (ever)					
0	0 (0.0%)	1 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2+	2 (100.0%)	3 (75.0%)	2 (100.0%)	1 (100.0%)	3 (100.0%)
Prior bDMARD use[a]	2 (100.0%)	3 (75.0%)	2 (100.0%)	1 (100.0%)	3 (100.0%)
Prior TNF bDMARD use	2 (100.0%)	2 (50.0%)	2 (100.0%)	1 (100.0%)	3 (100.0%)
Prior non-TNF bDMARD use	2 (100.0%)	2 (50.0%)	2 (100.0%)	0 (0.0%)	2 (66.7%)
DMARD, current (baseline)					
Concomitant non-methotrexate cDMARD use at baseline	0 (0.0%)	1 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate, concomitant use at baseline	1 (50.0%)	2 (50.0%)	1 (50.0%)	1 (100.0%)	2 (66.7%)
Post-index Medication (Prior to MACE)					

	Pre-matched		Matched		
	Baricitinib (N=2)	TNFi (N=4)	Baricitinib (N=2)	TNFi (N=1)	Total (N=3)
Concomitant methotrexate use during exposure (regardless of use at index date)	1 (50.0%)	2 (50.0%)	1 (50.0%)	1 (100.0%)	2 (66.7%)
Concomitant non-methotrexate cDMARD during exposure (regardless of use at index date)	0 (0.0%)	1 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event (MI (myocardial infarction) and stroke); Max = maximum; Min = minimum; N = count of patients in category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to the CorEvitas registry and have therefore not been included in this table.

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Table 53_Cor_US. Time to First MACE (Months*) - excludes patients with a MACE within 6 months prior to index date or on anticoagulant [COR_US]

	Pre-matched		Matched		
	Baricitinib (N=2)	TNFi (N=4)	Baricitinib (N=2)	TNFi (N=1)	Total (N=3)
n	2	4	2	1	3
Mean ± SD	6.5 ± 6.4	5.6 ± 5.3	6.5 ± 6.4	4.0 ±.	5.7 ± 4.7
Median	6.5	4.5	6.5	4.0	4.0
Min, Max	2.0, 11.0	0.5, 13.0	2.0, 11.0	4.0, 4.0	2.0, 11.0
25th percentile, 75th percentile	2.0, 11.0	2.3, 9.0	2.0, 11.0	4.0, 4.0	2.0, 11.0

Abbreviations: MACE = major adverse cardiovascular event; Min = minimum; Max = maximum; N = count of patients in category; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

* CorEvitas RA US registry collects drug information at the month-level so time is reported in months. A rough conversion to days can be made by multiplying the values in this table by a factor of 30.4375 (the average number of days in a month)

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Table 56_Cor_US. Baseline Clinical Characteristics of RA Patients with Serious Infection, Serious Infection-matched Population -excludes patients with a Serious Infection within 6 months prior to index date [COR_US]

	Baricitinib (N=3)	TNFi (N=0)	Total (N=3)
Age [yrs]			
n	3	0	3
Mean ± SD	71.3 ± 5.5	0.0 ± 0.0	71.3 ± 5.5
Median	71.0	0.0	71.0
Min, Max	66.0, 77.0	0.0, 0.0	66.0, 77.0
Gender			
Male	1 (33.3%)	0 (0.0%)	1 (33.3%)
Female	2 (66.7%)	0 (0.0%)	2 (66.7%)
History of MD-reported comorbidities (ever experienced)			
Cancer, Non-NMSC	1 (33.3%)	0 (0.0%)	1 (33.3%)
Cancer, NMSC only	1 (33.3%)	0 (0.0%)	1 (33.3%)
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	1 (33.3%)	0 (0.0%)	1 (33.3%)
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	1 (33.3%)	0 (0.0%)	1 (33.3%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)

	Baricitinib (N=3)	TNFi (N=0)	Total (N=3)
Congestive heart failure (hospitalized & non-hospitalized)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	1 (33.3%)	0 (0.0%)	1 (33.3%)
Ischemic heart disease	1 (33.3%)	0 (0.0%)	1 (33.3%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyperlipidaemia	1 (33.3%)	0 (0.0%)	1 (33.3%)
Hypertension (hospitalized & non-hospitalized)	1 (33.3%)	0 (0.0%)	1 (33.3%)
Immune disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)
Secondary Sjogren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity, current	1 (33.3%)	0 (0.0%)	1 (33.3%)
Pregnancy, recent (current or since last visit)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Smoking (current or former)	3 (100.0%)	0 (0.0%)	0 (0.0%)
RA severity (CDAI)			
n	3	0	3
Mean ± SD	14.2 ± 7.2	0.0 ± 0.0	14.2 ± 7.2
Median	12.5	0.0	12.5
Min, Max	8.0, 22.1	0.0, 0.0	8.0, 22.1
Prevalent outcomes			
VTE (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MACE (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Myocardial infarction	0 (0.0%)	0 (0.0%)	0 (0.0%)
Stroke	0 (0.0%)	0 (0.0%)	0 (0.0%)
Serious infection (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prescription medication use, current (baseline)			
Other prescription medications			
Cardiovascular medications			
Anticoagulant (coumadin/warfarin; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antihypertensives (blood pressure lowering medication(s); patient-reported)	1 (33.3%)	0 (0.0%)	1 (33.3%)
Antiplatelet (Plavix; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nitrates (angina/nitrate medications; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal Medication HRT (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents (cholesterol medication; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA-related			
Aspirin (includes non-prescription)	3 (100.0%)	0 (0.0%)	0 (0.0%)
Celebrex (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prednisone	1 (33.3%)	0 (0.0%)	1 (33.3%)
Vaccinations			
Influenza (baseline) (in RA US only)	1 (100.0%)	0 (0.0%)	1 (100.0%)

	Baricitinib (N=3)	TNFi (N=0)	Total (N=3)
Pneumonia (ever) (in RA US only)	1 (100.0%)	0 (0.0%)	1 (100.0%)
Shingles (ever)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Occurrence			
Cancer diagnosis within 90 days after Serious Infection	0 (0.0%)	0 (0.0%)	0 (0.0%)
Concomitant Methotrexate in 1 month prior to Serious Infection	2 (66.7%)	0 (0.0%)	2 (66.7%)

Abbreviations: CDAI = clinical disease activity index; cDMARD = conventional disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; HRT = hormone replacement therapy; MACE = major adverse cardiovascular event (MI (myocardial infarction) and stroke); Max = maximum; Min = minimum; N = count of patients in category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

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Table 57_Cor_US. Pattern of RA Medication Use in Patients with Serious Infection – excludes patients with a serious infection within 6 months prior to index date [COR_US]

	Pre-matched		Matched		
	Baricitinib (N=3)	TNFi (N=44)	Baricitinib (N=3)	TNFi (N=0)	Total (N=3)
Baseline Medication					
DMARD history					
Number of cDMARDs used (ever)					
0	0 (0.0%)	4 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
1	0 (0.0%)	11 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2+	3 (100.0%)	29 (65.9%)	3 (100.0%)	0 (0.0%)	3 (100.0%)
Methotrexate (prior use)	3 (100.0%)	37 (84.1%)	3 (100.0%)	0 (0.0%)	3 (100.0%)
Number of bDMARDs used (ever)					
0	0 (0.0%)	15 (34.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
1	0 (0.0%)	18 (40.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2+	3 (100.0%)	11 (25.0%)	3 (100.0%)	0 (0.0%)	3 (100.0%)
Prior bDMARD usea	3 (100.0%)	29 (65.9%)	3 (100.0%)	0 (0.0%)	3 (100.0%)
Prior TNF bDMARD use	3 (100.0%)	24 (54.5%)	3 (100.0%)	0 (0.0%)	3 (100.0%)
Prior non-TNF bDMARD use	2 (66.7%)	15 (34.1%)	2 (66.7%)	0 (0.0%)	2 (66.7%)
DMARD, current (baseline)					
Concomitant non-methotrexate cDMARD use at baseline	1 (33.3%)	18 (40.9%)	1 (33.3%)	0 (0.0%)	1 (33.3%)
Methotrexate, concomitant use at baseline	2 (66.7%)	21 (47.7%)	2 (66.7%)	0 (0.0%)	2 (66.7%)
Post-index Medication (Prior to Serious Infection)					
Concomitant methotrexate use during exposure (regardless of use at index date)	2 (66.7%)	21 (47.7%)	2 (66.7%)	0 (0.0%)	2 (66.7%)
Concomitant non-methotrexate cDMARD during exposure (regardless of use at index date)	1 (33.3%)	19 (43.2%)	1 (33.3%)	0 (0.0%)	1 (33.3%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = conventional disease-modifying antirheumatic drugs; N = count of patients in category; RA = rheumatoid arthritis; TNFi = tumour necrosis factor inhibitor.

a Per CorEvitas' contractual obligations, reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

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Table 58_Cor_US. Time to First Serious Infection Event (Months*) – excludes patients with a serious infection within 6 months prior to index date [COR_US]

	Pre-matched		Matched		
	Baricitinib (N=3)	TNFi (N=44)	Baricitinib (N=3)	TNFi (N=0)	Total (N=3)
n	3	44	3	0	3
Mean ± SD	7.7 ± 2.5	6.1 ± 4.5	7.7 ± 2.5	0.0 ± 0.0	7.7 ± 2.5
Median	8.0	4.3	8.0	0.0	8.0
Min, Max	5.0, 10.0	0.5, 21.0	5.0, 10.0	0.0, 0.0	5.0, 10.0
25th percentile, 75th percentile	5.0, 10.0	2.8, 9.5	5.0, 10.0	0.0, 0.0	5.0, 10.0

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism: defined as either pulmonary embolism or deep vein thrombosis.

* CorEvitas RA US registry collects drug information at the month-level so time is reported in months. A rough conversion to days can be made by multiplying the values in this table by a factor of 30.4375 (the average number of days in a month)

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II. Variable Ratio Matching

All prior tables presented in this annex were based on propensity score matched baricitinib:TNFi cohorts using a 1:1 matching strategy. In this section of the annex, the tables include results that are based on a variable ratio matching (VRM) approach as described in Section 9.9.6.1 of the final study report.

The main analysis was modified to use 1:1 matching, as this allows the results in the meta-analysis to be directly proportional to the amount of baricitinib exposure in each data source. For transparency, comparative results generated using VRM prior to the adoption of the 1:1 matching are included here.

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Analysis Results from the CorEvitas US Rheumatoid Arthritis Registry: 1:3-Matched Population

Prepared for: Lilly

Report Date: 17 August 2021

Prepared by: Bernice Gershenson, MPH, Robert Magner, MPH, Emily A. Scherer, PhD, Alina Onofrei, MS, Nicole Foster, MS, Christine J. Barr, BSN, MPH, and Celeste A. Lemay, RN, MPH.

Available Data through: 31 December 2020

COR_US Table 6.1. Baseline Demographics, Pre-matched Population [CorEvitas US]

	Baricitinib (N=118)	TNFi (N=1897)	Std. Diff.
Age [yrs]			
n	118	1897	0.094
Mean±SD	60.2 ± 11.4	59.0 ± 13.0	
Median	61.0	60.0	
Min, Max	27.0, 81.0	18.0, 90.0	
≥ 65 years	43 (36.4%)	716 (37.7%)	0.027
Gender			
Male	29 (24.6%)	396 (20.9%)	0.088
Female	89 (75.4%)	1501 (79.1%)	
BMI			
n	116	1860	0.069
Mean±SD	30.0 ± 7.5	30.5 ± 7.4	
Median	28.8	29.5	
Min, Max	16.1, 50.9	15.2, 64.0	
Smoking (current or former)	66 (55.9%)	882 (47.1%)	0.177
Alcohol use	42 (35.6%)	870 (45.9%)	0.212
Education			
College/university	56 (50.0%)	1123 (62.0%)	0.244

Abbreviations: Max = maximum; Min = minimum; SD = standard deviation; Std Diff = absolute value of the standardized difference; TNFi = tumor necrosis factor inhibitor.

COR_US Table 6.2. Baseline Demographics, VTE-matched Population [CorEvitas US]- also excludes patients with VTE within 6 months prior to index date or currently taking anticoagulant.

	Baricitinib (N=112)	TNFi (N=323)	Std. Diff.	Total (N=435)
Age [yrs]				
n	112	323	0.019	435
Mean±SD	59.8 ±11.4	59.6 ±12.6		59.6 ±12.3
Median	60.5	60.0		60.0
Min, Max	27.0, 81.0	22.0, 90.0		22.0, 90.0
≥ 65 years	40 (35.7%)	125 (38.7%)	0.062	165 (37.9%)
Gender				
Male	27 (24.1%)	65 (20.1%)	0.096	92 (21.1%)
Female	85 (75.9%)	258 (79.9%)		343 (78.9%)
BMI				
n	110	317	0.015	427
Mean±SD	30.2 ± 7.6	30.0 ± 7.1		30.1 ± 7.2
Median	28.9	28.8		28.8
Min, Max	16.1, 50.9	16.8, 57.9		16.1, 57.9
Smoking (current or former)	62 (55.4%)	164 (50.8%)	0.092	226 (52.0%)
Alcohol use	39 (34.8%)	140 (43.3%)	0.175	179 (41.1%)
Education				
College/university	52 (49.1%)	195 (62.1%)	0.265	247 (58.8%)

Abbreviations: Max = maximum; Min = minimum; SD = standard deviation; Std Diff = absolute value of the standardized difference; TNFi = tumor necrosis factor inhibitor.

COR_US Table 6.3. Baseline Demographics, MACE-matched Population [CorEvitas US]- also excludes patients with MACE within 6 months prior to index date or currently taking anticoagulant.

	Baricitinib (N=114)	TNFi (N=328)	Std. Diff.	Total (N=442)
Age [yrs]				
n	114	328	0.047	442
Mean±SD	59.7 ±11.3	60.3 ±12.0		60.1 ±11.8
Median	60.0	61.0		61.0
Min, Max	27.0, 81.0	21.0, 87.0		21.0, 87.0
≥ 65 years	40 (35.1%)	136 (41.5%)	0.131	176 (39.8%)
Gender				
Male	27 (23.7%)	66 (20.1%)	0.086	93 (21.0%)
Female	87 (76.3%)	262 (79.9%)		349 (79.0%)
BMI				
n	112	327	0.037	439
Mean±SD	30.2 ± 7.6	29.9 ± 7.2		30.0 ± 7.3
Median	28.9	28.6		28.8
Min, Max	16.1, 50.9	16.3, 57.4		16.1, 57.4
Smoking (current or former)	63 (55.3%)	175 (53.4%)	0.038	238 (53.8%)
Alcohol use	40 (35.1%)	107 (32.6%)	0.052	147 (33.3%)
Education				
College/university	53 (49.1%)	195 (60.7%)	0.236	248 (57.8%)

Abbreviations: Max = maximum; Min = minimum; SD = standard deviation; Std Diff = absolute value of the standardized difference; TNFi = tumor necrosis factor inhibitor.

COR_US Table 6.4. Baseline Demographics, Serious infection-matched Population [CorEvitas US]- also excludes patients with serious infection within 6 months prior to index date.

	Baricitinib (N=114)	TNFi (N=335)	Std. Diff.	Total (N=449)
Age [yrs]				
n	114	335	0.017	449
Mean±SD	60.2 ±11.4	60.5 ±12.7		60.4 ±12.4
Median	61.0	62.0		61.0
Min, Max	27.0, 81.0	22.0, 88.0		22.0, 88.0
≥ 65 years	42 (36.8%)	140 (41.8%)	0.101	182 (40.5%)
Gender				
Male	27 (23.7%)	74 (22.1%)	0.038	101 (22.5%)
Female	87 (76.3%)	261 (77.9%)		348 (77.5%)
BMI				
n	112	328	0.050	440
Mean±SD	29.8 ± 7.3	29.4 ± 7.3		29.5 ± 7.3
Median	28.8	28.1		28.3
Min, Max	16.1, 50.9	16.8, 64.0		16.1, 64.0
Smoking (current or former)	63 (55.3%)	182 (54.3%)	0.019	245 (54.6%)
Alcohol use	39 (34.2%)	148 (44.2%)	0.205	187 (41.6%)
Education				
College/university	54 (50.0%)	223 (68.4%)	0.381	277 (63.8%)

Abbreviations: Max = maximum; Min = minimum; SD = standard deviation; Std Diff = absolute value of the standardized difference; TNFi = tumor necrosis factor inhibitor.

COR_US Table 6.5. Baseline Demographics, Hospitalized Tuberculosis-matched Population [CorEvitas US]- also excludes patients with a hospitalized TB within 6 months prior to index date.

	Baricitinib (N=117)	TNFi (N=343)	Std. Diff.	Total (N=460)
Age [yrs]				
n	117	343	0.008	460
Mean±SD	60.0 ±11.3	60.1 ±12.6		60.1 ±12.3
Median	61.0	61.0		61.0
Min, Max	27.0, 81.0	22.0, 88.0		22.0, 88.0
≥ 65 years	42 (35.9%)	142 (41.4%)	0.113	184 (40.0%)
Gender				
Male	29 (24.8%)	70 (20.4%)	0.105	99 (21.5%)
Female	88 (75.2%)	273 (79.6%)		361 (78.5%)
BMI				
n	115	335	0.023	450
Mean±SD	30.1 ± 7.5	29.9 ± 7.8		29.9 ± 7.7
Median	28.9	28.1		28.5
Min, Max	16.1, 50.9	16.0, 61.6		16.0, 61.6
Smoking (current or former)	65 (55.6%)	190 (55.4%)	0.003	255 (55.4%)
Alcohol use	42 (35.9%)	149 (43.6%)	0.157	191 (41.6%)
Education				
College/university	55 (49.5%)	212 (63.5%)	0.284	267 (60.0%)

Abbreviations: Max = maximum; Min = minimum; SD = standard deviation; Std Diff = absolute value of the standardized difference; TB = tuberculosis; TNFi = tumor necrosis factor inhibitor.

COR_US Table 6.6. Clinical history at baseline, Pre-matched Population [CorEvitas US]

	Baricitinib (N=118)	TNFi (N=1897)	Std. Diff.
History of MD-reported comorbidities (ever experienced)			
Cancer, Non-NMSC	7 (5.9%)	138 (7.3%)	0.054
Cancer, NMSC only	13 (11.0%)	107 (5.6%)	0.196
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	12 (10.2%)	196 (10.3%)	0.005
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	5 (4.2%)	58 (3.1%)	0.063
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	10 (8.5%)	123 (6.5%)	0.076
Cardiovascular revascularization	2 (1.7%)	44 (2.3%)	0.045
Congestive heart failure (hospitalized & non-hospitalized)	4 (3.4%)	24 (1.3%)	0.141
Coronary artery disease	6 (5.1%)	68 (3.6%)	0.074
Ischemic heart disease	7 (5.9%)	92 (4.8%)	0.048
TIA	1 (0.8%)	22 (1.2%)	0.031
Unstable angina	0 (0.0%)	11 (0.6%)	0.108
Ventricular arrhythmia	1 (0.8%)	13 (0.7%)	0.019
Diabetes mellitus	13 (11.0%)	220 (11.6%)	0.018
Hyperlipidemia	27 (22.9%)	331 (17.4%)	0.136
Hypertension (hospitalized & non-hospitalized)	48 (40.7%)	673 (35.5%)	0.107
Immune disorders	31 (26.3%)	352 (18.8%)	0.180
Secondary Sjogren Syndrome	31 (26.3%)	352 (18.8%)	0.180
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	5 (4.2%)	54 (2.8%)	0.075
Obesity, current	42 (36.2%)	875 (47.0%)	0.221
Pregnancy, recent (current or since last visit)	0 (0.0%)	11 (0.6%)	0.111
RA severity (CDAI)			
n	118	1897	0.188
Mean±SD	19.0 ±11.7	16.7 ±13.0	
Median	17.4	14.0	
25th percentile, 75th percentile	11.0, 25.0	6.5, 24.0	
Min, Max	0.8, 51.2	0.0, 72.5	

	Baricitinib (N=118)	TNFi (N=1897)	Std. Diff.
Prevalent outcomes			
VTE (at any time in the past)	6 (5.1%)	34 (1.8%)	0.181
MACE (at any time in the past)	3 (2.5%)	65 (3.4%)	0.052
Myocardial infarction	3 (2.5%)	33 (1.7%)	0.055
Stroke	0 (0.0%)	34 (1.8%)	0.191
Serious infection (at any time in the past)	10 (8.5%)	174 (9.2%)	0.025
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)	
DMARD history			
Number of cDMARDs used (ever)			
0	3 (2.5%)	73 (3.8%)	0.074
1	40 (33.9%)	843 (44.4%)	0.217
2+	75 (63.6%)	981 (51.7%)	0.241
Methotrexate (prior use)	108 (91.5%)	1653 (87.1%)	0.142
Number of bDMARDs used (ever)			
0	15 (12.7%)	908 (47.9%)	0.828
1	19 (16.1%)	550 (29.0%)	0.312
2+	84 (71.2%)	439 (23.1%)	1.098
Prior bDMARD use[a]	103 (87.3%)	989 (52.1%)	0.828
Prior TNFi bDMARD use	100 (84.7%)	906 (47.8%)	0.850
Prior non-TNFi bDMARD use	72 (61.0%)	404 (21.3%)	0.882
DMARD, current (baseline)			
cDMARD, concomitant use at baseline	73 (61.9%)	1346 (71.0%)	0.193
Methotrexate, concomitant use at baseline	53 (44.9%)	980 (51.7%)	0.135
Prescription medication use, current (baseline)			
Other prescription medications			
Cardiovascular medications			
Anticoagulant (coumadin/warfarin; patient-reported)	3 (2.5%)	30 (1.6%)	0.068
Antihypertensives (blood pressure lowering medication(s); patient-reported)	55 (46.6%)	768 (40.5%)	0.124
Antiplatelet (Plavix; patient-reported)	2 (1.7%)	41 (2.2%)	0.034
Nitrates (angina/nitrate medications; patient-reported)	2 (1.7%)	17 (0.9%)	0.071
Hormonal Medication HRT (in RA US only)	1 (0.8%)	17 (0.9%)	0.005
Lipid-lowering agents (cholesterol medication; patient-reported)	31 (26.3%)	395 (20.8%)	0.129
RA-related			
Aspirin (includes non-prescription)	19 (16.1%)	253 (13.3%)	0.078

	Baricitinib (N=118)	TNFi (N=1897)	Std. Diff.
Celebrex (in RA US only)	12 (10.2%)	107 (5.6%)	0.168
Prednisone	43 (36.4%)	526 (27.7%)	0.187
Vaccinations			
Influenza (baseline) (in RA US only	45 (45.0%)	702 (41.4%)	0.072
Pneumonia (ever) (in RA US only)	27 (26.2%)	442 (25.3%)	0.021
Shingles (ever)	23 (21.7%)	386 (21.5%)	0.005

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; CDAI = clinical disease activity index; cDMARD = classical disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event; Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; Std Diff = absolute value of the standardized difference; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

a. Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

COR_US Table 6.7. Baseline Demographics, VTE-matched Population [CorEvitas US]- also excludes patients with VTE within 6 months prior to index date or currently taking anticoagulant.

	Baricitinib (N=112)	TNFi (N=323)	Std. Diff.	Total (N=435)
History of MD-reported comorbidities (ever experienced)				
Cancer, Non-NMSC	6 (5.4%)	16 (5.0%)	0.018	22 (5.1%)
Cancer, NMSC only	10 (8.9%)	24 (7.4%)	0.055	34 (7.8%)
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	11 (9.8%)	34 (10.5%)	0.023	45 (10.3%)
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	4 (3.6%)	10 (3.1%)	0.026	14 (3.2%)
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	8 (7.1%)	23 (7.1%)	0.001	31 (7.1%)
Cardiovascular revascularization	2 (1.8%)	11 (3.4%)	0.102	13 (3.0%)
Congestive heart failure (hospitalized & non-hospitalized)	2 (1.8%)	6 (1.9%)	0.005	8 (1.8%)
Coronary artery disease	5 (4.5%)	13 (4.0%)	0.022	18 (4.1%)
Ischemic heart disease	6 (5.4%)	18 (5.6%)	0.009	24 (5.5%)
TIA	1 (0.9%)	4 (1.2%)	0.034	5 (1.1%)
Unstable angina	0 (0.0%)	3 (0.9%)	0.137	3 (0.7%)
Ventricular arrhythmia	0 (0.0%)	2 (0.6%)	0.112	2 (0.5%)
Diabetes mellitus	12 (10.7%)	35 (10.8%)	0.004	47 (10.8%)
Hyperlipidemia	23 (20.5%)	55 (17.0%)	0.090	78 (17.9%)
Hypertension (hospitalized & non-hospitalized)	46 (41.1%)	122 (37.8%)	0.068	168 (38.6%)
Immune disorders	29 (25.9%)	79 (24.5%)	0.033	108 (24.8%)
Secondary Sjogren Syndrome	29 (25.9%)	79 (24.5%)	0.033	108 (24.8%)
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	4 (3.6%)	13 (4.0%)	0.024	17 (3.9%)
Obesity, current	41 (37.3%)	128 (40.4%)	0.064	169 (39.6%)
Pregnancy, recent (current or since last visit)	0 (0.0%)	1 (0.3%)	0.082	1 (0.2%)
RA severity (CDAI)				
n	112	323	0.058	435
Mean±SD	18.8 ±11.6	19.6 ±14.9		19.4 ±14.2
Median	16.5	16.5		16.5
25th percentile, 75th percentile	10.8, 25.0	8.0, 27.5		8.5, 27.0
Min, Max	0.8, 51.2	0.0, 72.5		0.0, 72.5

	Baricitinib (N=112)	TNFi (N=323)	Std. Diff.	Total (N=435)
Prevalent outcomes				
VTE (at any time in the past)	3 (2.7%)	8 (2.5%)	0.013	11 (2.5%)
MACE (at any time in the past)	2 (1.8%)	15 (4.6%)	0.163	17 (3.9%)
Myocardial infarction	2 (1.8%)	8 (2.5%)	0.048	10 (2.3%)
Stroke	0 (0.0%)	7 (2.2%)	0.210	7 (1.6%)
Serious infection (at any time in the past)	10 (8.9%)	42 (13.0%)	0.131	52 (12.0%)
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)		0 (0.0%)
DMARD history				
Number of cDMARDs used (ever)				
0	3 (2.7%)	4 (1.2%)	0.104	7 (1.6%)
1	38 (33.9%)	119 (36.8%)	0.061	157 (36.1%)
2+	71 (63.4%)	200 (61.9%)	0.030	271 (62.3%)
Methotrexate (prior use)	102 (91.1%)	289 (89.5%)	0.054	391 (89.9%)
Number of bDMARDs used (ever)				
0	15 (13.4%)	49 (15.2%)	0.051	64 (14.7%)
1	19 (17.0%)	46 (14.2%)	0.075	65 (14.9%)
2+	78 (69.6%)	228 (70.6%)	0.021	306 (70.3%)
Prior bDMARD use[a]	97 (86.6%)	274 (84.8%)	0.051	371 (85.3%)
Prior TNFi bDMARD use	94 (83.9%)	261 (80.8%)	0.082	355 (81.6%)
Prior non-TNFi bDMARD use	66 (58.9%)	187 (57.9%)	0.021	253 (58.2%)
DMARD, current (baseline)				
cDMARD, concomitant use at baseline	69 (61.6%)	221 (68.4%)	0.143	290 (66.7%)
Methotrexate, concomitant use at baseline	50 (44.6%)	146 (45.2%)	0.011	196 (45.1%)
Prescription medication use, current (baseline)				
Other prescription medications				
Cardiovascular medications				
Anticoagulant (coumadin/warfarin; patient-reported)	0 (0.0%)	0 (0.0%)		0 (0.0%)
Antihypertensives (blood pressure lowering medication(s); patient-reported)	51 (45.5%)	146 (45.2%)	0.007	197 (45.3%)
Antiplatelet (Plavix; patient-reported)	2 (1.8%)	8 (2.5%)	0.048	10 (2.3%)
Nitrates (angina/nitrate medications; patient-reported)	2 (1.8%)	8 (2.5%)	0.048	10 (2.3%)
Hormonal Medication HRT (in RA US only)	0 (0.0%)	2 (0.6%)	0.112	2 (0.5%)
Lipid-lowering agents (cholesterol medication; patient-reported)	26 (23.2%)	72 (22.3%)	0.022	98 (22.5%)
RA-related				
Aspirin (includes non-prescription)	18 (16.1%)	46 (14.2%)	0.051	64 (14.7%)
Celebrex (in RA US only)	11 (9.8%)	28 (8.7%)	0.040	39 (9.0%)

	Baricitinib (N=112)	TNFi (N=323)	Std. Diff.	Total (N=435)
Prednisone	39 (34.8%)	98 (30.3%)	0.096	137 (31.5%)
Vaccinations				
Influenza (baseline) (in RA US only)	44 (46.3%)	122 (42.1%)	0.086	166 (43.1%)
Pneumonia (ever) (in RA US only)	25 (25.8%)	66 (22.0%)	0.089	91 (22.9%)
Shingles (ever)	22 (22.0%)	64 (20.8%)	0.028	86 (21.1%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; CDAI = clinical disease activity index; cDMARD = classical disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event; Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; Std Diff = absolute value of the standardized difference; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 66 for each outcome, e.g., congestive heart failure for VTE. Other factors are included for descriptive purposes only and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., diabetes for VTE.

a. Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

COR_US Table 6.8. Baseline Demographics, MACE-matched Population [CorEvitas US]- also excludes patients with MACE within 6 months prior to index date or currently taking anticoagulant.

	Baricitinib (N=114)	TNFi (N=328)	Std. Diff.	Total (N=442)
History of MD-reported comorbidities (ever experienced)				
Cancer, Non-NMSC	6 (5.3%)	30 (9.1%)	0.151	36 (8.1%)
Cancer, NMSC only	10 (8.8%)	21 (6.4%)	0.090	31 (7.0%)
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	11 (9.6%)	29 (8.8%)	0.028	40 (9.0%)
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	5 (4.4%)	10 (3.0%)	0.071	15 (3.4%)
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	9 (7.9%)	26 (7.9%)	0.001	35 (7.9%)
Cardiovascular revascularization	2 (1.8%)	12 (3.7%)	0.118	14 (3.2%)
Congestive heart failure (hospitalized & non-hospitalized)	2 (1.8%)	5 (1.5%)	0.018	7 (1.6%)
Coronary artery disease	5 (4.4%)	16 (4.9%)	0.023	21 (4.8%)
Ischemic heart disease	6 (5.3%)	20 (6.1%)	0.036	26 (5.9%)
TIA	1 (0.9%)	6 (1.8%)	0.082	7 (1.6%)
Unstable angina	0 (0.0%)	3 (0.9%)	0.136	3 (0.7%)
Ventricular arrhythmia	1 (0.9%)	2 (0.6%)	0.031	3 (0.7%)
Diabetes mellitus	12 (10.5%)	32 (9.8%)	0.026	44 (10.0%)
Hyperlipidemia	25 (21.9%)	65 (19.8%)	0.052	90 (20.4%)
Hypertension (hospitalized & non-hospitalized)	47 (41.2%)	131 (39.9%)	0.026	178 (40.3%)
Immune disorders	30 (26.3%)	84 (25.6%)	0.016	114 (25.8%)
Secondary Sjogren Syndrome	30 (26.3%)	84 (25.6%)	0.016	114 (25.8%)
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	4 (3.5%)	15 (4.6%)	0.054	19 (4.3%)
Obesity, current	42 (37.5%)	132 (40.4%)	0.059	174 (39.6%)
Pregnancy, recent (current or since last visit)	0 (0.0%)	4 (1.3%)	0.162	4 (1.0%)
RA severity (CDAI)				
n	114	328	0.007	442
Mean±SD	18.8 ±11.5	18.9 ±14.5		18.9 ±13.8
Median	16.8	16.0		16.5
25^{th} percentile, 75^{th} percentile	11.0, 25.0	7.5, 28.5		8.3, 26.8
Min, Max	0.8, 51.2	0.0, 72.5		0.0, 72.5

	Baricitinib (N=114)	TNFi (N=328)	Std. Diff.	Total (N=442)
Prevalent outcomes				
VTE (at any time in the past)	5 (4.4%)	5 (1.5%)	0.170	10 (2.3%)
MACE (at any time in the past)	2 (1.8%)	10 (3.0%)	0.085	12 (2.7%)
Myocardial infarction	2 (1.8%)	6 (1.8%)	0.006	8 (1.8%)
Stroke	0 (0.0%)	4 (1.2%)	0.157	4 (0.9%)
Serious infection (at any time in the past)	10 (8.8%)	44 (13.4%)	0.148	54 (12.2%)
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)		0 (0.0%)
DMARD history				
Number of cDMARDs used (ever)				
0	3 (2.6%)	13 (4.0%)	0.075	16 (3.6%)
1	39 (34.2%)	96 (29.3%)	0.106	135 (30.5%)
2+	72 (63.2%)	219 (66.8%)	0.076	291 (65.8%)
Methotrexate (prior use)	104 (91.2%)	291 (88.7%)	0.084	395 (89.4%)
Number of bDMARDs used (ever)				
0	15 (13.2%)	42 (12.8%)	0.011	57 (12.9%)
1	19 (16.7%)	53 (16.2%)	0.014	72 (16.3%)
2+	80 (70.2%)	233 (71.0%)	0.019	313 (70.8%)
Prior bDMARD use[a]	99 (86.8%)	286 (87.2%)	0.011	385 (87.1%)
Prior TNFi bDMARD use	96 (84.2%)	269 (82.0%)	0.059	365 (82.6%)
Prior non-TNFi bDMARD use	68 (59.6%)	189 (57.6%)	0.041	257 (58.1%)
DMARD, current (baseline)				
cDMARD, concomitant use at baseline	71 (62.3%)	191 (58.2%)	0.083	262 (59.3%)
Methotrexate, concomitant use at baseline	51 (44.7%)	119 (36.3%)	0.173	170 (38.5%)
Prescription medication use, current (baseline)				
Other prescription medications				
Cardiovascular medications				
Anticoagulant (coumadin/warfarin; patient-reported)	0 (0.0%)	0 (0.0%)		0 (0.0%)
Antihypertensives (blood pressure lowering medication(s); patient-reported)	53 (46.5%)	157 (47.9%)	0.028	210 (47.5%)
Antiplatelet (Plavix; patient-reported)	2 (1.8%)	7 (2.1%)	0.028	9 (2.0%)
Nitrates (angina/nitrate medications; patient-reported)	2 (1.8%)	4 (1.2%)	0.044	6 (1.4%)
Hormonal Medication HRT (in RA US only)	0 (0.0%)	2 (0.6%)	0.111	2 (0.5%)
Lipid-lowering agents (cholesterol medication; patient-reported)	28 (24.6%)	76 (23.2%)	0.033	104 (23.5%)
RA-related				
Aspirin (includes non-prescription)	18 (15.8%)	42 (12.8%)	0.085	60 (13.6%)
Celebrex (in RA US only)	12 (10.5%)	26 (7.9%)	0.090	38 (8.6%)

	Baricitinib (N=114)	TNFi (N=328)	Std. Diff.	Total (N=442)
Prednisone	40 (35.1%)	113 (34.5%)	0.013	153 (34.6%)
Vaccinations				
Influenza (baseline) (in RA US only)	45 (46.4%)	112 (38.2%)	0.166	157 (40.3%)
Pneumonia (ever) (in RA US only)	27 (27.3%)	75 (24.9%)	0.054	102 (25.5%)
Shingles (ever)	22 (21.6%)	70 (22.8%)	0.030	92 (22.5%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; CDAI = clinical disease activity index; cDMARD = classical disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event; Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; Std Diff = absolute value of the standardized difference; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 66 for each outcome, e.g., congestive heart failure for VTE. Other factors are included for descriptive purposes only and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., diabetes for VTE.

a. Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

COR_US Table 6.9. Baseline Demographics, Serious infection-matched Population [CorEvitas US]- also excludes patients with serious infection within 6 months prior to index date.

	Baricitinib (N=114)	TNFi (N=335)	Std. Diff.	Total (N=449)
History of MD-reported comorbidities (ever experienced)				
Cancer, Non-NMSC	6 (5.3%)	31 (9.3%)	0.154	37 (8.2%)
Cancer, NMSC only	12 (10.5%)	19 (5.7%)	0.179	31 (6.9%)
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	11 (9.6%)	34 (10.1%)	0.017	45 (10.0%)
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	5 (4.4%)	16 (4.8%)	0.019	21 (4.7%)
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	9 (7.9%)	28 (8.4%)	0.017	37 (8.2%)
Cardiovascular revascularization	2 (1.8%)	13 (3.9%)	0.129	15 (3.3%)
Congestive heart failure (hospitalized & non-hospitalized)	3 (2.6%)	11 (3.3%)	0.038	14 (3.1%)
Coronary artery disease	5 (4.4%)	16 (4.8%)	0.019	21 (4.7%)
Ischemic heart disease	6 (5.3%)	21 (6.3%)	0.043	27 (6.0%)
TIA	1 (0.9%)	4 (1.2%)	0.031	5 (1.1%)
Unstable angina	0 (0.0%)	3 (0.9%)	0.134	3 (0.7%)
Ventricular arrhythmia	1 (0.9%)	2 (0.6%)	0.033	3 (0.7%)
Diabetes mellitus	12 (10.5%)	38 (11.3%)	0.026	50 (11.1%)
Hyperlipidemia	25 (21.9%)	62 (18.5%)	0.085	87 (19.4%)
Hypertension (hospitalized & non-hospitalized)	45 (39.5%)	113 (33.7%)	0.119	158 (35.2%)
Immune disorders	30 (26.3%)	82 (24.5%)	0.042	112 (24.9%)
Secondary Sjogren Syndrome	30 (26.3%)	82 (24.5%)	0.042	112 (24.9%)
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	5 (4.4%)	17 (5.1%)	0.032	22 (4.9%)
Obesity, current	40 (35.7%)	121 (36.9%)	0.024	161 (36.6%)
Pregnancy, recent (current or since last visit)	0 (0.0%)	0 (0.0%)		0 (0.0%)
RA severity (CDAI)				
n	114	335	0.134	449
Mean±SD	19.2 ±11.8	17.6 ±13.3		18.0 ±12.9
Median	17.9	15.0		16.0
25^{th} percentile, 75^{th} percentile	11.0, 25.0	7.0, 25.5		8.0, 25.2
Min, Max	0.8, 51.2	0.0, 72.5		0.0, 72.5

	Baricitinib (N=114)	TNFi (N=335)	Std. Diff.	Total (N=449)
Prevalent outcomes				
VTE (at any time in the past)	6 (5.3%)	3 (0.9%)	0.255	9 (2.0%)
MACE (at any time in the past)	3 (2.6%)	14 (4.2%)	0.085	17 (3.8%)
Myocardial infarction	3 (2.6%)	6 (1.8%)	0.057	9 (2.0%)
Stroke	0 (0.0%)	8 (2.4%)	0.221	8 (1.8%)
Serious infection (at any time in the past)	7 (6.1%)	24 (7.2%)	0.041	31 (6.9%)
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)		0 (0.0%)
DMARD history				
Number of cDMARDs used (ever)				
0	3 (2.6%)	8 (2.4%)	0.016	11 (2.4%)
1	39 (34.2%)	115 (34.3%)	0.002	154 (34.3%)
2+	72 (63.2%)	212 (63.3%)	0.003	284 (63.3%)
Prior cDMARD use				
Methotrexate (prior use)	104 (91.2%)	301 (89.9%)	0.047	405 (90.2%)
Number of bDMARDs used (ever)				
0	15 (13.2%)	52 (15.5%)	0.068	67 (14.9%)
1	19 (16.7%)	41 (12.2%)	0.126	60 (13.4%)
2+	80 (70.2%)	242 (72.2%)	0.046	322 (71.7%)
Prior bDMARD use[a]	99 (86.8%)	283 (84.5%)	0.068	382 (85.1%)
Prior TNFi bDMARD use	96 (84.2%)	269 (80.3%)	0.103	365 (81.3%)
Prior non-TNFi bDMARD use	68 (59.6%)	197 (58.8%)	0.017	265 (59.0%)
DMARD, current (baseline)				
cDMARD, concomitant use at baseline	71 (62.3%)	220 (65.7%)	0.071	291 (64.8%)
Methotrexate, concomitant use at baseline	52 (45.6%)	141 (42.1%)	0.071	193 (43.0%)
Prescription medication use, current (baseline)				
Other prescription medications				
Cardiovascular medications				
Anticoagulant (coumadin/warfarin; patient-reported)	2 (1.8%)	5 (1.5%)	0.021	7 (1.6%)
Antihypertensives (blood pressure lowering medication(s); patient-reported)	52 (45.6%)	146 (43.6%)	0.041	198 (44.1%)
Antiplatelet (Plavix; patient-reported)	2 (1.8%)	8 (2.4%)	0.045	10 (2.2%)
Nitrates (angina/nitrate medications; patient-reported)	2 (1.8%)	8 (2.4%)	0.045	10 (2.2%)
Hormonal Medication HRT (in RA US only)	1 (0.9%)	4 (1.2%)	0.031	5 (1.1%)
Lipid-lowering agents (cholesterol medication; patient-reported)	28 (24.6%)	75 (22.4%)	0.051	103 (22.9%)
RA-related				
Aspirin (includes non-prescription)	19 (16.7%)	42 (12.5%)	0.117	61 (13.6%)

	Baricitinib (N=114)	TNFi (N=335)	Std. Diff.	Total (N=449)
Celebrex (in RA US only)	12 (10.5%)	23 (6.9%)	0.130	35 (7.8%)
Prednisone	42 (36.8%)	122 (36.4%)	0.009	164 (36.5%)
Vaccinations				
Influenza (baseline) (in RA US only)	44 (45.8%)	139 (45.3%)	0.011	183 (45.4%)
Pneumonia (ever) (in RA US only)	26 (26.3%)	70 (22.2%)	0.096	96 (23.1%)
Shingles (ever)	22 (21.6%)	81 (25.2%)	0.087	103 (24.3%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; CDAI = clinical disease activity index; cDMARD = classical disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event; Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; Std Diff = absolute value of the standardized difference; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 66 for each outcome, e.g., congestive heart failure for VTE. Other factors are included for descriptive purposes only and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., diabetes for VTE.

a. Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

COR_US Table 6.10. Baseline Demographics, Hospitalized Tuberculosis-matched Population [CorEvitas US]- also excludes patients with serious infection within 6 months prior to index date.

	Baricitinib (N=117)	TNFi (N=343)	Std. Diff.	Total (N=460)
History of MD-reported comorbidities (ever experienced)				
Cancer, Non-NMSC	7 (6.0%)	30 (8.7%)	0.106	37 (8.0%)
Cancer, NMSC only	12 (10.3%)	21 (6.1%)	0.151	33 (7.2%)
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	12 (10.3%)	36 (10.5%)	0.008	48 (10.4%)
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	5 (4.3%)	14 (4.1%)	0.010	19 (4.1%)
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	10 (8.5%)	32 (9.3%)	0.027	42 (9.1%)
Cardiovascular revascularization	2 (1.7%)	11 (3.2%)	0.097	13 (2.8%)
Congestive heart failure (hospitalized & non-hospitalized)	3 (2.6%)	11 (3.2%)	0.038	14 (3.0%)
Coronary artery disease	6 (5.1%)	16 (4.7%)	0.021	22 (4.8%)
Ischemic heart disease	7 (6.0%)	22 (6.4%)	0.018	29 (6.3%)
TIA	1 (0.9%)	5 (1.5%)	0.056	6 (1.3%)
Unstable angina	0 (0.0%)	4 (1.2%)	0.154	4 (0.9%)
Ventricular arrhythmia	1 (0.9%)	4 (1.2%)	0.031	5 (1.1%)
Diabetes mellitus	13 (11.1%)	36 (10.5%)	0.020	49 (10.7%)
Hyperlipidemia	27 (23.1%)	56 (16.3%)	0.170	83 (18.0%)
Hypertension (hospitalized & non-hospitalized)	48 (41.0%)	128 (37.3%)	0.076	176 (38.3%)
Immune disorders	31 (26.5%)	107 (31.2%)	0.104	138 (30.0%)
Secondary Sjogren Syndrome	31 (26.5%)	107 (31.2%)	0.104	138 (30.0%)
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	5 (4.3%)	14 (4.1%)	0.010	19 (4.1%)
Obesity, current	42 (36.5%)	120 (35.8%)	0.015	162 (36.0%)
Pregnancy, recent (current or since last visit)	0 (0.0%)	1 (0.3%)	0.080	1 (0.2%)
RA severity (CDAI)				
n	117	343	0.003	460
Mean±SD	19.0 ±11.7	18.9 ±14.1		19.0 ±13.5
Median	17.1	16.1		16.5
25^{th} percentile, 75^{th} percentile	11.0, 25.0	7.5, 27.0		8.1, 26.5
Min, Max	0.8, 51.2	0.0, 72.5		0.0, 72.5

	Baricitinib (N=117)	TNFi (N=343)	Std. Diff.	Total (N=460)
Prevalent outcomes				
VTE (at any time in the past)	6 (5.1%)	10 (2.9%)	0.113	16 (3.5%)
MACE (at any time in the past)	3 (2.6%)	15 (4.4%)	0.099	18 (3.9%)
Myocardial infarction	3 (2.6%)	7 (2.0%)	0.035	10 (2.2%)
Stroke	0 (0.0%)	8 (2.3%)	0.219	8 (1.7%)
Serious infection (at any time in the past)	10 (8.5%)	33 (9.6%)	0.037	43 (9.3%)
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)		0 (0.0%)
DMARD history				
Number of cDMARDs used (ever)				
0	3 (2.6%)	6 (1.7%)	0.056	9 (2.0%)
1	39 (33.3%)	102 (29.7%)	0.077	141 (30.7%)
2+	75 (64.1%)	235 (68.5%)	0.093	310 (67.4%)
Prior cDMARD use				
Methotrexate (prior use)	107 (91.5%)	308 (89.8%)	0.057	415 (90.2%)
Number of bDMARDs used (ever)				
0	15 (12.8%)	41 (12.0%)	0.026	56 (12.2%)
1	19 (16.2%)	61 (17.8%)	0.041	80 (17.4%)
2+	83 (70.9%)	241 (70.3%)	0.015	324 (70.4%)
Prior bDMARD use[a]	102 (87.2%)	302 (88.0%)	0.026	404 (87.8%)
Prior TNFi bDMARD use	99 (84.6%)	282 (82.2%)	0.065	381 (82.8%)
Prior non-TNFi bDMARD use	71 (60.7%)	195 (56.9%)	0.078	266 (57.8%)
DMARD, current (baseline)				
cDMARD, concomitant use at baseline	73 (62.4%)	215 (62.7%)	0.006	288 (62.6%)
Methotrexate, concomitant use at baseline	53 (45.3%)	131 (38.2%)	0.144	184 (40.0%)
Prescription medication use, current (baseline)				
Other prescription medications				
Cardiovascular medications				
Anticoagulant (coumadin/warfarin; patient-reported)	2 (1.7%)	9 (2.6%)	0.063	11 (2.4%)
Antihypertensives (blood pressure lowering medication(s); patient-reported)	55 (47.0%)	148 (43.1%)	0.078	203 (44.1%)
Antiplatelet (Plavix; patient-reported)	2 (1.7%)	7 (2.0%)	0.024	9 (2.0%)
Nitrates (angina/nitrate medications; patient-reported)	2 (1.7%)	6 (1.7%)	0.003	8 (1.7%)
Hormonal Medication HRT (in RA US only)	0 (0.0%)	4 (1.2%)	0.154	4 (0.9%)
Lipid-lowering agents (cholesterol medication; patient-reported)	31 (26.5%)	70 (20.4%)	0.144	101 (22.0%)
RA-related				
Aspirin (includes non-prescription)	19 (16.2%)	52 (15.2%)	0.030	71 (15.4%)

	Baricitinib (N=117)	TNFi (N=343)	Std. Diff.	Total (N=460)
Celebrex (in RA US only)	12 (10.3%)	17 (5.0%)	0.201	29 (6.3%)
Prednisone	42 (35.9%)	106 (30.9%)	0.106	148 (32.2%)
Vaccinations				
Influenza (baseline) (in RA US only)	45 (45.5%)	138 (44.5%)	0.019	183 (44.7%)
Pneumonia (ever) (in RA US only)	27 (26.5%)	69 (21.6%)	0.115	96 (22.7%)
Shingles (ever)	23 (21.9%)	64 (19.6%)	0.058	87 (20.1%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; CDAI = clinical disease activity index; cDMARD = classical disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event; Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; Std Diff = absolute value of the standardized difference; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 66 for each outcome, e.g., congestive heart failure for VTE. Other factors are included for descriptive purposes only and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., diabetes for VTE.

a. Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvias' RA Registry and have therefore not been included in this table.

COR_US Table 6.11. Baseline Healthcare Resource Utilization, Unmatched [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.12. Baseline Healthcare Resource Utilization Primary VTE Cohorts, Matched [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.13. Baseline Healthcare Resource Utilization MACE Cohorts, Matched [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.14. Baseline Healthcare Resource Utilization Incident Serious Infection Cohorts, Matched [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.15. Baseline Healthcare Resource Utilization Hospitalized Tuberculosis Cohorts, Matched [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.16. Baseline Prevalence of Outcomes [CorEvitas US]

	Pre-matched			Matched*			
	Baricitinib (N= 118)	**TNFi (N=1,897)**	**Std. Diff.**	**Baricitinib**	**TNFi**	**Std. Diff.**	**Total**
VTE	6 (5.1%)	34 (1.8%)	0.181	N= 112 3 (2.7%)	N= 323 8 (2.5%)	0.013	N= 435 11 (2.5%)
MACE	3 (2.5%)	65 (3.4%)	0.052	N= 114 2 (1.8%)	N= 328 10 (3.0%)	0.085	N= 442 12 (2.7%)
Serious Infection	10 (8.5%)	174 (9.2%)	0.025	N= 114 7 (6.1%)	N= 335 24 (7.2%)	0.041	N= 449 31 (6.9%)
Hospitalized Tuberculosis	0 (0.0%)	0 (0.0%)		N= 117 0 (0.0%)	N= 343 0 (0.0%)		N= 460 0 (0.0%)

Abbreviations: VTE = venous thromboembolism; MACE = Major Cardiovascular Event; TNFi = tumor necrosis factor inhibitor.
* matched refers to the outcome-specific matched population

COR_US Table 6.17. Duration of Exposure (Months*), in Pre-matched Population [CorEvitas US] exposure ends at discontinuation/last follow-up visit.

	Baricitinib (N=118)	TNFi (N=1897)	Std. Diff.
N	118	1897	
Mean±SD	8.1 ± 6.4	9.2 ± 6.4	0.173
Median	6.0	7.0	
Min, Max	1.0, 27.0	1.0, 30.0	

* CorEvitas' RA US Registry collects drug information at the month-level so time is reported in months. A rough conversion to days can be made by multiplying the values in this table by a factor of 30.4375 (the average number of days in a month)
Abbreviations: Max = maximum; Min = minimum; SD = standard deviation; Std Diff = absolute value of standardized difference; TNFi = tumor necrosis factor inhibitor.

COR_US Table 6.18. Duration of Exposure (Months*), in VTE-matched Population [CorEvitas US] exposure ends at discontinuation/last follow-up visit; excludes patients with VTE within 6 months prior to index date or currently taking anticoagulant.

	Baricitinib (N=112)	TNFi (N=323)	Std. Diff.
N	112	323	
Mean±SD	8.2 ± 6.4	9.0 ± 6.4	0.127
Median	6.0	7.0	
Min, Max	1.0, 27.0	1.0, 29.0	
Reason for censoring			
Discontinue index medication (and did not start another b/tsDMARD within 30 days)	20 (17.86%)	94 (29.10%)	
Discontinue index medication (and started another b/tsDMARD within 30 days)	34 (30.36%)	50(15.48%)	
End of follow-up for that patient	58 (51.79%)	178 (55.11%)	
Death	n/a	n/a	
Incident event (VTE)	0 (0.00%)	1 (0.31%)	

* CorEvitas' RA US Registry collects drug information at the month-level so time is reported in months. A rough conversion to days can be made by multiplying the values in this table by a factor of 30.4375 (the average number of days in a month)
Abbreviations: Max = maximum; Min = minimum; SD = standard deviation; Std Diff = absolute value of standardized difference; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

COR_US Table 6.19. Duration of Follow-up Period (Days) Alternate VTE Cohorts (Case Definition I), Matched [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.20. Duration of Follow-up Period (Days) Alternate VTE Cohorts (Case Definition II), Matched [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.21. Duration of Exposure (Months*), in MACE-matched Population [CorEvitas US] exposure ends at discontinuation/last follow-up visit; excludes patients with MACE within 6 months prior to index date or taking anticoagulant.

	Baricitinib (N=114)	TNFi (N=328)	Std. Diff.
N	114	328	
Mean±SD	8.1 ± 6.4	8.9 ± 6.1	0.131
Median	6.0	7.0	
Min, Max	1.0, 27.0	1.0, 28.0	
Reason for censoring			
Discontinue index medication (and did not start another b/tsDMARD within 30 days)	21 (18.42%)	98 (29.88%)	
Discontinue index medication (and started another b/tsDMARD within 30 days)	34 (29.82%)	54 (16.46%)	
End of follow-up for that patient	57 (50.00%)	173 (52.74%)	
Death	n/a	n/a	
Incident event (MACE)	2 (1.75%)	3 (0.91%)	

* CorEvitas' RA US Registry collects drug information at the month-level so time is reported in months. A rough conversion to days can be made by multiplying the values in this table by a factor of 30.4375 (the average number of days in a month)
Abbreviations: MACE = major adverse cardiovascular event; Max = maximum; Min = minimum; SD = standard deviation; Std Diff = absolute value of standardized difference; TNFi = tumor necrosis factor inhibitor.

COR_US Table 6.22. Duration of Exposure (Months*), in Serious Infection-matched Population [CorEvitas US] exposure ends at discontinuation/last follow-up visit; excludes patients with serious infection within 6 months prior to index date.

	Baricitinib (N=114)	TNFi (N=335)	Std. Diff.
N	114	335	
Mean±SD	8.3 ± 6.5	8.7 ± 6.0	0.075
Median	6.0	7.0	
Min, Max	1.0, 27.0	1.0, 30.0	
Reason for censoring			
Discontinue index medication (and did not start another b/tsDMARD within 30 days)	21 (18.42%)	99 (29.55%)	
Discontinue index medication (and started another b/tsDMARD within 30 days)	32 (28.07%)	53 (15.82%)	
End of follow-up for that patient	58 (50.88%)	177 (52.84%)	
Death	n/a	n/a	
Incident event (serious infection)	3 (2.63%)	6 (1.79%)	

* CorEvitas' RA US Registry collects drug information at the month-level so time is reported in months. A rough conversion to days can be made by multiplying the values in this table by a factor of 30.4375 (the average number of days in a month)
Abbreviations: Max = maximum; Min = minimum; SD = standard deviation; Std Diff = absolute value of standardized difference; TNFi = tumor necrosis factor inhibitor.

COR_US Table 6.23. Duration of Exposure (Months*), in Hospitalized Tuberculosis-matched Population [CorEvitas US] exposure ends at discontinuation/last follow-up visit; excludes patients with hospitalized TB within 6 months prior to index date.

	Baricitinib (N=117)	TNFi (N=343)	Std. Diff.
N	117	343	
Mean±SD	8.1 ± 6.4	8.7 ± 6.1	0.097
Median	6.0	7.0	
Min, Max	1.0, 27.0	1.0, 28.0	
Reason for censoring			
Discontinue index medication (and did not start another b/tsDMARD within 30 days)	22 (18.80%)	109 (31.78%)	
Discontinue index medication (and started another b/tsDMARD within 30 days)	34 (29.06%)	57 (16.62%)	
End of follow-up for that patient	61 (52.14%)	177 (51.60%)	
Death	n/a	n/a	
Incident event (hospitalized TB)	0 (0.00%)	0 (0.00%)	

* CorEvitas' RA US Registry collects drug information at the month-level so time is reported in months. A rough conversion to days can be made by multiplying the values in this table by a factor of 30.4375 (the average number of days in a month)
Abbreviations: Max = maximum; Min = minimum; SD = standard deviation; Std Diff = absolute value of standardized difference; TB = tuberculosis; TNFi = tumor necrosis factor inhibitor.

COR_US Table 6.24. Baseline Clinical Characteristics by Exposure Duration, Pre-matched Population [CorEvitas US] - exposure ends at discontinuation/last follow-up visit.

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 55)	TNFi (N= 684)	Std. Diff.	Baricitinib (N= 34)	TNFi (N= 619)	Std. Diff.	Baricitinib (N= 25)	TNFi (N= 536)	Std. Diff.	Baricitinib (N= 4)	TNFi (N= 58)	Std. Diff.
Age [yrs]												
n	55	684	0.04	34	619	0.14	25	536	0.61	4	58	0.47
Mean±SD	59.2 ± 12.0	58.7 ± 13.4		56.7 ± 11.2	58.5 ± 13.4		65.8 ± 7.8	59.7 ± 12.1		67.5 ± 11.6	62.5 ± 9.7	
Median	61.0	60.0		57.0	59.0		66.0	61.0		68.0	64.0	
Min, Max	27.0, 79.0	19.0, 90.0		31.0, 81.0	18.0, 90.0		53.0, 79.0	20.0, 87.0		56.0, 78.0	37.0, 82.0	
≥ 65 years	17 (30.9%)	246 (36.0%)	0.11	8 (23.5%)	226 (36.5%)	0.29	16 (64.0%)	218 (40.7%)	0.48	2 (50.0%)	26 (44.8%)	0.10
Gender												
Male	13 (23.6%)	140 (20.5%)	0.08	7 (20.6%)	124 (20.0%)	0.01	5 (20.0%)	118 (22.0%)	0.05	4 (100.0%)	14 (24.1%)	2.51
Female	42 (76.4%)	544 (79.5%)		27 (79.4%)	495 (80.0%)		20 (80.0%)	418 (78.0%)		0 (0.0%)	44 (75.9%)	
History of MD-reported comorbidities (ever experienced)												
Cancer, Non-NMSC	4 (7.3%)	44 (6.4%)	0.03	1 (2.9%)	39 (6.3%)	0.16	2 (8.0%)	48 (9.0%)	0.03	0 (0.0%)	7 (12.1%)	0.52
Cancer, NMSC only	4 (7.3%)	38 (5.6%)	0.07	3 (8.8%)	38 (6.1%)	0.10	5 (20.0%)	29 (5.4%)	0.45	1 (25.0%)	2 (3.4%)	0.65
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	4 (7.3%)	57 (8.3%)	0.04	6 (17.6%)	79 (12.8%)	0.14	2 (8.0%)	56 (10.4%)	0.08	0 (0.0%)	4 (6.9%)	0.38
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	3 (5.5%)	22 (3.2%)	0.11	1 (2.9%)	17 (2.7%)	0.01	0 (0.0%)	18 (3.4%)	0.26	1 (25.0%)	1 (1.7%)	0.73
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	7 (12.7%)	48 (7.0%)	0.19	1 (2.9%)	38 (6.1%)	0.15	1 (4.0%)	34 (6.3%)	0.11	1 (25.0%)	3 (5.2%)	0.58
Cardiovascular revascularization	2 (3.6%)	22 (3.2%)	0.02	0 (0.0%)	11 (1.8%)	0.19	0 (0.0%)	11 (2.1%)	0.20	0 (0.0%)	0 (0.0%)	
Congestive heart failure (hospitalized & non-hospitalized)	4 (7.3%)	4 (0.6%)	0.35	0 (0.0%)	9 (1.5%)	0.17	0 (0.0%)	10 (1.9%)	0.19	0 (0.0%)	1 (1.7%)	0.19
Coronary artery disease	3 (5.5%)	30 (4.4%)	0.05	1 (2.9%)	20 (3.2%)	0.02	1 (4.0%)	18 (3.4%)	0.03	1 (25.0%)	0 (0.0%)	0.82
Ischemic heart disease	4 (7.3%)	37 (5.4%)	0.08	1 (2.9%)	31 (5.0%)	0.11	1 (4.0%)	24 (4.5%)	0.02	1 (25.0%)	0 (0.0%)	0.82
TIA	1 (1.8%)	9 (1.3%)	0.04	0 (0.0%)	8 (1.3%)	0.16	0 (0.0%)	3 (0.6%)	0.11	0 (0.0%)	2 (3.4%)	0.27
Unstable angina	0 (0.0%)	1 (0.1%)	0.05	0 (0.0%)	4 (0.6%)	0.11	0 (0.0%)	6 (1.1%)	0.15	0 (0.0%)	0 (0.0%)	
Ventricular arrhythmia	1 (1.8%)	8 (1.2%)	0.05	0 (0.0%)	1 (0.2%)	0.06	0 (0.0%)	4 (0.7%)	0.12	0 (0.0%)	0 (0.0%)	
Diabetes mellitus	11 (20.0%)	86 (12.6%)	0.20	1 (2.9%)	70 (11.3%)	0.33	1 (4.0%)	59 (11.0%)	0.27	0 (0.0%)	5 (8.6%)	0.43
Hyperlipidemia	11 (20.0%)	129 (18.9%)	0.03	10 (29.4%)	104 (16.8%)	0.30	6 (24.0%)	88 (16.4%)	0.19	0 (0.0%)	10 (17.2%)	0.65
Hypertension (hospitalized & non-hospitalized)	21 (38.2%)	254 (37.1%)	0.02	18 (52.9%)	218 (35.2%)	0.36	7 (28.0%)	178 (33.2%)	0.11	2 (50.0%)	23 (39.7%)	0.21
Immune disorders	13 (23.6%)	127 (19.0%)	0.11	10 (29.4%)	124 (20.2%)	0.22	8 (32.0%)	93 (17.4%)	0.34	0 (0.0%)	8 (13.8%)	0.57
Secondary Sjogren Syndrome	13 (23.6%)	127 (19.0%)	0.11	10 (29.4%)	124 (20.2%)	0.22	8 (32.0%)	93 (17.4%)	0.34	0 (0.0%)	8 (13.8%)	0.57

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 55)	TNFi (N= 684)	Std. Diff.	Baricitinib (N= 34)	TNFi (N= 619)	Std. Diff.	Baricitinib (N= 25)	TNFi (N= 536)	Std. Diff.	Baricitinib (N= 4)	TNFi (N= 58)	Std. Diff.
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	1 (1.8%)	21 (3.1%)	0.08	1 (2.9%)	21 (3.4%)	0.03	3 (12.0%)	10 (1.9%)	0.41	0 (0.0%)	2 (3.4%)	0.27
Obesity, current	17 (31.5%)	315 (47.2%)	0.33	14 (42.4%)	280 (46.4%)	0.08	10 (40.0%)	259 (48.8%)	0.18	1 (25.0%)	21 (36.8%)	0.26
Pregnancy, recent (current or since last visit)	0 (0.0%)	4 (0.6%)	0.11	0 (0.0%)	2 (0.3%)	0.08	0 (0.0%)	5 (1.0%)	0.14	0 (0.0%)	0 (0.0%)	
Smoking (current or former)	32 (58.2%)	307 (45.4%)	0.26	15 (44.1%)	297 (48.8%)	0.09	17 (68.0%)	250 (47.1%)	0.43	2 (50.0%)	28 (49.1%)	0.02
RA severity (CDAI)												
n	55	684	0.17	34	619	0.17	25	536	0.26	4	58	0.10
Mean±SD	18.9 ± 10.8	16.9 ± 13.3		19.3 ± 12.8	17.2 ± 12.9		19.3 ± 12.5	16.1 ± 12.8		15.5 ± 11.8	14.3 ± 12.2	
Median	15.8	14.0		20.4	14.7		18.0	13.0		16.3	11.3	
Min, Max	4.0, 51.2	0.0, 70.2		1.0, 49.0	0.0, 66.0		2.1, 48.5	0.0, 72.5		0.8, 28.6	0.0, 48.0	
Prevalent outcomes												
VTE (at any time in the past)	4 (7.3%)	14 (2.0%)	0.25	1 (2.9%)	9 (1.5%)	0.10	1 (4.0%)	11 (2.1%)	0.11	0 (0.0%)	0 (0.0%)	
MACE (at any time in the past)	1 (1.8%)	29 (4.2%)	0.14	0 (0.0%)	17 (2.7%)	0.24	2 (8.0%)	16 (3.0%)	0.22	0 (0.0%)	3 (5.2%)	0.33
Myocardial infarction	1 (1.8%)	16 (2.3%)	0.04	0 (0.0%)	11 (1.8%)	0.19	2 (8.0%)	6 (1.1%)	0.33	0 (0.0%)	0 (0.0%)	
Stroke	0 (0.0%)	14 (2.0%)	0.20	0 (0.0%)	6 (1.0%)	0.14	0 (0.0%)	11 (2.1%)	0.20	0 (0.0%)	3 (5.2%)	0.33
Serious infection (at any time in the past)	5 (9.1%)	66 (9.6%)	0.02	3 (8.8%)	54 (8.7%)	0.00	2 (8.0%)	44 (8.2%)	0.01	0 (0.0%)	10 (17.2%)	0.65
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
DMARD history												
Number of cDMARDs used (ever)												
0	0 (0.0%)	25 (3.7%)	0.28	1 (2.9%)	28 (4.5%)	0.08	1 (4.0%)	17 (3.2%)	0.04	1 (25.0%)	3 (5.2%)	0.58
1	19 (34.5%)	302 (44.2%)	0.20	10 (29.4%)	264 (42.6%)	0.28	9 (36.0%)	248 (46.3%)	0.21	2 (50.0%)	29 (50.0%)	0.00
2+	36 (65.5%)	357 (52.2%)	0.27	23 (67.6%)	327 (52.8%)	0.31	15 (60.0%)	271 (50.6%)	0.19	1 (25.0%)	26 (44.8%)	0.43
Methotrexate (prior use)	51 (92.7%)	598 (87.4%)	0.18	32 (94.1%)	540 (87.2%)	0.24	22 (88.0%)	462 (86.2%)	0.05	3 (75.0%)	53 (91.4%)	0.45
Number of bDMARDs used (ever)												
0	5 (9.1%)	300 (43.9%)	0.86	5 (14.7%)	324 (52.3%)	0.87	4 (16.0%)	254 (47.4%)	0.72	1 (25.0%)	30 (51.7%)	0.57
1	8 (14.5%)	206 (30.1%)	0.38	5 (14.7%)	167 (27.0%)	0.31	6 (24.0%)	157 (29.3%)	0.12	0 (0.0%)	20 (34.5%)	1.03
2+	42 (76.4%)	178 (26.0%)	1.17	24 (70.6%)	128 (20.7%)	1.16	15 (60.0%)	125 (23.3%)	0.80	3 (75.0%)	8 (13.8%)	1.56
Prior bDMARD use[a]	50 (90.9%)	384 (56.1%)	0.86	29 (85.3%)	295 (47.7%)	0.87	21 (84.0%)	282 (52.6%)	0.72	3 (75.0%)	28 (48.3%)	0.57
Prior TNFi bDMARD use	49 (89.1%)	349 (51.0%)	0.91	27 (79.4%)	271 (43.8%)	0.79	21 (84.0%)	262 (48.9%)	0.80	3 (75.0%)	24 (41.4%)	0.73
Prior non-TNFi bDMARD use	39 (70.9%)	163 (23.8%)	1.07	21 (61.8%)	125 (20.2%)	0.93	10 (40.0%)	105 (19.6%)	0.46	2 (50.0%)	11 (19.0%)	0.69
DMARD, current (baseline)												
cDMARD, concomitant use at baseline	33 (60.0%)	476 (69.6%)	0.20	22 (64.7%)	447 (72.2%)	0.16	17 (68.0%)	386 (72.0%)	0.09	1 (25.0%)	37 (63.8%)	0.85
Methotrexate, concomitant use at baseline	21 (38.2%)	343 (50.1%)	0.24	17 (50.0%)	322 (52.0%)	0.04	14 (56.0%)	283 (52.8%)	0.06	1 (25.0%)	32 (55.2%)	0.65
Prescription medication use, current (baseline)												
Other prescription medications												
Cardiovascular medications												
Anticoagulant (coumadin/warfarin; patient-reported)	3 (5.5%)	15 (2.2%)	0.17	0 (0.0%)	8 (1.3%)	0.16	0 (0.0%)	7 (1.3%)	0.16	0 (0.0%)	0 (0.0%)	

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 55)	TNFi (N= 684)	Std. Diff.	Baricitinib (N= 34)	TNFi (N= 619)	Std. Diff.	Baricitinib (N= 25)	TNFi (N= 536)	Std. Diff.	Baricitinib (N= 4)	TNFi (N= 58)	Std. Diff.
Antihypertensives (blood pressure lowering medication(s); patient-reported)	24 (43.6%)	278 (40.6%)	0.06	19 (55.9%)	249 (40.2%)	0.32	12 (48.0%)	218 (40.7%)	0.15	0 (0.0%)	23 (39.7%)	1.15
Antiplatelet (Plavix; patient-reported)	1 (1.8%)	13 (1.9%)	0.01	1 (2.9%)	10 (1.6%)	0.09	0 (0.0%)	17 (3.2%)	0.26	0 (0.0%)	1 (1.7%)	0.19
Nitrates (angina/nitrate medications; patient-reported)	0 (0.0%)	10 (1.5%)	0.17	2 (5.9%)	5 (0.8%)	0.29	0 (0.0%)	2 (0.4%)	0.09	0 (0.0%)	0 (0.0%)	
Hormonal Medication HRT (in RA US only)	1 (1.8%)	6 (0.9%)	0.08	0 (0.0%)	8 (1.3%)	0.16	0 (0.0%)	3 (0.6%)	0.11	0 (0.0%)	0 (0.0%)	
Lipid-lowering agents (cholesterol medication; patient-reported)	15 (27.3%)	149 (21.8%)	0.13	8 (23.5%)	127 (20.5%)	0.07	8 (32.0%)	108 (20.1%)	0.27	0 (0.0%)	11 (19.0%)	0.68
RA-related												
Aspirin (includes non-prescription)	6 (10.9%)	87 (12.7%)	0.06	5 (14.7%)	69 (11.1%)	0.11	6 (24.0%)	92 (17.2%)	0.17	2 (50.0%)	5 (8.6%)	1.02
Celebrex (in RA US only)	7 (12.7%)	42 (6.1%)	0.23	3 (8.8%)	39 (6.3%)	0.10	2 (8.0%)	23 (4.3%)	0.15	0 (0.0%)	3 (5.2%)	0.33
Prednisone	20 (36.4%)	205 (30.0%)	0.14	15 (44.1%)	172 (27.8%)	0.35	8 (32.0%)	139 (25.9%)	0.13	0 (0.0%)	10 (17.2%)	0.65
Vaccinations												
Influenza (baseline) (in RA US only)	24 (50.0%)	259 (42.3%)	0.15	10 (33.3%)	229 (40.9%)	0.16	11 (52.4%)	192 (40.9%)	0.23	0 (0.0%)	22 (41.5%)	1.19
Pneumonia (ever) (in RA US only)	13 (25.0%)	157 (25.1%)	0.00	9 (30.0%)	161 (27.9%)	0.05	5 (25.0%)	113 (23.1%)	0.04	0 (0.0%)	11 (20.4%)	0.72
Shingles (ever)	11 (20.8%)	136 (21.2%)	0.01	4 (13.3%)	132 (22.4%)	0.24	8 (38.1%)	107 (21.1%)	0.38	0 (0.0%)	11 (19.3%)	0.69

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; CDAI = clinical disease activity index; cDMARD = classical disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event (MI (myocardial infarction) and stroke); Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; Std Diff = absolute value of the standardized difference; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

a. Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

COR_US Table 6.25. Baseline Clinical Characteristics by Exposure Duration, VTE-matched Population [CorEvitas US] - exposure ends at discontinuation/last follow-up visit/VTE event; excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 51)	TNFi (N= 133)	Std. Diff.	Baricitinib (N= 33)	TNFi (N= 88)	Std. Diff.	Baricitinib (N= 24)	TNFi (N= 95)	Std. Diff.	Baricitinib (N= 4)	TNFi (N= 7)	Std. Diff.
Age [yrs]												
n	51	133	0.03	33	88	0.40	24	95	0.66	4	7	0.54
Mean±SD	58.3 ± 11.8	58.7 ± 12.9		56.7 ± 11.3	61.3 ± 12.0		66.0 ± 7.9	59.0± 12.7		67.5 ± 11.6	61.4 ± 10.8	
Median	61.0	59.0		57.0	61.5		67.0	60.0		68.0	64.0	
Min, Max	27.0, 78.0	22.0, 90.0		31.0, 81.0	31.0, 87.0		53.0, 79.0	28.0, 87.0		56.0, 78.0	44.0, 74.0	
≥ 65 years	14 (27.5%)	45 (33.8%)	0.14	8 (24.2%)	38 (43.2%)	0.41	16 (66.7%)	39 (41.1%)	0.53	2 (50.0%)	3 (42.9%)	0.14
Gender												
Male	12 (23.5%)	28 (21.1%)	0.06	7 (21.2%)	16 (18.2%)	0.08	4 (16.7%)	19 (20.0%)	0.09	4 (100.0%)	2 (28.6%)	2.24
Female	39 (76.5%)	105 (78.9%)		26 (78.8%)	72 (81.8%)		20 (83.3%)	76 (80.0%)		0 (0.0%)	5 (71.4%)	
History of MD-reported comorbidities (ever experienced)												
Cancer, Non-NMSC	3 (5.9%)	4 (3.0%)	0.14	1 (3.0%)	7 (8.0%)	0.22	2 (8.3%)	5 (5.3%)	0.12	0 (0.0%)	0 (0.0%)	
Cancer, NMSC only	2 (3.9%)	9 (6.8%)	0.13	3 (9.1%)	6 (6.8%)	0.08	4 (16.7%)	8 (8.4%)	0.25	1 (25.0%)	1 (14.3%)	0.27
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	3 (5.9%)	12 (9.0%)	0.12	6 (18.2%)	13 (14.8%)	0.09	2 (8.3%)	9 (9.5%)	0.04	0 (0.0%)	0 (0.0%)	
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	2 (3.9%)	4 (3.0%)	0.05	1 (3.0%)	3 (3.4%)	0.02	0 (0.0%)	3 (3.2%)	0.26	1 (25.0%)	0 (0.0%)	0.82
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	5 (9.8%)	8 (6.0%)	0.14	1 (3.0%)	9 (10.2%)	0.29	1 (4.2%)	6 (6.3%)	0.10	1 (25.0%)	0 (0.0%)	0.82
Cardiovascular revascularization	2 (3.9%)	5 (3.8%)	0.01	0 (0.0%)	4 (4.5%)	0.31	0 (0.0%)	2 (2.1%)	0.21	0 (0.0%)	0 (0.0%)	
Congestive heart failure (hospitalized & non-hospitalized)	2 (3.9%)	1 (0.8%)	0.21	0 (0.0%)	2 (2.3%)	0.22	0 (0.0%)	3 (3.2%)	0.26	0 (0.0%)	0 (0.0%)	
Coronary artery disease	2 (3.9%)	5 (3.8%)	0.01	1 (3.0%)	5 (5.7%)	0.13	1 (4.2%)	3 (3.2%)	0.05	1 (25.0%)	0 (0.0%)	0.82
Ischemic heart disease	3 (5.9%)	7 (5.3%)	0.03	1 (3.0%)	7 (8.0%)	0.22	1 (4.2%)	4 (4.2%)	0.00	1 (25.0%)	0 (0.0%)	0.82
TIA	1 (2.0%)	1 (0.8%)	0.10	0 (0.0%)	3 (3.4%)	0.27	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
Unstable angina	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	3 (3.2%)	0.26	0 (0.0%)	0 (0.0%)	
Ventricular arrhythmia	0 (0.0%)	2 (1.5%)	0.17	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
Diabetes mellitus	10 (19.6%)	18 (13.5%)	0.16	1 (3.0%)	8 (9.1%)	0.26	1 (4.2%)	9 (9.5%)	0.21	0 (0.0%)	0 (0.0%)	
Hyperlipidemia	9 (17.6%)	26 (19.5%)	0.05	9 (27.3%)	14 (15.9%)	0.28	5 (20.8%)	14 (14.7%)	0.16	0 (0.0%)	1 (14.3%)	0.58

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 51)	TNFi (N= 133)	Std. Diff.	Baricitinib (N= 33)	TNFi (N= 88)	Std. Diff.	Baricitinib (N= 24)	TNFi (N= 95)	Std. Diff.	Baricitinib (N= 4)	TNFi (N= 7)	Std. Diff.
Hypertension (hospitalized & non-hospitalized)	20 (39.2%)	53 (39.8%)	0.01	17 (51.5%)	35 (39.8%)	0.24	7 (29.2%)	31 (32.6%)	0.08	2 (50.0%)	3 (42.9%)	0.14
Immune disorders	12 (23.5%)	34 (25.6%)	0.05	9 (27.3%)	28 (31.8%)	0.10	8 (33.3%)	17 (17.9%)	0.36	0 (0.0%)	0 (0.0%)	
Secondary Sjogren Syndrome	12 (23.5%)	34 (25.6%)	0.05	9 (27.3%)	28 (31.8%)	0.10	8 (33.3%)	17 (17.9%)	0.36	0 (0.0%)	0 (0.0%)	
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	1 (2.0%)	7 (5.3%)	0.18	1 (3.0%)	4 (4.5%)	0.08	2 (8.3%)	2 (2.1%)	0.28	0 (0.0%)	0 (0.0%)	
Obesity, current	16 (32.0%)	56 (43.1%)	0.23	14 (43.8%)	34 (40.0%)	0.08	10 (41.7%)	36 (37.9%)	0.08	1 (25.0%)	2 (28.6%)	0.08
Pregnancy, recent (current or since last visit)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	1 (1.1%)	0.15	0 (0.0%)	0 (0.0%)	
Smoking (current or former)	29 (56.9%)	68 (51.1%)	0.12	15 (45.5%)	54 (61.4%)	0.32	16 (66.7%)	40 (42.1%)	0.51	2 (50.0%)	2 (28.6%)	0.45
RA severity (CDAI)												
n	51	133	0.14	33	88	0.12	24	95	0.11	4	7	0.09
Mean±SD	19.1 ± 11.1	21.1 ± 16.0		19.3 ± 13.0	20.9 ± 14.3		18.1 ± 11.2	16.7 ± 13.7		15.5 ± 11.8	14.4 ± 13.9	
Median	15.8	18.3		20.7	18.6		17.9	13.7		16.3	12.0	
Min, Max	4.0, 51.2	0.0, 67.5		1.0, 49.0	0.8, 61.4		2.1, 44.0	0.0, 72.5		0.8, 28.6	0.5, 39.0	
Prevalent outcomes												
VTE (at any time in the past)	2 (3.9%)	3 (2.3%)	0.10	0 (0.0%)	2 (2.3%)	0.22	1 (4.2%)	3 (3.2%)	0.05	0 (0.0%)	0 (0.0%)	
MACE (at any time in the past)	1 (2.0%)	8 (6.0%)	0.21	0 (0.0%)	4 (4.5%)	0.31	1 (4.2%)	3 (3.2%)	0.05	0 (0.0%)	0 (0.0%)	
Myocardial infarction	1 (2.0%)	3 (2.3%)	0.02	0 (0.0%)	4 (4.5%)	0.31	1 (4.2%)	1 (1.1%)	0.20	0 (0.0%)	0 (0.0%)	
Stroke	0 (0.0%)	5 (3.8%)	0.28	0 (0.0%)	0 (0.0%)		0 (0.0%)	2 (2.1%)	0.21	0 (0.0%)	0 (0.0%)	
Serious infection (at any time in the past)	5 (9.8%)	16 (12.0%)	0.07	3 (9.1%)	13 (14.8%)	0.18	2 (8.3%)	12 (12.6%)	0.14	0 (0.0%)	1 (14.3%)	0.58
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
DMARD history												
Number of cDMARDs used (ever)												
0	0 (0.0%)	3 (2.3%)	0.21	1 (3.0%)	1 (1.1%)	0.13	1 (4.2%)	0 (0.0%)	0.29	1 (25.0%)	0 (0.0%)	0.82
1	17 (33.3%)	48 (36.1%)	0.06	10 (30.3%)	31 (35.2%)	0.11	9 (37.5%)	38 (40.0%)	0.05	2 (50.0%)	2 (28.6%)	0.45
2+	34 (66.7%)	82 (61.7%)	0.10	22 (66.7%)	56 (63.6%)	0.06	14 (58.3%)	57 (60.0%)	0.03	1 (25.0%)	5 (71.4%)	1.05
Methotrexate (prior use)	47 (92.2%)	118 (88.7%)	0.12	31 (93.9%)	78 (88.6%)	0.19	21 (87.5%)	86 (90.5%)	0.10	3 (75.0%)	7 (100.0%)	0.82
Number of bDMARDs used (ever)												
0	5 (9.8%)	18 (13.5%)	0.12	5 (15.2%)	13 (14.8%)	0.01	4 (16.7%)	17 (17.9%)	0.03	1 (25.0%)	1 (14.3%)	0.27
1	8 (15.7%)	20 (15.0%)	0.02	5 (15.2%)	11 (12.5%)	0.08	6 (25.0%)	12 (12.6%)	0.32	0 (0.0%)	3 (42.9%)	1.22
2+	38 (74.5%)	95 (71.4%)	0.07	23 (69.7%)	64 (72.7%)	0.07	14 (58.3%)	66 (69.5%)	0.23	3 (75.0%)	3 (42.9%)	0.69
Prior bDMARD use[a]	46 (90.2%)	115 (86.5%)	0.12	28 (84.8%)	75 (85.2%)	0.01	20 (83.3%)	78 (82.1%)	0.03	3 (75.0%)	6 (85.7%)	0.27
Prior TNFi bDMARD use	45 (88.2%)	108 (81.2%)	0.20	26 (78.8%)	72 (81.8%)	0.08	20 (83.3%)	76 (80.0%)	0.09	3 (75.0%)	5 (71.4%)	0.08
Prior non-TNFi bDMARD use	35 (68.6%)	78 (58.6%)	0.21	20 (60.6%)	56 (63.6%)	0.06	9 (37.5%)	50 (52.6%)	0.31	2 (50.0%)	3 (42.9%)	0.14
DMARD, current (baseline)												
cDMARD, concomitant use at baseline	30 (58.8%)	83 (62.4%)	0.07	21 (63.6%)	64 (72.7%)	0.20	17 (70.8%)	68 (71.6%)	0.02	1 (25.0%)	6 (85.7%)	1.54
Methotrexate, concomitant use at baseline	18 (35.3%)	57 (42.9%)	0.16	17 (51.5%)	41 (46.6%)	0.10	14 (58.3%)	43 (45.3%)	0.26	1 (25.0%)	5 (71.4%)	1.05

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 51)	TNFi (N= 133)	Std. Diff.	Baricitinib (N= 33)	TNFi (N= 88)	Std. Diff.	Baricitinib (N= 24)	TNFi (N= 95)	Std. Diff.	Baricitinib (N= 4)	TNFi (N= 7)	Std. Diff.
Prescription medication use, current (baseline)												
Other prescription medications												
Cardiovascular medications												
Anticoagulant (coumadin/warfarin; patient-reported)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
Antihypertensives (blood pressure lowering medication(s); patient-reported)	21 (41.2%)	63 (47.4%)	0.12	18 (54.5%)	45 (51.1%)	0.07	12 (50.0%)	35 (36.8%)	0.27	0 (0.0%)	3 (42.9%)	1.22
Antiplatelet (Plavix; patient-reported)	1 (2.0%)	5 (3.8%)	0.11	1 (3.0%)	1 (1.1%)	0.13	0 (0.0%)	2 (2.1%)	0.21	0 (0.0%)	0 (0.0%)	
Nitrates (angina/nitrate medications; patient-reported)	0 (0.0%)	5 (3.8%)	0.28	2 (6.1%)	1 (1.1%)	0.27	0 (0.0%)	2 (2.1%)	0.21	0 (0.0%)	0 (0.0%)	
Hormonal Medication HRT (in RA US only)	0 (0.0%)	1 (0.8%)	0.12	0 (0.0%)	1 (1.1%)	0.15	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
Lipid-lowering agents (cholesterol medication; patient-reported)	12 (23.5%)	29 (21.8%)	0.04	7 (21.2%)	23 (26.1%)	0.12	7 (29.2%)	20 (21.1%)	0.19	0 (0.0%)	0 (0.0%)	
RA-related												
Aspirin (includes non-prescription)	6 (11.8%)	15 (11.3%)	0.02	5 (15.2%)	12 (13.6%)	0.04	5 (20.8%)	19 (20.0%)	0.02	2 (50.0%)	0 (0.0%)	1.41
Celebrex (in RA US only)	7 (13.7%)	8 (6.0%)	0.26	2 (6.1%)	13 (14.8%)	0.29	2 (8.3%)	6 (6.3%)	0.08	0 (0.0%)	1 (14.3%)	0.58
Prednisone	18 (35.3%)	40 (30.1%)	0.11	14 (42.4%)	35 (39.8%)	0.05	7 (29.2%)	23 (24.2%)	0.11	0 (0.0%)	0 (0.0%)	
Vaccinations												
Influenza (baseline) (in RA US only)	23 (51.1%)	54 (45.8%)	0.11	10 (34.5%)	30 (37.5%)	0.06	11 (55.0%)	37 (43.5%)	0.23	0 (0.0%)	1 (14.3%)	0.58
Pneumonia (ever) (in RA US only)	12 (25.0%)	32 (26.0%)	0.02	8 (27.6%)	14 (17.5%)	0.24	5 (26.3%)	19 (21.1%)	0.12	0 (0.0%)	1 (14.3%)	0.58
Shingles (ever)	10 (20.4%)	22 (17.9%)	0.06	4 (13.8%)	19 (22.4%)	0.22	8 (40.0%)	22 (23.9%)	0.35	0 (0.0%)	1 (14.3%)	0.58

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; CDAI = clinical disease activity index; cDMARD = classical disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event (MI (myocardial infarction) and stroke); Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; Std Diff = absolute value of the standardized difference; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

a. Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

COR_US Table 6.26. Baseline Characteristics by Exposure Duration, Alternate VTE Cohorts (Case Definition I), Matched [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.27. Baseline Characteristics by Exposure Duration, Alternate VTE Cohorts (Case Definition II), Matched [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.28. Baseline Clinical Characteristics by Time-to-Event Duration, MACE-matched Population [CorEvitas US] - exposure ends at discontinuation/last follow-up visit/MACE; excludes patients with a MACE within 6 months prior to index date or on anticoagulant.

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 52)	TNFi (N= 127)	Std. Diff.	Baricitinib (N= 35)	TNFi (N= 103)	Std. Diff.	Baricitinib (N= 24)	TNFi (N= 91)	Std. Diff.	Baricitinib (N= 3)	TNFi (N= 7)	Std. Diff.
Age [yrs]												
n	52	127	0.10	35	103	0.22	24	91	0.45	3	7	0.02
Mean±SD	58.2 ± 11.6	59.5 ± 12.4		57.3 ± 11.5	59.9± 12.2		66.0 ± 7.9	61.5± 11.7		64.3 ± 11.9	64.6 ± 7.3	
Median	60.0	60.0		57.0	61.0		67.0	63.0		59.0	67.0	
Min, Max	27.0, 78.0	22.0, 83.0		31.0, 81.0	21.0, 83.0		53.0, 79.0	32.0, 87.0		56.0, 78.0	51.0, 72.0	
≥ 65 years	14 (26.9%)	44 (34.6%)	0.17	9 (25.7%)	43 (41.7%)	0.34	16 (66.7%)	45 (49.5%)	0.35	1 (33.3%)	4 (57.1%)	0.49
Gender												
Male	12 (23.1%)	28 (22.0%)	0.02	8 (22.9%)	17 (16.5%)	0.16	4 (16.7%)	20 (22.0%)	0.13	3 (100.0%)	1 (14.3%)	3.46
Female	40 (76.9%)	99 (78.0%)		27 (77.1%)	86 (83.5%)		20 (83.3%)	71 (78.0%)		0 (0.0%)	6 (85.7%)	
History of MD-reported comorbidities (ever experienced)												
Cancer, Non-NMSC	3 (5.8%)	7 (5.5%)	0.01	1 (2.9%)	8 (7.8%)	0.22	2 (8.3%)	14 (15.4%)	0.22	0 (0.0%)	1 (14.3%)	0.58
Cancer, NMSC only	2 (3.8%)	9 (7.1%)	0.14	4 (11.4%)	6 (5.8%)	0.20	4 (16.7%)	6 (6.6%)	0.32	0 (0.0%)	0 (0.0%)	
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	3 (5.8%)	9 (7.1%)	0.05	6 (17.1%)	9 (8.7%)	0.25	2 (8.3%)	10 (11.0%)	0.09	0 (0.0%)	1 (14.3%)	0.58
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	3 (5.8%)	5 (3.9%)	0.09	2 (5.7%)	2 (1.9%)	0.20	0 (0.0%)	3 (3.3%)	0.26	0 (0.0%)	0 (0.0%)	
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	6 (11.5%)	10 (7.9%)	0.12	2 (5.7%)	5 (4.9%)	0.04	1 (4.2%)	11 (12.1%)	0.29	0 (0.0%)	0 (0.0%)	
Cardiovascular revascularization	2 (3.8%)	6 (4.7%)	0.04	0 (0.0%)	1 (1.0%)	0.14	0 (0.0%)	5 (5.5%)	0.34	0 (0.0%)	0 (0.0%)	
Congestive heart failure (hospitalized & non-hospitalized)	2 (3.8%)	1 (0.8%)	0.20	0 (0.0%)	1 (1.0%)	0.14	0 (0.0%)	3 (3.3%)	0.26	0 (0.0%)	0 (0.0%)	
Coronary artery disease	2 (3.8%)	8 (6.3%)	0.11	2 (5.7%)	2 (1.9%)	0.20	1 (4.2%)	6 (6.6%)	0.11	0 (0.0%)	0 (0.0%)	
Ischemic heart disease	3 (5.8%)	9 (7.1%)	0.05	2 (5.7%)	4 (3.9%)	0.09	1 (4.2%)	7 (7.7%)	0.15	0 (0.0%)	0 (0.0%)	
TIA	1 (1.9%)	1 (0.8%)	0.10	0 (0.0%)	3 (2.9%)	0.24	0 (0.0%)	2 (2.2%)	0.21	0 (0.0%)	0 (0.0%)	
Unstable angina	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	3 (3.3%)	0.26	0 (0.0%)	0 (0.0%)	
Ventricular arrhythmia	1 (1.9%)	1 (0.8%)	0.10	0 (0.0%)	0 (0.0%)		0 (0.0%)	1 (1.1%)	0.15	0 (0.0%)	0 (0.0%)	
Diabetes mellitus	10 (19.2%)	13 (10.2%)	0.26	1 (2.9%)	7 (6.8%)	0.18	1 (4.2%)	11 (12.1%)	0.29	0 (0.0%)	1 (14.3%)	0.58
Hyperlipidemia	10 (19.2%)	27 (21.3%)	0.05	10 (28.6%)	19 (18.4%)	0.24	5 (20.8%)	18 (19.8%)	0.03	0 (0.0%)	1 (14.3%)	0.58

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 52)	TNFi (N= 127)	Std. Diff.	Baricitinib (N= 35)	TNFi (N= 103)	Std. Diff.	Baricitinib (N= 24)	TNFi (N= 91)	Std. Diff.	Baricitinib (N= 3)	TNFi (N= 7)	Std. Diff.
Hypertension (hospitalized & non-hospitalized)	20 (38.5%)	46 (36.2%)	0.05	19 (54.3%)	40 (38.8%)	0.31	7 (29.2%)	41 (45.1%)	0.33	1 (33.3%)	4 (57.1%)	0.49
Immune disorders	12 (23.1%)	36 (28.3%)	0.12	10 (28.6%)	26 (25.2%)	0.08	8 (33.3%)	22 (24.2%)	0.20	0 (0.0%)	0 (0.0%)	
Secondary Sjogren Syndrome	12 (23.1%)	36 (28.3%)	0.12	10 (28.6%)	26 (25.2%)	0.08	8 (33.3%)	22 (24.2%)	0.20	0 (0.0%)	0 (0.0%)	
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	1 (1.9%)	7 (5.5%)	0.19	1 (2.9%)	5 (4.9%)	0.10	2 (8.3%)	2 (2.2%)	0.28	0 (0.0%)	1 (14.3%)	0.58
Obesity, current	17 (33.3%)	45 (35.4%)	0.04	14 (41.2%)	51 (50.0%)	0.18	10 (41.7%)	36 (39.6%)	0.04	1 (33.3%)	0 (0.0%)	1.00
Pregnancy, recent (current or since last visit)	0 (0.0%)	2 (1.7%)	0.19	0 (0.0%)	1 (1.0%)	0.14	0 (0.0%)	1 (1.2%)	0.16	0 (0.0%)	0 (0.0%)	
Smoking (current or former)	30 (57.7%)	69 (54.3%)	0.07	16 (45.7%)	59 (57.3%)	0.23	16 (66.7%)	43 (47.3%)	0.40	1 (33.3%)	4 (57.1%)	0.49
RA severity (CDAI)												
n	52	127	0.02	35	103	0.08	24	91	0.08	3	7	0.18
Mean±SD	19.1 ± 11.0	19.4 ± 14.5		19.1 ± 12.7	18.1 ± 13.5		18.1 ± 11.2	19.1 ± 15.4		16.5 ± 14.2	19.5 ± 19.4	
Median	15.8	16.0		20.0	16.0		17.9	16.5		20.0	14.4	
Min, Max	4.0, 51.2	0.0, 62.5		1.0, 49.0	0.1, 66.0		2.1, 44.0	0.0, 72.5		0.8, 28.6	0.0, 48.0	
Prevalent outcomes												
VTE (at any time in the past)	3 (5.8%)	2 (1.6%)	0.22	1 (2.9%)	2 (1.9%)	0.06	1 (4.2%)	1 (1.1%)	0.19	0 (0.0%)	0 (0.0%)	
MACE (at any time in the past)	1 (1.9%)	5 (3.9%)	0.12	0 (0.0%)	3 (2.9%)	0.24	1 (4.2%)	2 (2.2%)	0.11	0 (0.0%)	0 (0.0%)	
Myocardial infarction	1 (1.9%)	2 (1.6%)	0.03	0 (0.0%)	2 (1.9%)	0.20	1 (4.2%)	2 (2.2%)	0.11	0 (0.0%)	0 (0.0%)	
Stroke	0 (0.0%)	3 (2.4%)	0.22	0 (0.0%)	1 (1.0%)	0.14	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
Serious infection (at any time in the past)	5 (9.6%)	17 (13.4%)	0.12	3 (8.6%)	13 (12.6%)	0.13	2 (8.3%)	13 (14.3%)	0.19	0 (0.0%)	1 (14.3%)	0.58
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
DMARD history												
Number of cDMARDs used (ever)												
0	0 (0.0%)	3 (2.4%)	0.22	1 (2.9%)	5 (4.9%)	0.10	1 (4.2%)	4 (4.4%)	0.01	1 (33.3%)	1 (14.3%)	0.46
1	18 (34.6%)	38 (29.9%)	0.10	10 (28.6%)	29 (28.2%)	0.01	9 (37.5%)	27 (29.7%)	0.17	2 (66.7%)	2 (28.6%)	0.83
2+	34 (65.4%)	86 (67.7%)	0.05	24 (68.6%)	69 (67.0%)	0.03	14 (58.3%)	60 (65.9%)	0.16	0 (0.0%)	4 (57.1%)	1.63
Methotrexate (prior use)	48 (92.3%)	116 (91.3%)	0.04	33 (94.3%)	87 (84.5%)	0.32	21 (87.5%)	82 (90.1%)	0.08	2 (66.7%)	6 (85.7%)	0.46
Number of bDMARDs used (ever)												
0	5 (9.6%)	14 (11.0%)	0.05	5 (14.3%)	12 (11.7%)	0.08	4 (16.7%)	13 (14.3%)	0.07	1 (33.3%)	3 (42.9%)	0.20
1	8 (15.4%)	17 (13.4%)	0.06	5 (14.3%)	18 (17.5%)	0.09	6 (25.0%)	17 (18.7%)	0.15	0 (0.0%)	1 (14.3%)	0.58
2+	39 (75.0%)	96 (75.6%)	0.01	25 (71.4%)	73 (70.9%)	0.01	14 (58.3%)	61 (67.0%)	0.18	2 (66.7%)	3 (42.9%)	0.49
Prior bDMARD use[a]	47 (90.4%)	113 (89.0%)	0.05	30 (85.7%)	91 (88.3%)	0.08	20 (83.3%)	78 (85.7%)	0.07	2 (66.7%)	4 (57.1%)	0.20
Prior TNFi bDMARD use	46 (88.5%)	109 (85.8%)	0.08	28 (80.0%)	86 (83.5%)	0.09	20 (83.3%)	71 (78.0%)	0.13	2 (66.7%)	3 (42.9%)	0.49
Prior non-TNFi bDMARD use	36 (69.2%)	73 (57.5%)	0.25	22 (62.9%)	65 (63.1%)	0.01	9 (37.5%)	48 (52.7%)	0.31	1 (33.3%)	3 (42.9%)	0.20

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 52)	TNFi (N= 127)	Std. Diff.	Baricitinib (N= 35)	TNFi (N= 103)	Std. Diff.	Baricitinib (N= 24)	TNFi (N= 91)	Std. Diff.	Baricitinib (N= 3)	TNFi (N= 7)	Std. Diff.
DMARD, current (baseline)												
cDMARD, concomitant use at baseline	31 (59.6%)	70 (55.1%)	0.09	23 (65.7%)	62 (60.2%)	0.11	17 (70.8%)	56 (61.5%)	0.20	0 (0.0%)	3 (42.9%)	1.22
Methotrexate, concomitant use at baseline	19 (36.5%)	43 (33.9%)	0.06	18 (51.4%)	33 (32.0%)	0.40	14 (58.3%)	40 (44.0%)	0.29	0 (0.0%)	3 (42.9%)	1.22
Prescription medication use, current (baseline)												
Other prescription medications												
Cardiovascular medications												
Anticoagulant (coumadin/warfarin; patient-reported)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
Antihypertensives (blood pressure lowering medication(s); patient-reported)	22 (42.3%)	59 (46.5%)	0.08	19 (54.3%)	47 (45.6%)	0.17	12 (50.0%)	46 (50.5%)	0.01	0 (0.0%)	5 (71.4%)	2.24
Antiplatelet (Plavix; patient-reported)	1 (1.9%)	2 (1.6%)	0.03	1 (2.9%)	0 (0.0%)	0.24	0 (0.0%)	5 (5.5%)	0.34	0 (0.0%)	0 (0.0%)	
Nitrates (angina/nitrate medications; patient-reported)	0 (0.0%)	2 (1.6%)	0.18	2 (5.7%)	1 (1.0%)	0.27	0 (0.0%)	1 (1.1%)	0.15	0 (0.0%)	0 (0.0%)	
Hormonal Medication HRT (in RA US only)	0 (0.0%)	0 (0.0%)		0 (0.0%)	2 (1.9%)	0.20	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
Lipid-lowering agents (cholesterol medication; patient-reported)	13 (25.0%)	31 (24.4%)	0.01	8 (22.9%)	22 (21.4%)	0.04	7 (29.2%)	22 (24.2%)	0.11	0 (0.0%)	1 (14.3%)	0.58
RA-related												
Aspirin (includes non-prescription)	6 (11.5%)	15 (11.8%)	0.01	6 (17.1%)	9 (8.7%)	0.25	5 (20.8%)	18 (19.8%)	0.03	1 (33.3%)	0 (0.0%)	1.00
Celebrex (in RA US only)	7 (13.5%)	10 (7.9%)	0.18	3 (8.6%)	13 (12.6%)	0.13	2 (8.3%)	2 (2.2%)	0.28	0 (0.0%)	1 (14.3%)	0.58
Prednisone	18 (34.6%)	44 (34.6%)	0.00	15 (42.9%)	36 (35.0%)	0.16	7 (29.2%)	32 (35.2%)	0.13	0 (0.0%)	1 (14.3%)	0.58
Vaccinations												
Influenza (baseline) (in RA US only)	24 (52.2%)	43 (38.4%)	0.28	10 (33.3%)	39 (41.1%)	0.16	11 (55.0%)	28 (35.4%)	0.40	0 (0.0%)	2 (28.6%)	0.89
Pneumonia (ever) (in RA US only)	13 (26.5%)	30 (25.6%)	0.02	9 (30.0%)	28 (29.2%)	0.02	5 (26.3%)	16 (19.8%)	0.16	0 (0.0%)	1 (14.3%)	0.58
Shingles (ever)	10 (20.0%)	25 (21.2%)	0.03	4 (13.3%)	23 (23.5%)	0.26	8 (40.0%)	21 (25.0%)	0.32	0 (0.0%)	1 (14.3%)	0.58

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; CDAI = clinical disease activity index; cDMARD = classical disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event (MI (myocardial infarction) and stroke); Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; Std Diff = absolute value of the standardized difference TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

a. Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

COR_US Table 6.29. Baseline Clinical Characteristics by Time-to-Event Duration, Serious infection-matched Population [CorEvitas US] - exposure ends at discontinuation/last follow-up visit/serious infection event; excludes patients with a serious infection within 6 months prior to index date.

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 53)	TNFi (N= 136)	Std. Diff.	Baricitinib (N= 35)	TNFi (N= 105)	Std. Diff.	Baricitinib (N= 23)	TNFi (N= 86)	Std. Diff.	Baricitinib (N= 3)	TNFi (N= 8)	Std. Diff.
Age [yrs]												
n	53	136	0.06	35	105	0.22	23	86	0.45	3	8	0.17
Mean±SD	59.6 ± 12.0	60.4 ± 12.9		57.3 ± 11.4	60.0 ± 12.9		65.6 ± 8.0	60.9 ± 12.4		64.3 ± 11.9	62.4 ± 11.5	
Median	61.0	61.5		57.0	60.0		66.0	64.5		59.0	63.5	
Min, Max	27.0, 79.0	22.0, 88.0		31.0, 81.0	23.0, 84.0		53.0, 79.0	28.0, 82.0		56.0, 78.0	44.0, 76.0	
≥ 65 years	17 (32.1%)	54 (39.7%)	0.16	10 (28.6%)	39 (37.1%)	0.18	14 (60.9%)	43 (50.0%)	0.22	1 (33.3%)	4 (50.0%)	0.34
Gender												
Male	12 (22.6%)	31 (22.8%)	0.00	7 (20.0%)	21 (20.0%)	0.00	5 (21.7%)	21 (24.4%)	0.06	3 (100.0%)	1 (12.5%)	3.74
Female	41 (77.4%)	105 (77.2%)		28 (80.0%)	84 (80.0%)		18 (78.3%)	65 (75.6%)		0 (0.0%)	7 (87.5%)	
History of MD-reported comorbidities (ever experienced)												
Cancer, Non-NMSC	3 (5.7%)	7 (5.1%)	0.02	2 (5.7%)	12 (11.4%)	0.21	1 (4.3%)	11 (12.8%)	0.31	0 (0.0%)	1 (12.5%)	0.53
Cancer, NMSC only	4 (7.5%)	6 (4.4%)	0.13	3 (8.6%)	7 (6.7%)	0.07	5 (21.7%)	6 (7.0%)	0.43	0 (0.0%)	0 (0.0%)	
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	3 (5.7%)	15 (11.0%)	0.20	6 (17.1%)	12 (11.4%)	0.16	2 (8.7%)	7 (8.1%)	0.02	0 (0.0%)	0 (0.0%)	
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	4 (7.5%)	5 (3.7%)	0.17	1 (2.9%)	5 (4.8%)	0.10	0 (0.0%)	6 (7.0%)	0.39	0 (0.0%)	0 (0.0%)	
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	7 (13.2%)	8 (5.9%)	0.25	1 (2.9%)	10 (9.5%)	0.28	1 (4.3%)	10 (11.6%)	0.27	0 (0.0%)	0 (0.0%)	
Cardiovascular revascularization	2 (3.8%)	6 (4.4%)	0.03	0 (0.0%)	3 (2.9%)	0.24	0 (0.0%)	4 (4.7%)	0.31	0 (0.0%)	0 (0.0%)	
Congestive heart failure (hospitalized & non-hospitalized)	3 (5.7%)	1 (0.7%)	0.28	0 (0.0%)	4 (3.8%)	0.28	0 (0.0%)	6 (7.0%)	0.39	0 (0.0%)	0 (0.0%)	
Coronary artery disease	3 (5.7%)	7 (5.1%)	0.02	1 (2.9%)	4 (3.8%)	0.05	1 (4.3%)	5 (5.8%)	0.07	0 (0.0%)	0 (0.0%)	
Ischemic heart disease	4 (7.5%)	8 (5.9%)	0.07	1 (2.9%)	7 (6.7%)	0.18	1 (4.3%)	6 (7.0%)	0.11	0 (0.0%)	0 (0.0%)	
TIA	1 (1.9%)	0 (0.0%)	0.20	0 (0.0%)	3 (2.9%)	0.24	0 (0.0%)	1 (1.2%)	0.15	0 (0.0%)	0 (0.0%)	
Unstable angina	0 (0.0%)	0 (0.0%)		0 (0.0%)	1 (1.0%)	0.14	0 (0.0%)	2 (2.3%)	0.22	0 (0.0%)	0 (0.0%)	
Ventricular arrhythmia	1 (1.9%)	1 (0.7%)	0.10	0 (0.0%)	0 (0.0%)		0 (0.0%)	1 (1.2%)	0.15	0 (0.0%)	0 (0.0%)	
Diabetes mellitus	10 (18.9%)	15 (11.0%)	0.22	1 (2.9%)	10 (9.5%)	0.28	1 (4.3%)	12 (14.0%)	0.34	0 (0.0%)	1 (12.5%)	0.53
Hyperlipidemia	10 (18.9%)	29 (21.3%)	0.06	10 (28.6%)	19 (18.1%)	0.25	5 (21.7%)	12 (14.0%)	0.20	0 (0.0%)	2 (25.0%)	0.82

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 53)	TNFi (N= 136)	Std. Diff.	Baricitinib (N= 35)	TNFi (N= 105)	Std. Diff.	Baricitinib (N= 23)	TNFi (N= 86)	Std. Diff.	Baricitinib (N= 3)	TNFi (N= 8)	Std. Diff.
Hypertension (hospitalized & non-hospitalized)	19 (35.8%)	45 (33.1%)	0.06	18 (51.4%)	37 (35.2%)	0.33	7 (30.4%)	27 (31.4%)	0.02	1 (33.3%)	4 (50.0%)	0.34
Immune disorders	13 (24.5%)	36 (26.5%)	0.04	9 (25.7%)	26 (24.8%)	0.02	8 (34.8%)	19 (22.1%)	0.28	0 (0.0%)	1 (12.5%)	0.53
Secondary Sjogren Syndrome	13 (24.5%)	36 (26.5%)	0.04	9 (25.7%)	26 (24.8%)	0.02	8 (34.8%)	19 (22.1%)	0.28	0 (0.0%)	1 (12.5%)	0.53
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	1 (1.9%)	7 (5.1%)	0.18	1 (2.9%)	6 (5.7%)	0.14	3 (13.0%)	3 (3.5%)	0.35	0 (0.0%)	1 (12.5%)	0.53
Obesity, current	15 (28.8%)	46 (34.6%)	0.12	15 (44.1%)	44 (43.6%)	0.01	9 (39.1%)	29 (33.7%)	0.11	1 (33.3%)	2 (25.0%)	0.18
Pregnancy, recent (current or since last visit)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
Smoking (current or former)	31 (58.5%)	74 (54.4%)	0.08	16 (45.7%)	65 (61.9%)	0.33	15 (65.2%)	41 (47.7%)	0.36	1 (33.3%)	2 (25.0%)	0.18
RA severity (CDAI)												
n	53	136	0.12	35	105	0.15	23	86	0.14	3	8	0.04
Mean±SD	19.2 ± 10.9	17.7 ± 13.0		19.3 ± 12.7	17.3 ± 13.8		19.7 ± 12.8	17.8 ± 13.2		16.5 ± 14.2	15.9 ± 13.6	
Median	16.0	15.5		20.7	14.5		18.0	15.3		20.0	16.8	
Min, Max	4.0, 51.2	0.0, 62.5		1.0, 49.0	0.0, 66.0		2.1, 48.5	0.0, 72.5		0.8, 28.6	0.5, 39.0	
Prevalent outcomes												
VTE (at any time in the past)	4 (7.5%)	1 (0.7%)	0.35	1 (2.9%)	0 (0.0%)	0.24	1 (4.3%)	2 (2.3%)	0.11	0 (0.0%)	0 (0.0%)	
MACE (at any time in the past)	1 (1.9%)	6 (4.4%)	0.14	0 (0.0%)	3 (2.9%)	0.24	2 (8.7%)	5 (5.8%)	0.11	0 (0.0%)	0 (0.0%)	
Myocardial infarction	1 (1.9%)	3 (2.2%)	0.02	0 (0.0%)	3 (2.9%)	0.24	2 (8.7%)	0 (0.0%)	0.44	0 (0.0%)	0 (0.0%)	
Stroke	0 (0.0%)	3 (2.2%)	0.21	0 (0.0%)	0 (0.0%)		0 (0.0%)	5 (5.8%)	0.35	0 (0.0%)	0 (0.0%)	
Serious infection (at any time in the past)	3 (5.7%)	5 (3.7%)	0.09	2 (5.7%)	10 (9.5%)	0.14	2 (8.7%)	9 (10.5%)	0.06	0 (0.0%)	0 (0.0%)	
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
DMARD history												
Number of cDMARDs used (ever)												
0	0 (0.0%)	4 (2.9%)	0.25	1 (2.9%)	2 (1.9%)	0.06	1 (4.3%)	2 (2.3%)	0.11	1 (33.3%)	0 (0.0%)	1.00
1	19 (35.8%)	47 (34.6%)	0.03	9 (25.7%)	33 (31.4%)	0.13	9 (39.1%)	33 (38.4%)	0.02	2 (66.7%)	2 (25.0%)	0.92
2+	34 (64.2%)	85 (62.5%)	0.03	25 (71.4%)	70 (66.7%)	0.10	13 (56.5%)	51 (59.3%)	0.06	0 (0.0%)	6 (75.0%)	2.45
Methotrexate (prior use)	49 (92.5%)	121 (89.0%)	0.12	33 (94.3%)	97 (92.4%)	0.08	20 (87.0%)	75 (87.2%)	0.01	2 (66.7%)	8 (100.0%)	1.00
Number of bDMARDs used (ever)												
0	5 (9.4%)	18 (13.2%)	0.12	5 (14.3%)	18 (17.1%)	0.08	4 (17.4%)	15 (17.4%)	0.00	1 (33.3%)	1 (12.5%)	0.51
1	8 (15.1%)	15 (11.0%)	0.12	5 (14.3%)	11 (10.5%)	0.12	6 (26.1%)	13 (15.1%)	0.27	0 (0.0%)	2 (25.0%)	0.82
2+	40 (75.5%)	103 (75.7%)	0.01	25 (71.4%)	76 (72.4%)	0.02	13 (56.5%)	58 (67.4%)	0.23	2 (66.7%)	5 (62.5%)	0.09
Prior bDMARD use[a]	48 (90.6%)	118 (86.8%)	0.12	30 (85.7%)	87 (82.9%)	0.08	19 (82.6%)	71 (82.6%)	0.00	2 (66.7%)	7 (87.5%)	0.51
Prior TNFi bDMARD use	47 (88.7%)	111 (81.6%)	0.20	28 (80.0%)	84 (80.0%)	0.00	19 (82.6%)	68 (79.1%)	0.09	2 (66.7%)	6 (75.0%)	0.18
Prior non-TNFi bDMARD use	37 (69.8%)	87 (64.0%)	0.12	21 (60.0%)	65 (61.9%)	0.04	9 (39.1%)	40 (46.5%)	0.15	1 (33.3%)	5 (62.5%)	0.61
DMARD, current (baseline)												
cDMARD, concomitant use at baseline	32 (60.4%)	86 (63.2%)	0.06	23 (65.7%)	72 (68.6%)	0.06	16 (69.6%)	56 (65.1%)	0.09	0 (0.0%)	6 (75.0%)	2.45

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 53)	TNFi (N= 136)	Std. Diff.	Baricitinib (N= 35)	TNFi (N= 105)	Std. Diff.	Baricitinib (N= 23)	TNFi (N= 86)	Std. Diff.	Baricitinib (N= 3)	TNFi (N= 8)	Std. Diff.
Methotrexate, concomitant use at baseline	21 (39.6%)	55 (40.4%)	0.02	18 (51.4%)	45 (42.9%)	0.17	13 (56.5%)	35 (40.7%)	0.32	0 (0.0%)	6 (75.0%)	2.45
Prescription medication use, current (baseline)												
Other prescription medications												
Cardiovascular medications												
Anticoagulant (coumadin/warfarin; patient-reported)	2 (3.8%)	1 (0.7%)	0.21	0 (0.0%)	3 (2.9%)	0.24	0 (0.0%)	1 (1.2%)	0.15	0 (0.0%)	0 (0.0%)	
Antihypertensives (blood pressure lowering medication(s); patient-reported)	21 (39.6%)	56 (41.2%)	0.03	20 (57.1%)	50 (47.6%)	0.19	11 (47.8%)	36 (41.9%)	0.12	0 (0.0%)	4 (50.0%)	1.41
Antiplatelet (Plavix; patient-reported)	1 (1.9%)	4 (2.9%)	0.07	1 (2.9%)	0 (0.0%)	0.24	0 (0.0%)	4 (4.7%)	0.31	0 (0.0%)	0 (0.0%)	
Nitrates (angina/nitrate medications; patient-reported)	0 (0.0%)	5 (3.7%)	0.28	2 (5.7%)	2 (1.9%)	0.20	0 (0.0%)	1 (1.2%)	0.15	0 (0.0%)	0 (0.0%)	
Hormonal Medication HRT (in RA US only)	1 (1.9%)	1 (0.7%)	0.10	0 (0.0%)	2 (1.9%)	0.20	0 (0.0%)	1 (1.2%)	0.15	0 (0.0%)	0 (0.0%)	
Lipid-lowering agents (cholesterol medication; patient-reported)	13 (24.5%)	36 (26.5%)	0.04	7 (20.0%)	22 (21.0%)	0.02	8 (34.8%)	15 (17.4%)	0.40	0 (0.0%)	2 (25.0%)	0.82
RA-related												
Aspirin (includes non-prescription)	7 (13.2%)	16 (11.8%)	0.04	7 (20.0%)	12 (11.4%)	0.24	4 (17.4%)	14 (16.3%)	0.03	1 (33.3%)	0 (0.0%)	1.00
Celebrex (in RA US only)	7 (13.2%)	9 (6.6%)	0.22	3 (8.6%)	10 (9.5%)	0.03	2 (8.7%)	3 (3.5%)	0.22	0 (0.0%)	1 (12.5%)	0.53
Prednisone	20 (37.7%)	50 (36.8%)	0.02	15 (42.9%)	39 (37.1%)	0.12	7 (30.4%)	32 (37.2%)	0.14	0 (0.0%)	1 (12.5%)	0.53
Vaccinations												
Influenza (baseline) (in RA US only)	24 (53.3%)	53 (42.7%)	0.21	10 (33.3%)	46 (48.9%)	0.32	10 (50.0%)	37 (45.7%)	0.09	0 (0.0%)	3 (37.5%)	1.10
Pneumonia (ever) (in RA US only)	12 (24.5%)	33 (26.0%)	0.03	10 (33.3%)	23 (23.2%)	0.23	4 (21.1%)	12 (14.6%)	0.17	0 (0.0%)	2 (25.0%)	0.82
Shingles (ever)	10 (20.0%)	32 (25.0%)	0.12	4 (13.3%)	25 (24.5%)	0.29	8 (40.0%)	23 (27.7%)	0.26	0 (0.0%)	1 (12.5%)	0.53

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; CDAI = clinical disease activity index; cDMARD = classical disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event; Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; TB = tuberculosis; TIA = transient ischemic attack; SD = standard deviation; Std Diff = absolute value of the standardized difference; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism;.

a. Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

COR_US Table 6.30. Baseline Clinical Characteristics by Time-to-Event Duration, TB Hospitalized infection-matched Population [CorEvitas US] - exposure ends at discontinuation/last follow-up visit/tb hospitalized infection event; excludes patients with a TB infection within 6 months prior to index date.

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 54)	TNFi (N= 136)	Std. Diff.	Baricitinib (N= 34)	TNFi (N= 108)	Std. Diff.	Baricitinib (N= 25)	TNFi (N= 89)	Std. Diff.	Baricitinib (N= 4)	TNFi (N= 10)	Std. Diff.
Age [yrs]												
n	54	136	0.17	34	108	0.26	25	89	0.64	4	10	0.71
Mean±SD	58.8 ± 11.8	60.9 ± 13.4		56.7 ± 11.2	59.7 ± 11.9		65.8 ± 7.8	59.3 ± 12.4		67.5 ± 11.6	60.2 ± 8.6	
Median	61.0	62.0		57.0	60.5		66.0	62.0		68.0	61.0	
Min, Max	27.0, 78.0	22.0, 88.0		31.0, 81.0	23.0, 82.0		53.0, 79.0	32.0, 87.0		56.0, 78.0	44.0, 72.0	
≥ 65 years	16 (29.6%)	59 (43.4%)	0.29	8 (23.5%)	42 (38.9%)	0.34	16 (64.0%)	38 (42.7%)	0.44	2 (50.0%)	3 (30.0%)	0.42
Gender												
Male	13 (24.1%)	27 (19.9%)	0.10	7 (20.6%)	23 (21.3%)	0.02	5 (20.0%)	18 (20.2%)	0.01	4 (100.0%)	2 (20.0%)	2.83
Female	41 (75.9%)	109 (80.1%)		27 (79.4%)	85 (78.7%)		20 (80.0%)	71 (79.8%)		0 (0.0%)	8 (80.0%)	
History of MD-reported comorbidities (ever experienced)												
Cancer, Non-NMSC	4 (7.4%)	8 (5.9%)	0.06	1 (2.9%)	9 (8.3%)	0.24	2 (8.0%)	12 (13.5%)	0.18	0 (0.0%)	1 (10.0%)	0.47
Cancer, NMSC only	3 (5.6%)	8 (5.9%)	0.01	3 (8.8%)	6 (5.6%)	0.13	5 (20.0%)	7 (7.9%)	0.36	1 (25.0%)	0 (0.0%)	0.82
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	4 (7.4%)	11 (8.1%)	0.03	6 (17.6%)	15 (13.9%)	0.10	2 (8.0%)	10 (11.2%)	0.11	0 (0.0%)	0 (0.0%)	
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	3 (5.6%)	6 (4.4%)	0.05	1 (2.9%)	3 (2.8%)	0.01	0 (0.0%)	5 (5.6%)	0.35	1 (25.0%)	0 (0.0%)	0.82
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	7 (13.0%)	12 (8.8%)	0.13	1 (2.9%)	12 (11.1%)	0.32	1 (4.0%)	8 (9.0%)	0.20	1 (25.0%)	0 (0.0%)	0.82
Cardiovascular revascularization	2 (3.7%)	6 (4.4%)	0.04	0 (0.0%)	2 (1.9%)	0.19	0 (0.0%)	3 (3.4%)	0.26	0 (0.0%)	0 (0.0%)	
Congestive heart failure (hospitalized & non-hospitalized)	3 (5.6%)	2 (1.5%)	0.22	0 (0.0%)	4 (3.7%)	0.28	0 (0.0%)	5 (5.6%)	0.35	0 (0.0%)	0 (0.0%)	
Coronary artery disease	3 (5.6%)	8 (5.9%)	0.01	1 (2.9%)	4 (3.7%)	0.04	1 (4.0%)	4 (4.5%)	0.02	1 (25.0%)	0 (0.0%)	0.82
Ischemic heart disease	4 (7.4%)	9 (6.6%)	0.03	1 (2.9%)	8 (7.4%)	0.20	1 (4.0%)	5 (5.6%)	0.08	1 (25.0%)	0 (0.0%)	0.82
TIA	1 (1.9%)	0 (0.0%)	0.19	0 (0.0%)	4 (3.7%)	0.28	0 (0.0%)	1 (1.1%)	0.15	0 (0.0%)	0 (0.0%)	
Unstable angina	0 (0.0%)	0 (0.0%)		0 (0.0%)	2 (1.9%)	0.19	0 (0.0%)	2 (2.2%)	0.21	0 (0.0%)	0 (0.0%)	
Ventricular arrhythmia	1 (1.9%)	3 (2.2%)	0.03	0 (0.0%)	0 (0.0%)		0 (0.0%)	1 (1.1%)	0.15	0 (0.0%)	0 (0.0%)	
Diabetes mellitus	11 (20.4%)	16 (11.8%)	0.24	1 (2.9%)	10 (9.3%)	0.27	1 (4.0%)	10 (11.2%)	0.28	0 (0.0%)	0 (0.0%)	
Hyperlipidemia	11 (20.4%)	25 (18.4%)	0.05	10 (29.4%)	20 (18.5%)	0.26	6 (24.0%)	11 (12.4%)	0.31	0 (0.0%)	0 (0.0%)	

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 54)	TNFi (N= 136)	Std. Diff.	Baricitinib (N= 34)	TNFi (N= 108)	Std. Diff.	Baricitinib (N= 25)	TNFi (N= 89)	Std. Diff.	Baricitinib (N= 4)	TNFi (N= 10)	Std. Diff.
Hypertension (hospitalized & non-hospitalized)	21 (38.9%)	51 (37.5%)	0.03	18 (52.9%)	42 (38.9%)	0.28	7 (28.0%)	31 (34.8%)	0.15	2 (50.0%)	4 (40.0%)	0.20
Immune disorders	13 (24.1%)	42 (30.9%)	0.15	10 (29.4%)	36 (33.3%)	0.08	8 (32.0%)	28 (31.5%)	0.01	0 (0.0%)	1 (10.0%)	0.47
Secondary Sjogren Syndrome	13 (24.1%)	42 (30.9%)	0.15	10 (29.4%)	36 (33.3%)	0.08	8 (32.0%)	28 (31.5%)	0.01	0 (0.0%)	1 (10.0%)	0.47
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	1 (1.9%)	8 (5.9%)	0.21	1 (2.9%)	3 (2.8%)	0.01	3 (12.0%)	3 (3.4%)	0.33	0 (0.0%)	0 (0.0%)	
Obesity, current	17 (32.1%)	44 (33.3%)	0.03	14 (42.4%)	39 (37.1%)	0.11	10 (40.0%)	33 (37.5%)	0.05	1 (25.0%)	4 (40.0%)	0.32
Pregnancy, recent (current or since last visit)	0 (0.0%)	1 (0.8%)	0.13	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
Smoking (current or former)	31 (57.4%)	77 (56.6%)	0.02	15 (44.1%)	64 (59.3%)	0.31	17 (68.0%)	44 (49.4%)	0.38	2 (50.0%)	5 (50.0%)	0.00
RA severity (CDAI)												
n	54	136	0.12	34	108	0.12	25	89	0.04	4	10	0.35
Mean±SD	18.9 ± 10.9	20.5 ± 15.2		19.3 ± 12.8	17.8 ± 13.2		19.3 ± 12.5	18.8 ± 13.5		15.5 ± 11.8	11.4 ± 11.6	
Median	15.8	18.1		20.4	15.3		18.0	14.5		16.3	7.9	
Min, Max	4.0, 51.2	0.5, 62.5		1.0, 49.0	0.0, 61.4		2.1, 48.5	0.5, 72.5		0.8, 28.6	0.5, 39.0	
Prevalent outcomes												
VTE (at any time in the past)	4 (7.4%)	4 (2.9%)	0.20	1 (2.9%)	2 (1.9%)	0.07	1 (4.0%)	4 (4.5%)	0.02	0 (0.0%)	0 (0.0%)	
MACE (at any time in the past)	1 (1.9%)	6 (4.4%)	0.15	0 (0.0%)	4 (3.7%)	0.28	2 (8.0%)	5 (5.6%)	0.09	0 (0.0%)	0 (0.0%)	
Myocardial infarction	1 (1.9%)	2 (1.5%)	0.03	0 (0.0%)	4 (3.7%)	0.28	2 (8.0%)	1 (1.1%)	0.33	0 (0.0%)	0 (0.0%)	
Stroke	0 (0.0%)	4 (2.9%)	0.25	0 (0.0%)	0 (0.0%)		0 (0.0%)	4 (4.5%)	0.31	0 (0.0%)	0 (0.0%)	
Serious infection (at any time in the past)	5 (9.3%)	14 (10.3%)	0.03	3 (8.8%)	10 (9.3%)	0.02	2 (8.0%)	9 (10.1%)	0.07	0 (0.0%)	0 (0.0%)	
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
DMARD history												
Number of cDMARDs used (ever)												
0	0 (0.0%)	4 (2.9%)	0.25	1 (2.9%)	2 (1.9%)	0.07	1 (4.0%)	0 (0.0%)	0.29	1 (25.0%)	0 (0.0%)	0.82
1	18 (33.3%)	38 (27.9%)	0.12	10 (29.4%)	30 (27.8%)	0.04	9 (36.0%)	31 (34.8%)	0.02	2 (50.0%)	3 (30.0%)	0.42
2+	36 (66.7%)	94 (69.1%)	0.05	23 (67.6%)	76 (70.4%)	0.06	15 (60.0%)	58 (65.2%)	0.11	1 (25.0%)	7 (70.0%)	1.01
Methotrexate (prior use)	50 (92.6%)	120 (88.2%)	0.15	32 (94.1%)	97 (89.8%)	0.16	22 (88.0%)	81 (91.0%)	0.10	3 (75.0%)	10 (100.0%)	0.82
Number of bDMARDs used (ever)												
0	5 (9.3%)	14 (10.3%)	0.03	5 (14.7%)	14 (13.0%)	0.05	4 (16.0%)	9 (10.1%)	0.18	1 (25.0%)	4 (40.0%)	0.32
1	8 (14.8%)	22 (16.2%)	0.04	5 (14.7%)	22 (20.4%)	0.15	6 (24.0%)	15 (16.9%)	0.18	0 (0.0%)	2 (20.0%)	0.71
2+	41 (75.9%)	100 (73.5%)	0.06	24 (70.6%)	72 (66.7%)	0.08	15 (60.0%)	65 (73.0%)	0.28	3 (75.0%)	4 (40.0%)	0.76
Prior bDMARD use[a]	49 (90.7%)	122 (89.7%)	0.03	29 (85.3%)	94 (87.0%)	0.05	21 (84.0%)	80 (89.9%)	0.18	3 (75.0%)	6 (60.0%)	0.32
Prior TNFi bDMARD use	48 (88.9%)	113 (83.1%)	0.17	27 (79.4%)	89 (82.4%)	0.08	21 (84.0%)	74 (83.1%)	0.02	3 (75.0%)	6 (60.0%)	0.32
Prior non-TNFi bDMARD use	38 (70.4%)	81 (59.6%)	0.23	21 (61.8%)	65 (60.2%)	0.03	10 (40.0%)	46 (51.7%)	0.24	2 (50.0%)	3 (30.0%)	0.42
DMARD, current (baseline)												
cDMARD, concomitant use at baseline	33 (61.1%)	78 (57.4%)	0.08	22 (64.7%)	73 (67.6%)	0.06	17 (68.0%)	56 (62.9%)	0.11	1 (25.0%)	8 (80.0%)	1.32

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 54)	TNFi (N= 136)	Std. Diff.	Baricitinib (N= 34)	TNFi (N= 108)	Std. Diff.	Baricitinib (N= 25)	TNFi (N= 89)	Std. Diff.	Baricitinib (N= 4)	TNFi (N= 10)	Std. Diff.
Methotrexate, concomitant use at baseline	21 (38.9%)	47 (34.6%)	0.09	17 (50.0%)	41 (38.0%)	0.24	14 (56.0%)	35 (39.3%)	0.34	1 (25.0%)	8 (80.0%)	1.32
Prescription medication use, current (baseline)												
Other prescription medications												
Cardiovascular medications												
Anticoagulant (coumadin/warfarin; patient-reported)	2 (3.7%)	6 (4.4%)	0.04	0 (0.0%)	2 (1.9%)	0.19	0 (0.0%)	1 (1.1%)	0.15	0 (0.0%)	0 (0.0%)	
Antihypertensives (blood pressure lowering medication(s); patient-reported)	24 (44.4%)	55 (40.4%)	0.08	19 (55.9%)	46 (42.6%)	0.27	12 (48.0%)	42 (47.2%)	0.02	0 (0.0%)	5 (50.0%)	1.41
Antiplatelet (Plavix; patient-reported)	1 (1.9%)	4 (2.9%)	0.07	1 (2.9%)	0 (0.0%)	0.25	0 (0.0%)	3 (3.4%)	0.26	0 (0.0%)	0 (0.0%)	
Nitrates (angina/nitrate medications; patient-reported)	0 (0.0%)	4 (2.9%)	0.25	2 (5.9%)	0 (0.0%)	0.35	0 (0.0%)	2 (2.2%)	0.21	0 (0.0%)	0 (0.0%)	
Hormonal Medication HRT (in RA US only)	0 (0.0%)	1 (0.7%)	0.12	0 (0.0%)	3 (2.8%)	0.24	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
Lipid-lowering agents (cholesterol medication; patient-reported)	15 (27.8%)	33 (24.3%)	0.08	8 (23.5%)	21 (19.4%)	0.10	8 (32.0%)	15 (16.9%)	0.36	0 (0.0%)	1 (10.0%)	0.47
RA-related												
Aspirin (includes non-prescription)	6 (11.1%)	19 (14.0%)	0.09	5 (14.7%)	14 (13.0%)	0.05	6 (24.0%)	19 (21.3%)	0.06	2 (50.0%)	0 (0.0%)	1.41
Celebrex (in RA US only)	7 (13.0%)	7 (5.1%)	0.27	3 (8.8%)	6 (5.6%)	0.13	2 (8.0%)	3 (3.4%)	0.20	0 (0.0%)	1 (10.0%)	0.47
Prednisone	19 (35.2%)	40 (29.4%)	0.12	15 (44.1%)	39 (36.1%)	0.16	8 (32.0%)	26 (29.2%)	0.06	0 (0.0%)	1 (10.0%)	0.47
Vaccinations												
Influenza (baseline) (in RA US only)	24 (51.1%)	57 (45.6%)	0.11	10 (33.3%)	43 (46.2%)	0.27	11 (52.4%)	35 (42.2%)	0.21	0 (0.0%)	3 (33.3%)	1.00
Pneumonia (ever) (in RA US only)	13 (25.5%)	30 (23.6%)	0.04	9 (30.0%)	24 (23.3%)	0.15	5 (25.0%)	14 (17.5%)	0.18	0 (0.0%)	1 (10.0%)	0.47
Shingles (ever)	11 (21.2%)	27 (21.1%)	0.00	4 (13.3%)	21 (20.0%)	0.18	8 (38.1%)	16 (19.0%)	0.43	0 (0.0%)	0 (0.0%)	

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; CDAI = clinical disease activity index; cDMARD = classical disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event (MI (myocardial infarction) and stroke); Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; TB = tuberculosis; TIA = transient ischemic attack; SD = standard deviation; Std Diff = absolute value of the standardized difference; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism;.

a. Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

COR_US Table 6.31. Baseline Healthcare Resource Utilization by Exposure Duration, Unmatched [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.32. Baseline Healthcare Resource Utilization by Exposure Duration, Primary VTE Cohorts [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.33. Baseline Healthcare Resource Utilization by Exposure Duration, Alternate VTE Cohorts (Case Definition I) [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.34. Baseline Healthcare Resource Utilization by Exposure Duration, Alternate VTE Cohorts (Case Definition II) [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.35. Baseline Healthcare Resource Utilization by Exposure Duration, MACE Cohorts [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.36. Baseline Healthcare Resource Utilization by Exposure Duration, Incident Serious Infections [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.37. Baseline Healthcare Resource Utilization by Exposure Duration, Hospitalized Tuberculosis [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.38. Primary (Main) Case Definition for VTE and Alternate Case Definitions for Sensitivity Analyses [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.39. Pattern of VTE and Related Diagnostic Codes in Patients with RA [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.40. Baseline Clinical Characteristics of RA Patients with VTE, VTE-matched Population [CorEvitas US]- excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

	Baricitinib (N=0)	TNFi (N=1)	Total (N=1)
Age [yrs]			
n	0	1	1
Mean±SD	0.0 ±0.0	44.0 ±.	44.0 ±.
Median	0.0	44.0	44.0
Min, Max	0.0, 0.0	44.0, 44.0	44.0, 44.0
Gender			
Male	0 (0.0%)	1 (100.0%)	1 (100.0%)
Female	0 (0.0%)	0 (0.0%)	0 (0.0%)
History of MD-reported comorbidities (ever experienced)			
Cancer, Non-NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cancer, NMSC only	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure (hospitalized & non-hospitalized)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyperlipidemia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertension (hospitalized & non-hospitalized)	0 (0.0%)	0 (0.0%)	0 (0.0%)

	Baricitinib (N=0)	TNFi (N=1)	Total (N=1)
Immune disorders	0 (0.0%)	1 (100.0%)	1 (100.0%)
Secondary Sjogren Syndrome	0 (0.0%)	1 (100.0%)	1 (100.0%)
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity, current	0 (0.0%)	1 (100.0%)	1 (100.0%)
Pregnancy, recent (current or since last visit)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Smoking (current or former)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA severity (CDAI)			
n	0	1	1
Mean	0.0 ±0.0	19.3 ±.	19.3 ±.
Median	0.0	19.3	19.3
Min, Max	0.0, 0.0	19.3, 19.3	19.3, 19.3
Prevalent outcomes			
VTE (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MACE (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Myocardial infarction	0 (0.0%)	0 (0.0%)	0 (0.0%)
Stroke	0 (0.0%)	0 (0.0%)	0 (0.0%)
Serious infection (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prescription medication use, current (baseline)			
Other prescription medications			
Cardiovascular medications			
Anticoagulant (coumadin/warfarin; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antihypertensives (blood pressure lowering medication(s); patient-reported)	0 (0.0%)	1 (100.0%)	1 (100.0%)
Antiplatelet (Plavix; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nitrates (angina/nitrate medications; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal Medication HRT (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents (cholesterol medication; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA-related			
Aspirin (includes non-prescription)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Celebrex (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prednisone	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vaccinations			
Influenza (baseline) (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)

	Baricitinib (N=0)	TNFi (N=1)	Total (N=1)
Pneumonia (ever) (in RA US only)	0 (0.0%)	1 (100.0%)	1 (100.0%)
Shingles (ever)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Occurrence			
Cancer diagnosis within 90 days after VTE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Concomitant Methotrexate in 1 month prior to VTE	0 (0.0%)	1 (100.0%)	1 (100.0%)

Abbreviations: COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event; Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

COR_US Table 6.41. Pattern of RA Medication Use in Patients with VTE [CorEvitas US] – excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

	Pre-matched		Matched		
	Baricitinib (N= 0)	TNFi (N= 7)	Baricitinib (N= 0)	TNFi (N= 1)	Total (N= 1)
Baseline Medication					
DMARD history					
Number of cDMARDs used (ever)					
0	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
1	0 (0.0%)	3 (42.9%)	0 (0.0%)	1 (100.0%)	1 (100.0%)
2+	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate (prior use)	0 (0.0%)	5 (71.4%)	0 (0.0%)	1 (100.0%)	1 (100.0%)
Number of bDMARDs used (ever)					
0	0 (0.0%)	4 (57.1%)	0 (0.0%)	1 (100.0%)	1 (100.0%)
1	0 (0.0%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2+	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prior bDMARD use[a]	0 (0.0%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prior TNFi bDMARD use	0 (0.0%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prior non-TNFi bDMARD use	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DMARD, current (baseline)					
cDMARD (non-methotrexate), concomitant use at baseline	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate, concomitant use at baseline	0 (0.0%)	3 (42.9%)	0 (0.0%)	1 (100.0%)	1 (100.0%)
Post-index Medication (Prior to VTE)					
Concomitant methotrexate use during exposure (regardless of use at index date)	0 (0.0%)	4 (57.1%)	0 (0.0%)	1 (100.0%)	1 (100.0%)
Concomitant non-methotrexate cDMARD during exposure (regardless of use at index date)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs; TNFi = tumor necrosis factor inhibitor.

a. Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

COR_US Table 6.42. Time to First VTE Event (Months*) [CorEvitas US] – excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

	Pre-matched		Matched		
	Baricitinib (N= 0)	TNFi (N= 7)	Baricitinib (N= 0)	TNFi (N= 1)	Total (N= 1)
n	0	7	0	1	1
Mean±SD	0.0 ± 0.0	1.5 ± 1.2	0.0 ± 0.0	0.5 ±.	0.5 ±.
Median	0.0	1.0	0.0	0.5	0.5
Min, Max	0.0, 0.0	0.5, 3.0	0.0, 0.0	0.5, 0.5	0.5, 0.5
25th percentile, 75th percentile	0.0, 0.0	0.5, 3.0	0.0, 0.0	0.5, 0.5	0.5, 0.5

Abbreviations: Min = minimum; Max = maximum; SD = standard deviation; VTE = venous thromboembolism; TNFi = tumor necrosis factor inhibitor.

* CorEvitas' RA US Registry collects drug information at the month-level so time is reported in months. A rough conversion to days can be made by multiplying the values in this table by a factor of 30.4375 (the average number of days in a month)

COR_US Table 6.43. Time to First VTE Event (Days), Alternate Definition I [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.44. Time to First VTE Event (Days), Alternate Definition II [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.45. Incidence Rates of First VTE Event [CorEvitas US] –excludes patients with VTE within 6 months prior to index date or currently taking anticoagulant.

	Pre-matched		Matched		
	Baricitinib (N= 115)	**TNFi (N=1,864)**	**Baricitinib (N= 112)**	**TNFi (N= 323)**	**Total (N= 435)**
Overall					
N	115	1,864	112	323	435
VTE Events	0	7	0	1	1
Person-Years	78.9	1428.5	76.2	241.5	317.7
VTE Events/100 PY	0.0	0.5	0.0	0.4	0.3
95% CI	0.0, 4.7	0.2, 1.0	0.0, 4.8	0.0, 2.3	0.0, 1.8
Incidence rate difference: baricitinib-TNFi (95% CI)					-0.4 (-1.2, 0.4)
bDMARD-naïve					
N	15	895	15	49	64
VTE Events	0	4	0	1	1
Person-Years	12.2	699.0	12.2	40.0	52.1
VTE Events/100 PY	0.0	0.6	0.0	2.5	1.9
95% CI	0.0, 30.2	0.2, 1.5	0.0, 30.2	0.1, 13.9	0.0, 10.7
Incidence rate difference: baricitinib-TNFi (95% CI)					-2.5 (-7.4, 2.4)
bDMARD-experienced					
N	100	969	97	274	371
VTE Events	0	3	0	0	0
Person-Years	66.7	729.4	64.0	201.5	265.5
VTE Events/100 PY	0.0	0.4	0.0	0.0	0.0
95% CI	0.0, 5.5	0.1, 1.2	0.0, 5.8	0.0, 1.8	0.0, 1.4
Incidence rate difference: baricitinib-TNFi (95% CI)					0.0 (0.0, 0.0)
Concomitant MTX Use at Index Date					
N	51	964	50	146	196
VTE Events	0	3	0	1	1
Person-Years	37.5	752.9	37.2	113.0	150.2
VTE Events/100 PY	0.0	0.4	0.0	0.9	0.7
95% CI	0.0, 9.8	0.1, 1.2	0.0, 9.9	0.0, 4.9	0.0, 3.7
Incidence rate difference: baricitinib-TNFi (95% CI)					-0.9 (-2.6, 0.8)
No concomitant MTX Use at Index Date					
N	64	900	62	177	239
VTE Events	0	4	0	0	0

	Pre-matched		Matched		
	Baricitinib (N= 115)	TNFi (N=1,864)	Baricitinib (N= 112)	TNFi (N= 323)	Total (N= 435)
Person-Years	41.4	675.6	39.0	128.4	167.5
VTE Events/100 PY	0.0	0.6	0.0	0.0	0.0
95% CI	0.0, 8.9	0.2, 1.5	0.0, 9.5	0.0, 2.9	0.0, 2.2
Incidence rate difference: baricitinib-TNFi (95% CI)					0.0 (0.0, 0.0)

Abbreviations: bDMARD = biologic disease-modifying anti-rheumatic drug; CI = confidence interval; MTX = methotrexate; PY = person-years; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

COR_US Table 6.46. Incidence Rates of Incident VTE Event, Alternate Definition I [CorEvitas US]

Not applicable in CorEvitas data

COR_US Table 6.47. Incidence Rates of Incident VTE Event, Alternate Definition II [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Table 6.48. Comparative Risk of Incident VTE, Primary Definition [CorEvitas US], VTE-matched population-excludes patients with prior VTE within 6 months prior to index date or anticoagulant.

Not applicable in CorEvitas data.

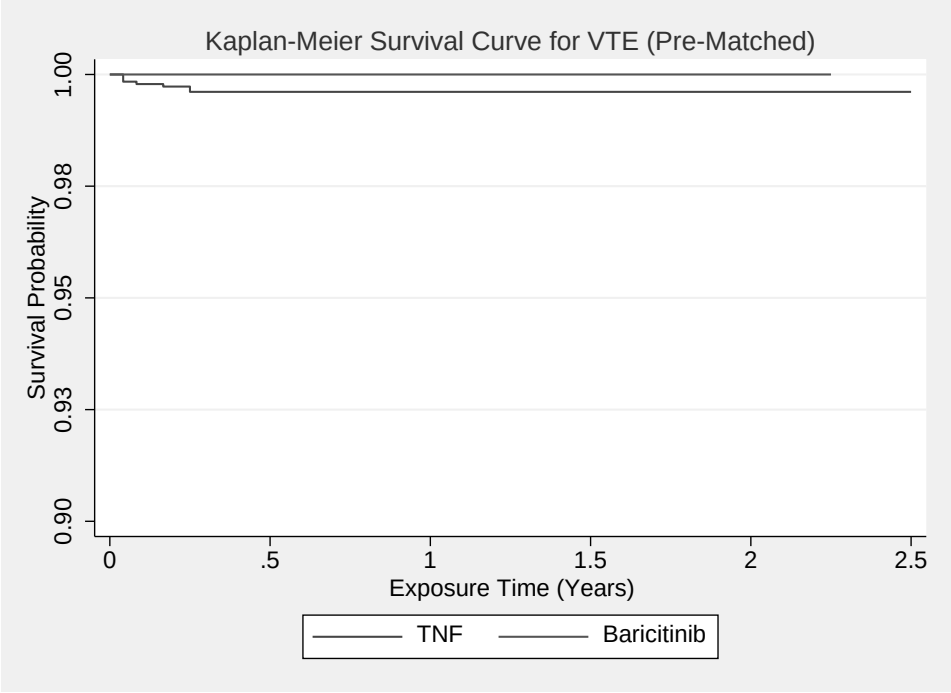
COR_US Table 6.49. Comparative Risk of Incident VTE, Alternate Definition I [CorEvitas US]

Not applicable in CorEvitas data.

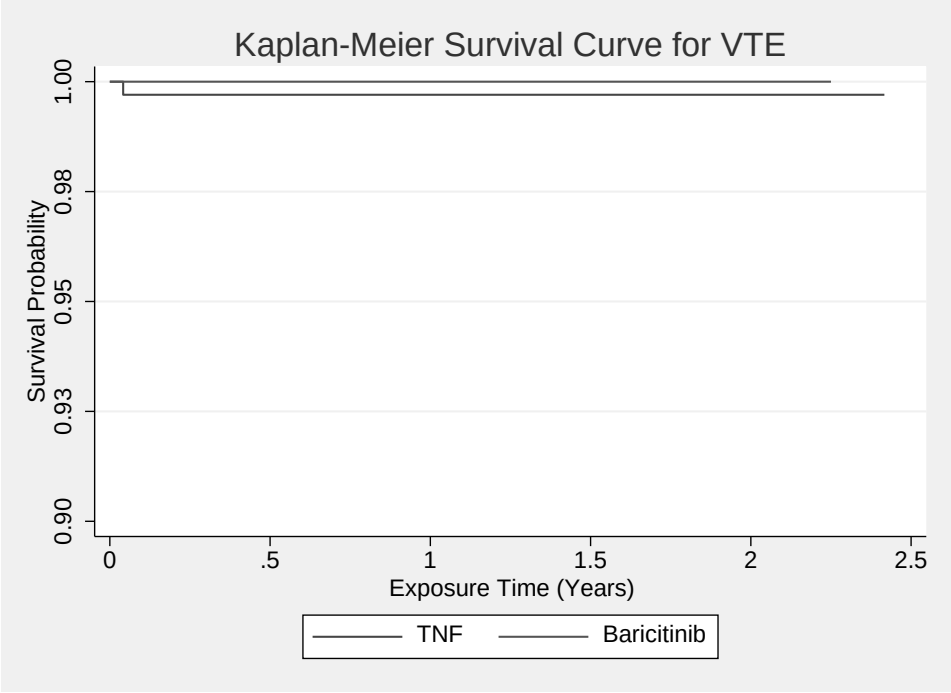
COR_US Table 6.50. Comparative Risk of Incident VTE, Alternate Definition II [CorEvitas US]

Not applicable in CorEvitas data.

COR_US Figure 2. Kaplan-Meier Curve of Time-to-First VTE Event [CorEvitas US], pre-matched VTE Population – excludes patients with prior VTE within 6 months prior to index date or on anticoagulant



COR_US Figure 3. Kaplan-Meier Curve of Time-to-First VTE Event [CorEvitas US], VTE-matched Population – excludes patients with prior VTE within 6 months prior to index date or on anticoagulant



COR_US Figure 4. Adjusted Survival Curve of Time-to-First VTE Event [CorEvitas US], VTE-matched Population – excludes patients with prior VTE within 6 months prior to index date or on anticoagulant

Not generated because < 20% difference in HR between unadjusted and model [1]

COR_US Table 6.51. Baseline Clinical Characteristics of RA Patients with MACE, MACE-matched Population [CorEvitas US]- excludes patients with a MACE within 6 months prior to index date or on anticoagulant.

	Baricitinib (N=2)	TNFi (N=3)	Total (N=5)
Age [yrs]			
n	2	3	5
Mean±SD	62.5 ±20.5	74.0 ± 3.0	69.4 ±12.2
Median	62.5	74.0	74.0
Min, Max	48.0, 77.0	71.0, 77.0	48.0, 77.0
Gender			
Male	2 (50.0%)	1 (33.3%)	3 (60.0%)
Female	0 (0.0%)	2 (66.7%)	2 (40.0%)
History of MD-reported comorbidities (ever experienced)			
Cancer, Non-NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cancer, NMSC only	1 (50.0%)	1 (33.3%)	2 (40.0%)
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	0 (0.0%)	1 (33.3%)	1 (20.0%)
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	1 (50.0%)	0 (0.0%)	1 (20.0%)
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	1 (50.0%)	0 (0.0%)	1 (20.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure (hospitalized & non-hospitalized)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	1 (50.0%)	0 (0.0%)	1 (20.0%)
Ischemic heart disease	1 (50.0%)	0 (0.0%)	1 (20.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyperlipidemia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertension (hospitalized & non-hospitalized)	1 (50.0%)	2 (66.7%)	3 (60.0%)
Immune disorders	0 (0.0%)	1 (33.3%)	1 (20.0%)

	Baricitinib (N=2)	TNFi (N=3)	Total (N=5)
Secondary Sjogren Syndrome	0 (0.0%)	1 (33.3%)	1 (20.0%)
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity, current	0 (0.0%)	1 (33.3%)	1 (20.0%)
Pregnancy, recent (current or since last visit)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Smoking (current or former)	1 (50.0%)	3 (100.0%)	4 (80.0%)
RA severity (CDAI)			
n	2	3	5
Mean±SD	13.0 ± 0.7	10.2 ± 2.3	11.3 ± 2.3
Median	13.0	10.0	12.5
Min, Max	12.5, 13.5	8.0, 12.5	8.0, 13.5
Prevalent outcomes			
VTE (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MACE (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Myocardial infarction	0 (0.0%)	0 (0.0%)	0 (0.0%)
Stroke	0 (0.0%)	0 (0.0%)	0 (0.0%)
Serious infection (at any time in the past)	0 (0.0%)	3 (100.0%)	3 (60.0%)
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prescription medication use, current (baseline)			
Other prescription medications			
Cardiovascular medications			
Anticoagulant (coumadin/warfarin; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antihypertensives (blood pressure lowering medication(s); patient-reported)	0 (0.0%)	2 (66.7%)	2 (40.0%)
Antiplatelet (Plavix; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nitrates (angina/nitrate medications; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal Medication HRT (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents (cholesterol medication; patient-reported)	0 (0.0%)	1 (33.3%)	1 (20.0%)
RA-related			
Aspirin (includes non-prescription)	1 (50.0%)	1 (33.3%)	2 (40.0%)
Celebrex (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prednisone	0 (0.0%)	1 (33.3%)	1 (20.0%)

	Baricitinib (N=2)	TNFi (N=3)	Total (N=5)
Vaccinations			
Influenza (baseline) (in RA US only)	1 (100.0%)	3 (100.0%)	4 (100.0%)
Pneumonia (ever) (in RA US only)	0 (0.0%)	1 (33.3%)	1 (25.0%)
Shingles (ever)	1 (100.0%)	1 (33.3%)	2 (50.0%)
Post-index Occurrence			
Concomitant Methotrexate in 1** month prior to MACE	1 (50.0%)	1 (33.3%)	2 (40.0%)

Abbreviations: COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event (MI (myocardial infarction) and stroke); Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.
** CorEvitas drug use information collected at the month-level, so “in 7 days prior to MACE” is replaced with “in 1 month prior to MACE”

COR_US Table 6.52. Pattern of RA Medication Use in Patients with MACE [CorEvitas US] – excludes patients with a MACE within 6 months prior to index date or on anticoagulant.

	Pre-matched		Matched		
	Baricitinib (N= 2)	TNFi (N= 4)	Baricitinib (N= 2)	TNFi (N= 3)	Total (N= 5)
Baseline Medication					
DMARD history					
Number of cDMARDs used (ever)					
0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
1	0 (0.0%)	1 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2+	2 (100.0%)	3 (75.0%)	2 (100.0%)	3 (100.0%)	5 (100.0%)
Methotrexate (prior use)	2 (100.0%)	4 (100.0%)	2 (100.0%)	3 (100.0%)	5 (100.0%)
Number of bDMARDs used (ever)					
0	0 (0.0%)	1 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2+	2 (100.0%)	3 (75.0%)	2 (100.0%)	3 (100.0%)	5 (100.0%)
Prior bDMARD use[a]	2 (100.0%)	3 (75.0%)	2 (100.0%)	3 (100.0%)	5 (100.0%)
Prior TNFi bDMARD use	2 (100.0%)	2 (50.0%)	2 (100.0%)	2 (66.7%)	4 (80.0%)
Prior non-TNFi bDMARD use	2 (100.0%)	2 (50.0%)	2 (100.0%)	2 (66.7%)	4 (80.0%)
DMARD, current (baseline)					
cDMARD (non-methotrexate), concomitant use at baseline	0 (0.0%)	1 (25.0%)	0 (0.0%)	1 (33.3%)	1 (20.0%)
Methotrexate, concomitant use at baseline	1 (50.0%)	2 (50.0%)	1 (50.0%)	1 (33.3%)	2 (40.0%)
Post-index Medication (Prior to MACE)					
Concomitant methotrexate use during exposure (regardless of use at index date)	1 (50.0%)	2 (50.0%)	1 (50.0%)	1 (33.3%)	2 (40.0%)
Concomitant non-methotrexate cDMARD during exposure (regardless of use at index date)	0 (0.0%)	1 (25.0%)	0 (0.0%)	1 (33.3%)	1 (20.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs; MACE = major adverse cardiovascular event; TNFi = tumor necrosis factor inhibitor.
a. Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

COR_US Table 6.53. Time to First MACE(Months*) [CorEvitas US] - excludes patients with a MACE within 6 months prior to index date or on anticoagulant.

	Pre-matched		Matched		
	Baricitinib (N= 2)	**TNFi (N= 4)**	**Baricitinib (N= 2)**	**TNFi (N= 3)**	**Total (N= 5)**
n	2	4	2	3	5
Mean±SD	6.5 ± 6.4	5.6 ± 5.3	6.5 ± 6.4	7.3 ± 4.9	7.0 ± 4.7
Median	6.5	4.5	6.5	5.0	5.0
Min, Max	2.0, 11.0	0.5, 13.0	2.0, 11.0	4.0, 13.0	2.0, 13.0
25th percentile, 75th percentile	2.0, 11.0	2.3, 9.0	2.0, 11.0	4.0, 13.0	4.0, 11.0

* CorEvitas' RA US Registry collects drug information at the month-level so time is reported in months. A rough conversion to days can be made by multiplying the values in this table by a factor of 30.4375 (the average number of days in a month)
Abbreviations: MACE = major adverse cardiovascular event; Min = minimum; Max = maximum; SD = standard deviation; TNFi = tumor necrosis factor inhibitor.

COR_US Table 6.54. Incidence Rates of First MACE [CorEvitas US] –excludes patients with MACE within 6 months prior to index date or currently taking anticoagulant.

	Pre-matched		Matched		
	Baricitinib (N= 114)	**TNFi (N=1,864)**	**Baricitinib (N= 114)**	**TNFi (N= 328)**	**Total (N= 442)**
Overall					
N	114	1,864	114	328	442
MACE Events	2	4	2	3	5
Person-Years	76.0	1426.3	76.0	241.0	317.0
MACE Events/100 PY	2.6	0.3	2.6	1.2	1.6
95% CI	0.3, 9.5	0.1, 0.7	0.3, 9.5	0.3, 3.6	0.5, 3.7
Incidence rate difference: baricitinib-TNFi (95% CI)					1.4 (-2.5, 5.3)
MI					
N	114	1,864	114	328	442
MI Events	2	2	2	1	3
Person-Years	76.0	1428.7	76.0	243.4	319.5
MI Events/100 PY	2.6	0.1	2.6	0.4	0.9
95% CI	0.3, 9.5	0.0, 0.5	0.3, 9.5	0.0, 2.3	0.2, 2.7
Incidence rate difference: baricitinib-TNFi (95% CI)					2.2 (-1.5, 6.0)
Stroke					
N	114	1,864	114	328	442
Stroke Events	0	2	0	2	2
Person-Years	77.1	1427.2	77.1	241.7	318.8
Stroke Events/100 PY	0.0	0.1	0.0	0.8	0.6
95% CI	0.0, 4.8	0.0, 0.5	0.0, 4.8	0.1, 3.0	0.1, 2.3
Incidence rate difference: baricitinib-TNFi (95% CI)					-0.8 (-2.0, 0.3)
Concomitant MTX Use at Index Date					
N	51	966	51	119	170
MACE Events	1	2	1	1	2
Person-Years	36.4	753.8	36.4	94.8	131.2
MACE Events/100 PY	2.7	0.3	2.7	1.1	1.5
95% CI	0.1, 15.3	0.0, 1.0	0.1, 15.3	0.0, 5.9	0.2, 5.5
Incidence rate difference: baricitinib-TNFi (95% CI)					1.7 (-4.1, 7.5)
No concomitant MTX Use at Index Date					
N	63	898	63	209	272
MACE Events	1	2	1	2	3
Person-Years	39.6	672.5	39.6	146.2	185.8
MACE Events/100 PY	2.5	0.3	2.5	1.4	1.6
95% CI	0.1, 14.1	0.0, 1.1	0.1, 14.1	0.2, 4.9	0.3, 4.7
Incidence rate difference: baricitinib-TNFi (95% CI)					1.2 (-4.1, 6.5)

Abbreviations: CI = confidence interval; MI = myocardial infarction; MACE = major adverse cardiovascular event; MTX = methotrexate; PY = person-years; TNFi = tumor necrosis factor inhibitor.

COR_US Table 6.55. Comparative Risk of Incident MACE [CorEvitas US], MACE-matched population- excludes patients with prior MACE within 6 months prior to index date or anticoagulant.

	TNFi	Baricitinib HR (95% CI)	P-value
Base model	Ref	1.40 (0.18, 10.96)	0.75
Adjusted- Model [1]	Ref	1.75 (0.22, 14.15)	0.60
Adjusted- Model [2]	Ref	1.66 (0.20, 13.60)	0.64
Non-mtx cDMARD use	Ref	0.40 (0.01, 15.30)	0.62
Mtx cDMARD use	Ref	1.24 (0.15, 10.16)	0.84
Prednisone use	Ref	0.25 (0.01, 8.91)	0.45
Adjusted- Model [3]	Ref	1.76 (0.22, 14.14)	0.60
Prednisone use	Ref	0.24 (0.01, 8.56)	0.43
Adjusted- Model [4]	Ref	2.18 (0.24, 19.65)	0.49
RA severity (CDAI)	Ref	0.94 (0.83, 1.05)	0.27
Adjusted- Model [5]	Ref	2.67 (0.27, 26.88)	0.40
Adjusted- Model [6]	Ref	1.48 (0.19, 11.88)	0.71

Abbreviations: CDAI = clinical disease activity index; cDMARD = classical disease-modifying anti-rheumatic drug; CI = confidence interval; HR = hazard ratio;. mtx = methotrexate; Ref = Referent group; TNFi = tumor necrosis factor inhibitor.

Base model: no adjusting covariates

Model [1]: adjusted with covariates specified in SAP COR_US Table 66 and remaining imbalanced after matching

Model [2]: Model [1] + time-varying concomitant non-methotrexate cDMARD use + time-varying concomitant methotrexate use + time-varying prednisone use

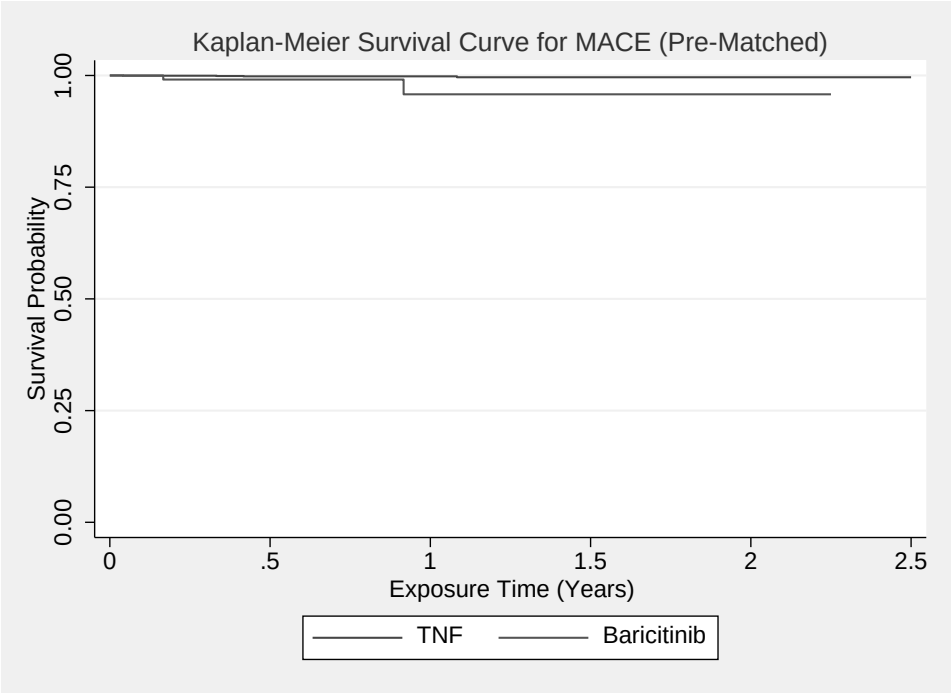
Model [3]: Model [1] + time-varying prednisone use.

Model [4]: Model [1] + RA severity (CDAI)

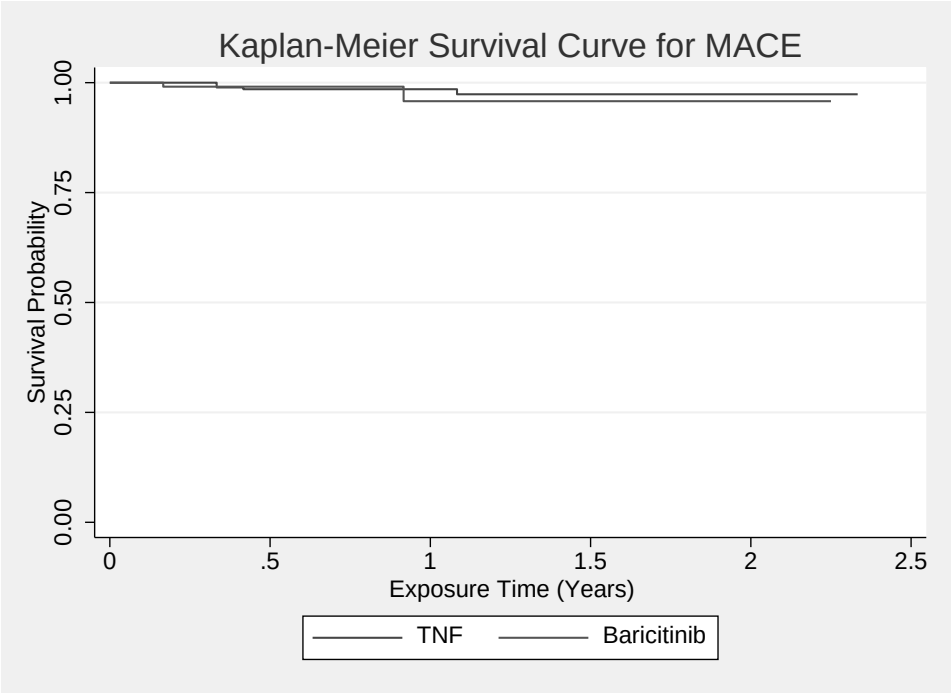
Model [5]: Model [4] + BMI + smoking status

Model [5]: Model [1] + aspirin use

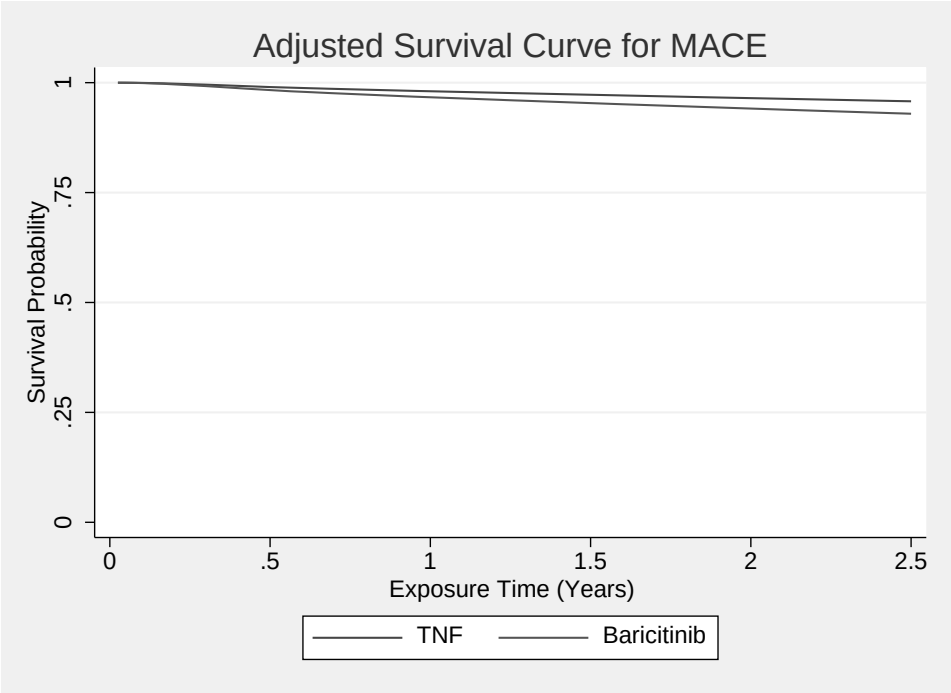
COR_US Figure 5. Kaplan-Meier Curve of Time-to-First MACE [CorEvitas US], pre-matched MACE Population – excludes patients with prior MACE within 6 months prior to index date or on anticoagulant



COR_US Figure 6. Kaplan-Meier Curve of Time-to-First MACE Event [CorEvitas US], MACE-matched Population – excludes patients with prior MACE within 6 months prior to index date or on anticoagulant



COR_US Figure 7. Adjusted Survival Curve of Time-to-First MACE [CorEvitas US], MACE-matched Population – excludes patients with prior MACE within 6 months prior to index date or on anticoagulant



COR_US Table 6.56. Baseline Clinical Characteristics of RA Patients with Serious Infection, Serious Infection-matched Population [CorEvitas US]-excludes patients with a Serious Infection within 6 months prior to index date.

	Baricitinib (N=3)	TNFi (N=6)	Total (N=9)
Age [yrs]			
n	3	6	9
Mean±SD	71.3 ± 5.5	69.8 ± 8.9	70.3 ± 7.6
Median	71.0	72.5	71.0
Min, Max	66.0, 77.0	56.0, 78.0	56.0, 78.0
Gender			
Male	1 (33.3%)	1 (16.7%)	2 (22.2%)
Female	2 (66.7%)	5 (83.3%)	7 (77.8%)
History of MD-reported comorbidities (ever experienced)			
Cancer, Non-NMSC	1 (33.3%)	1 (16.7%)	2 (22.2%)
Cancer, NMSC only	1 (33.3%)	1 (16.7%)	2 (22.2%)
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	0 (0.0%)	4 (66.7%)	4 (44.4%)
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	1 (33.3%)	0 (0.0%)	1 (11.1%)
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	1 (33.3%)	0 (0.0%)	1 (11.1%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure (hospitalized & non-hospitalized)	0 (0.0%)	1 (16.7%)	1 (11.1%)
Coronary artery disease	1 (33.3%)	0 (0.0%)	1 (11.1%)
Ischemic heart disease	1 (33.3%)	0 (0.0%)	1 (11.1%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyperlipidemia	1 (33.3%)	2 (33.3%)	3 (33.3%)
Hypertension (hospitalized & non-hospitalized)	1 (33.3%)	5 (83.3%)	6 (66.7%)
Immune disorders	0 (0.0%)	1 (16.7%)	1 (11.1%)
Secondary Sjogren Syndrome	0 (0.0%)	1 (16.7%)	1 (11.1%)
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	0 (0.0%)	0 (0.0%)	0 (0.0%)

	Baricitinib (N=3)	TNFi (N=6)	Total (N=9)
Obesity, current	1 (33.3%)	2 (33.3%)	3 (33.3%)
Pregnancy, recent (current or since last visit)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Smoking (current or former)	3 (100.0%)	2 (33.3%)	5 (55.6%)
RA severity (CDAI)			
n	3	6	9
Mean±SD	14.2 ± 7.2	19.3 ± 6.7	17.6 ± 6.9
Median	12.5	20.3	19.5
Min, Max	8.0, 22.1	6.5, 25.0	6.5, 25.0
Prevalent outcomes			
VTE (at any time in the past)	0 (0.0%)	1 (16.7%)	1 (11.1%)
MACE (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Myocardial infarction	0 (0.0%)	0 (0.0%)	0 (0.0%)
Stroke	0 (0.0%)	0 (0.0%)	0 (0.0%)
Serious infection (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prescription medication use, current (baseline)			
Other prescription medications			
Cardiovascular medications			
Anticoagulant (coumadin/warfarin; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antihypertensives (blood pressure lowering medication(s); patient-reported)	1 (33.3%)	5 (83.3%)	6 (66.7%)
Antiplatelet (Plavix; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nitrates (angina/nitrate medications; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal Medication HRT (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents (cholesterol medication; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA-related			
Aspirin (includes non-prescription)	3 (100.0%)	2 (33.3%)	5 (55.6%)
Celebrex (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prednisone	1 (33.3%)	3 (50.0%)	4 (44.4%)
Vaccinations			
Influenza (baseline) (in RA US only)	1 (100.0%)	3 (50.0%)	4 (57.1%)
Pneumonia (ever) (in RA US only)	1 (100.0%)	3 (50.0%)	4 (57.1%)
Shingles (ever)	0 (0.0%)	3 (60.0%)	3 (50.0%)

Abbreviations: CDAI = clinical disease activity index; cDMARD = classical disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event (MI (myocardial infarction) and stroke); Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

COR_US Table 6.57. Pattern of RA Medication Use in Patients with Serious Infection [CorEvitas US] – excludes patients with a serious infection within 6 months prior to index date.

	Pre-matched		Matched		
	Baricitinib (N= 3)	TNFi (N= 44)	Baricitinib (N= 3)	TNFi (N= 6)	Total (N= 9)
Baseline Medication					
DMARD history					
Number of cDMARDs used (ever)					
0	0 (0.0%)	4 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
1	0 (0.0%)	11 (25.0%)	0 (0.0%)	1 (16.7%)	1 (11.1%)
2+	3 (100.0%)	29 (65.9%)	3 (100.0%)	5 (83.3%)	8 (88.9%)
Methotrexate (prior use)	3 (100.0%)	37 (84.1%)	3 (100.0%)	6 (100.0%)	9 (100.0%)
Number of bDMARDs used (ever)					
0	0 (0.0%)	15 (34.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
1	0 (0.0%)	18 (40.9%)	0 (0.0%)	1 (16.7%)	1 (11.1%)
2+	3 (100.0%)	11 (25.0%)	3 (100.0%)	5 (83.3%)	8 (88.9%)
Prior bDMARD use[a]	3 (100.0%)	29 (65.9%)	3 (100.0%)	6 (100.0%)	9 (100.0%)
Prior TNFi bDMARD use	3 (100.0%)	24 (54.5%)	3 (100.0%)	4 (66.7%)	7 (77.8%)
Prior non-TNFi bDMARD use	2 (66.7%)	15 (34.1%)	2 (66.7%)	6 (100.0%)	8 (88.9%)
DMARD, current (baseline)					
cDMARD (non-methotrexate), concomitant use at baseline	1 (33.3%)	18 (40.9%)	1 (33.3%)	1 (16.7%)	2 (22.2%)
Methotrexate, concomitant use at baseline	2 (66.7%)	21 (47.7%)	2 (66.7%)	2 (33.3%)	4 (44.4%)
Post-index Medication (Prior to Serious Infection)					
Concomitant methotrexate use during exposure (regardless of use at index date)	2 (66.7%)	21 (47.7%)	2 (66.7%)	2 (33.3%)	4 (44.4%)
Concomitant non-methotrexate cDMARD during exposure (regardless of use at index date)	1 (33.3%)	19 (43.2%)	1 (33.3%)	1 (16.7%)	2 (22.2%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs; TNFi = tumor necrosis factor inhibitor.

a. Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

COR_US Table 6.58. Time to First Serious Infection Event (Months*) [CorEvitas US] – excludes patients with a serious infection within 6 months prior to index date.

	Pre-matched		Matched		
	Baricitinib (N= 3)	**TNFi (N= 44)**	**Baricitinib (N= 3)**	**TNFi (N= 6)**	**Total (N= 9)**
n	3	44	3	6	9
Mean±SD	7.7 ± 2.5	6.1 ± 4.5	7.7 ± 2.5	8.5 ± 5.1	8.2 ± 4.2
Median	8.0	4.3	8.0	7.0	8.0
Min, Max	5.0, 10.0	0.5, 21.0	5.0, 10.0	4.0, 16.0	4.0, 16.0
25th percentile, 75th percentile	5.0, 10.0	2.8, 9.5	5.0, 10.0	4.0, 13.0	5.0, 10.0

* CorEvitas' RA US Registry collects drug information at the month-level so time is reported in months. A rough conversion to days can be made by multiplying the values in this table by a factor of 30.4375 (the average number of days in a month)
Abbreviations: Min = minimum; Max = maximum; SD = standard deviation; TNFi = tumor necrosis factor inhibitor.

COR_US Table 6.59. Incidence Rates of First Serious Infection Event [CorEvitas US] – excludes patients with a serious infection within 6 months prior to index date.

	Pre-matched		Matched		
	Baricitinib (N= 115)	**TNFi (N=1,881)**	**Baricitinib (N= 114)**	**TNFi (N= 335)**	**Total (N= 449)**
Overall					
N	115	1,881	114	335	449
SI Events	3	44	3	6	9
Person-Years	75.0	1423.6	74.9	241.7	316.5
SI Events/100 PY	4.0	3.1	4.0	2.5	2.8
95% CI	0.8, 11.7	2.2, 4.1	0.8, 11.7	0.9, 5.4	1.3, 5.4
Incidence rate difference: baricitinib-TNFi (95% CI)					1.5 (-3.4, 6.5)

Abbreviations: CI = confidence interval; PY = person-years; SI = serious Infection defined as infection; TNFi = tumor necrosis factor inhibitor.

COR_US Table 6.60. Serious Infection Events Per Patient During Baricitinib and TNF Exposure* [CorEvitas US] – excludes patients with a serious infection within 6 months prior to index date.

	Pre-matched		Matched		
	Baricitinib (N= 3)	TNFi (N= 44)	Baricitinib (N= 3)	TNFi (N= 6)	Total (N= 9)
0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
1	3 (100.0%)	38 (86.4%)	3 (100.0%)	6 (100.0%)	9 (100.0%)
2	0 (0.0%)	5 (11.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
3	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

* All events after the first occur after the incident serious infection determining time to first serious infection event
Abbreviation: TNFi = tumor necrosis factor inhibitor.

COR_US Table 6.61. Comparative Risk of Incident Serious Infection [CorEvitas US], Serious Infection -matched population-excludes patients with prior serious infection within 6 months prior to index date.

	TNFi	Baricitinib HR (95% CI)	P-value
Base model	Ref	1.71 (0.28, 10.22)	0.56
Adjusted- Model [1]	Ref	1.71 (0.29, 10.23)	0.56
Adjusted- Model [2]	Ref	1.71 (0.26, 11.25)	0.58
Non-mtx cDMARD use	Ref	1.51 (0.18, 12.73)	0.70
Mtx cDMARD use	Ref	1.63 (0.27, 9.88)	0.60
Prednisone use	Ref	2.09 (0.34, 12.62)	0.42
Adjusted- Model [3]	Ref	1.60 (0.26, 9.66)	0.61
Prednisone use	Ref	2.12 (0.35, 12.81)	0.41
Adjusted- Model [4]	Ref	1.73 (0.29, 10.40)	0.55
RA severity (CDAI)	Ref	0.99 (0.92, 1.06)	0.72
Adjusted- Model [5]	Ref	1.86 (0.31, 11.26)	0.50

Abbreviations: CDAI = clinical disease activity index; cDMARD = classical disease-modifying anti-rheumatic drug; CI = confidence interval; HR = hazard ratio mtx = methotrexate; Ref = Referent group; TNFi = tumor necrosis factor inhibitor.

Base model: no adjusting covariates

Model [1]: adjusted with covariates specified in SAP COR_US Table 66 and remaining imbalanced after matching

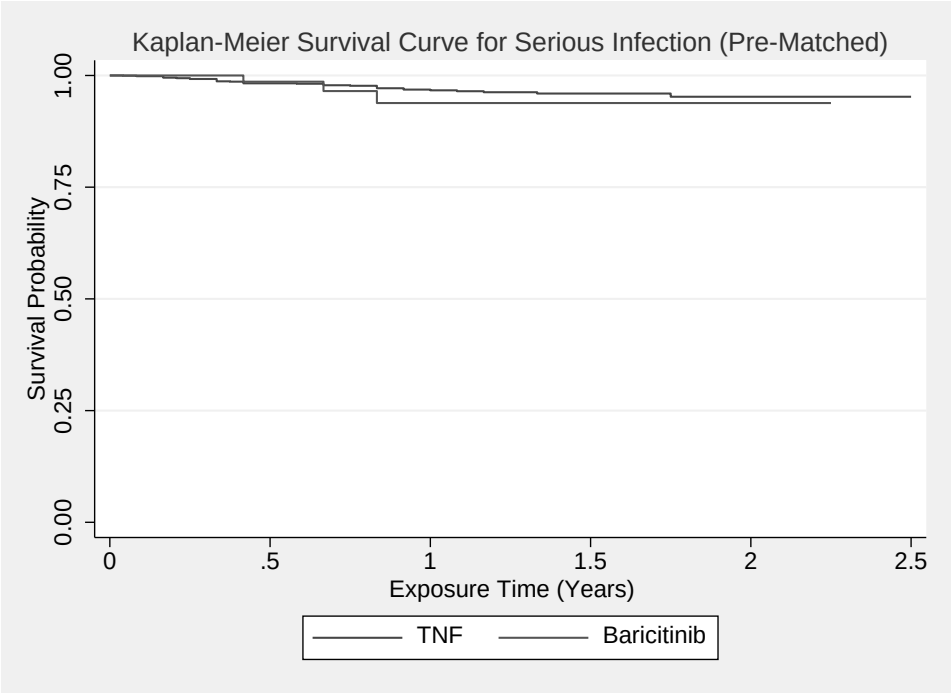
Model [2]: Model [1] + time-varying concomitant non-methotrexate cDMARD use + time-varying concomitant methotrexate use + time-varying prednisone use

Model [3]: Model [1] + time-varying prednisone use.

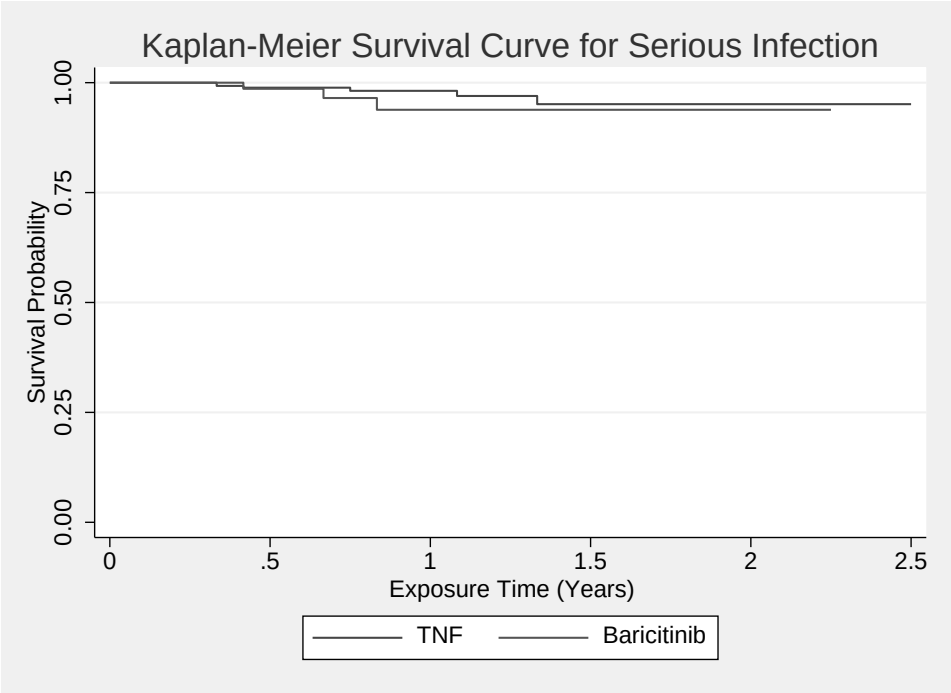
Model [4]: Model [1] + RA severity (CDAI)

Model [5]: Model [4] + BMI + smoking status

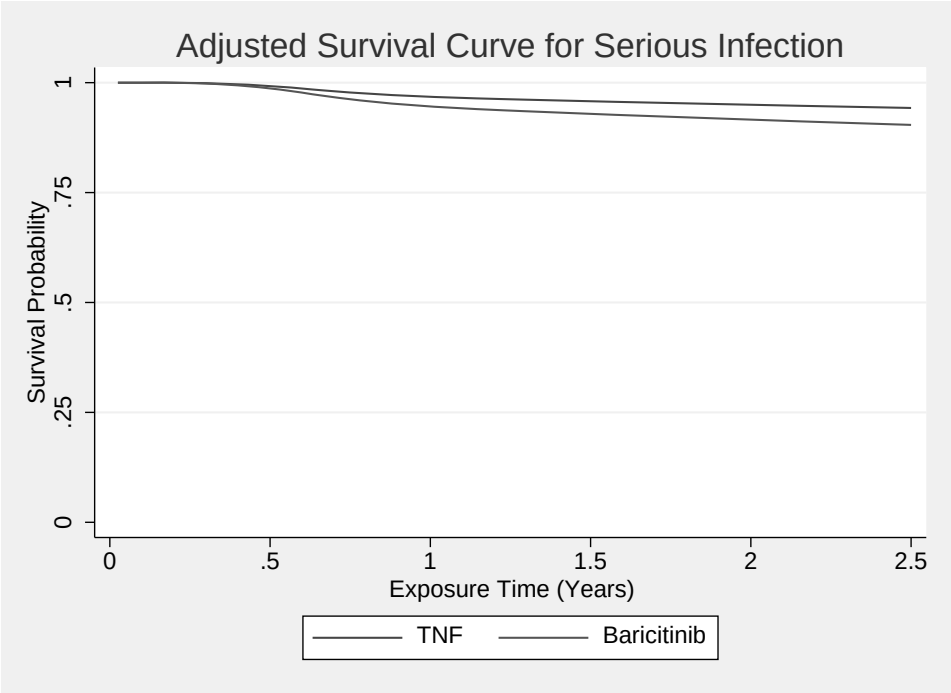
COR_US Figure 8. Kaplan-Meier Curve of Time-to-First Serious Infection [CorEvitas US], pre-matched Serious Infection Population – excludes patients with a serious infection within 6 months prior to index date



COR_US Figure 9. Kaplan-Meier Curve of Time-to-First Serious Infection [CorEvitas US], Serious Infection-matched Population – excludes patients with a serious infection within 6 months prior to index date



COR_US Figure 10. Adjusted Survival Curve of Time-to-First Serious Infection [CorEvitas US], Serious Infection-matched Population – excludes patients with a serious infection within 6 months prior to index date



COR_US Table 6.62. Pattern of RA Medication Use in Patients with Hospitalized TB Event [CorEvitas US]– excludes patients with a hospitalized TB within 6 months prior to index date.

Not applicable in CorEvitas data.

COR_US Table 6.63. Time to First Hospitalized TB Event (Month*) [CorEvitas US] – excludes patients with a hospitalized TB within 6 months prior to index date.

The table has been omitted as there are no TB events.

COR_US Table 6.64. Incidence Rates of First Hospitalized TB Event [CorEvitas US] – excludes patients with a hospitalized TB within 6 months prior to index date.

	Pre-matched		Matched		
	Baricitinib (N= 118)	**TNFi (N=1,897)**	**Baricitinib (N= 117)**	**TNFi (N= 343)**	**Total (N= 460)**
Overall					
N	118	1,897	117	343	460
TB Events	0	0	0	0	0
Person-Years	79.5	1453.0	79.3	249.8	329.1
TB Events/100 PY	0.0	0.0	0.0	0.0	0.0
95% CI	0.0, 4.6	0.0, 0.3	0.0, 4.7	0.0, 1.5	0.0, 1.1
Incidence rate difference: baricitinib-TNFi (95% CI)					0.0 (0.0, 0.0)

Abbreviations: CI = confidence interval; PY = person-years; TB = [hospitalized] tuberculosis; TNFi = tumor necrosis factor.

COR_US Table 6.65. Hospitalized TB Events per Patient During Baricitinib and TNF Exposure * [CorEvitas US] – excludes patients with a hospitalized TB within 6 months prior to index date.

Not applicable in CorEvitas data.

COR_US Figure 11. Kaplan-Meier Curve of Time-to-First Hospitalized TB Event [CorEvitas US], pre-matched Hospitalized TB Population – excludes patients with a hospitalized TB within 6 months prior to index date

Not applicable for CorEvitas data because there were not hospitalized TB events observed.

COR_US Figure 12. Kaplan-Meier Curve of Time-to-First Hospitalized TB Event [CorEvitas US], Hospitalized TB-matched Population – excludes patients with a hospitalized TB within 6 months prior to index date

Not applicable for CorEvitas data because there were not hospitalized TB events observed.

COR_US Figure 13. Adjusted Survival Curve of Time-to-First Hospitalized TB Event [CorEvitas US], Hospitalized TB-matched Population – excludes patients with a hospitalized TB within 6 months prior to index date

Not applicable for CorEvitas data.

COR_US Table 6.67. Incidence Rates of VTE Prior to Cohort Entry [CorEvitas US], VTE-matched* Population – does not exclude patients with prior VTE within 6 months prior to index date or patients on anticoagulant.

Treatment Group	Patients (N)	Events (n)/PY	Incidence Rate (per 100 PY)	95% CI	Incidence rate difference: baricitinib – TNFi (95% CI)
3 months prior[a]					
baricitinib	n/a	n/a	n/a	n/a	
TNFi	n/a	n/a	n/a	n/a	
6 months prior[b]					
baricitinib	n/a	n/a	n/a	n/a	
TNFi	n/a	n/a	n/a	n/a	
12 months prior					
baricitinib	117	0/117.0	0.0	0.0, 3.2	-0.3 (-0.9, 0.3)
TNFi	326	1/325.2	0.3	0.0, 1.7	

* Matched population is matched using a propensity score population that excludes the variable indicating history of VTE
Abbreviations: CI = confidence interval; PY = person-years; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.
[a] Due to small event counts, incidence rates of VTE in the 3 months prior to cohort entry will not be performed
[b] Due to small event counts, incidence rates of VTE in the 6 months prior to cohort entry will not be performed

COR_US Table 6.68. Incidence Rates of VTE, by Dose. Pre-matched VTE population [CorEvitas US]

Not applicable in CorEvitas RA US data.

COR_US Table 6.69. Incidence Rates of VTE, by Dose. Pre-matched VTE population [CorEvitas US]

Not applicable in CorEvitas RA US data.

COR_US Table 6.70. bDMARD-Experienced: Baseline Demographics, Pre-matched Population [CorEvitas US]

Not applicable in CorEvitas RA US data.

COR_US Table 6.71. bDMARD-Naïve: Baseline Demographics, Pre-matched Population [CorEvitas US]

Not applicable in CorEvitas RA US data.

COR_US Table 6.72. bDMARD-Experienced: Baseline Demographics, VTE-matched Population [CorEvitas US] – also excludes patients with VTE within 6 months of index date or currently taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.73. bDMARD-Naïve: Baseline Demographics, VTE-matched Population [CorEvitas US] – also excludes patients with VTE within 6 months of index date or currently taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.74. bDMARD-Experienced: Baseline Demographics, MACE-matched Population [CorEvitas US] – also excludes patients with MACE within 6 months of index date or currently taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.75. bDMARD-Naïve: Baseline Demographics, MACE-matched Population [CorEvitas US] – also excludes patients with VTE within 6 months of index date or currently taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.76. bDMARD-Experienced: Baseline Demographics, Serious infection-matched Population [CorEvitas US] – also excludes patients with Serious infection within 6 months of index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.77. bDMARD-Naïve: Baseline Demographics, Serious infection-matched Population [CorEvitas US] – also excludes patients with Serious infection within 6 months of index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.78. bDMARD-Experienced: Baseline Demographics, Hospitalized Tuberculosis-matched Population [CorEvitas US] – also excludes patients with Hospitalized Tuberculosis within 6 months of index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.79. bDMARD-Naïve: Baseline Demographics, Hospitalized Tuberculosis-matched Population [CorEvitas US] – also excludes patients with Hospitalized Tuberculosis within 6 months of index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.80. bDMARD-Experienced: Clinical history at baseline, Pre-matched Population [CorEvitas US]

Not applicable in CorEvitas RA US data.

COR_US Table 6.81. bDMARD-Naïve: Clinical history at baseline, Pre-matched Population [CorEvitas US]

Not applicable in CorEvitas RA US data.

COR_US Table 6.82. bDMARD-Experienced: Baseline Clinical Characteristics, VTE-matched Population [CorEvitas US] – also excludes patients with VTE within 6 months prior to index date or currently taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.83. bDMARD-Naïve: Baseline Clinical Characteristics, VTE-matched Population [CorEvitas US] – also excludes patients with VTE within 6 months prior to index date or currently taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.84. bDMARD-Experienced: Baseline Clinical Characteristics, MACE-matched Population [CorEvitas US] – also excludes patients with MACE within 6 months prior to index date or currently taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.85. bDMARD-Naïve: Baseline Clinical Characteristics, MACE-matched Population [CorEvitas US] – also excludes patients with MACE within 6 months prior to index date or currently taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.86. bDMARD-Experienced: Baseline Clinical Characteristics, Serious infection-matched Population [CorEvitas US] – also excludes patients with Serious infection within 6 months of index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.87. bDMARD-Naïve: Baseline Clinical Characteristics, Serious infection-matched Population [CorEvitas US] – also excludes patients with Serious infection within 6 months of index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.88. bDMARD-Experienced: Baseline Clinical Characteristics, Hospitalized Tuberculosis-matched Population [CorEvitas US] – also excludes patients with Hospitalized Tuberculosis within 6 months of index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.89. bDMARD-Naïve: Baseline Clinical Characteristics, Hospitalized Tuberculosis-matched Population [CorEvitas US] – also excludes patients with Hospitalized Tuberculosis within 6 months of index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.90. bDMARD-Experienced: Baseline Healthcare Resource Utilization, Pre-matched Population [CorEvitas US]

Not applicable in CorEvitas RA US data.

COR_US Table 6.91. bDMARD-Naïve: Baseline Healthcare Resource Utilization, Pre-matched Population [CorEvitas US]

Not applicable in CorEvitas RA US data.

COR_US Table 6.92. bDMARD-Experienced: Baseline Healthcare Resource Utilization, VTE-matched Population [CorEvitas US] – also excludes patients with VTE within 6 months prior to index date or currently taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.93. bDMARD-Naïve: Baseline Healthcare Resource Utilization, VTE-matched Population [CorEvitas US] – also excludes patients with VTE within 6 months prior to index date or currently taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.94. bDMARD-Experienced: Baseline Healthcare Resource Utilization, MACE-matched Population [CorEvitas US] – also excludes patients with MACE within 6 months prior to index date or currently taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.95. bDMARD-Naïve: Baseline Healthcare Resource Utilization, MACE-matched Population [CorEvitas US] – also excludes patients with MACE within 6 months prior to index date or currently taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.96. bDMARD-Experienced: Baseline Healthcare Resource Utilization, Serious infection-matched Population [CorEvitas US] – also excludes patients with Serious infection within 6 months of index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.97. bDMARD-Naïve: Baseline Healthcare Resource Utilization, Serious infection-matched Population [CorEvitas US] – also excludes patients with Serious infection within 6 months of index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.98. bDMARD-Experienced: Baseline Healthcare Resource Utilization, Hospitalized Tuberculosis-matched Population [CorEvitas US] – also excludes patients with Hospitalized Tuberculosis within 6 months of index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.99. bDMARD-Naïve: Baseline Healthcare Resource Utilization, Hospitalized Tuberculosis-matched Population [CorEvitas US] – also excludes patients with Hospitalized Tuberculosis within 6 months of index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.100. bDMARD-Experienced: Baseline Prevalence of Outcomes [CorEvitas US]

Not applicable in CorEvitas RA US data.

COR_US Table 6.101. bDMARD-Naïve: Baseline Prevalence of Outcomes [CorEvitas US]

Not applicable in CorEvitas RA US data.

COR_US Table 6.102. bDMARD-Experienced: Duration of Exposure (Days) in Pre-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit

Not applicable in CorEvitas RA US data.

COR_US Table 6.103. bDMARD-Naïve: Duration of Exposure (Days) in Pre-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit

Not applicable in CorEvitas RA US data.

COR_US Table 6.104. bDMARD-Experienced: Duration of Exposure (Days), VTE-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit, excludes patients with VTE within 6 months prior to index date or currently taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.105. bDMARD-Naïve: Duration of Exposure (Days), VTE-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit, excludes patients with VTE within 6 months prior to index date or currently taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.106. bDMARD-Experienced: Duration of Exposure (Days), MACE-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit, excludes patients with MACE within 6 months prior to index date or taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.107. bDMARD-Naïve: Duration of Exposure (Days), MACE-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit, excludes patients with MACE within 6 months prior to index date or taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.108. bDMARD-Experienced: Duration of Exposure (Days), Serious infection-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit, excludes patients with serious infection within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.109. bDMARD-Naïve: Duration of Exposure (Days), Serious infection-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit, excludes patients with serious infection within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.110. bDMARD-Experienced: Duration of Exposure (Days), Hospitalized Tuberculosis-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit, excludes patients with hospitalized TB within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.111. bDMARD-Naïve: Duration of Exposure (Days), Hospitalized Tuberculosis-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit, excludes patients with hospitalized TB within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.112. bDMARD-Experienced: Baseline Clinical Characteristics by Exposure Duration in Pre-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit

Not applicable in CorEvitas RA US data.

COR_US Table 6.113. bDMARD-Naïve: Baseline Clinical Characteristics by Exposure Duration in Pre-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit

Not applicable in CorEvitas RA US data.

COR_US Table 6.114. bDMARD-Experienced: Baseline Clinical Characteristics by Exposure Duration, VTE-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit/VTE event; excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.115. bDMARD-Naïve: Baseline Clinical Characteristics by Exposure Duration, VTE-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit/VTE event; excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.116. bDMARD-Experienced: Baseline Clinical Characteristics by Exposure Duration, MACE-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit/MACE; excludes patients with a MACE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.117. bDMARD-Naïve: Baseline Clinical Characteristics by Exposure Duration, MACE-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit/MACE; excludes patients with a MACE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.118. bDMARD-Experienced: Baseline Clinical Characteristics by Exposure Duration, Serious infection-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit/serious infection event; excludes patients with a serious infection within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.119. bDMARD-Naïve: Baseline Clinical Characteristics by Exposure Duration, Serious infection-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit/serious infection event; excludes patients with a serious infection within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.120. bDMARD-Experienced: Baseline Clinical Characteristics by Exposure Duration, Hospitalized Tuberculosis-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit/TB event; excludes patients with a hospitalized TB within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.121. bDMARD-Naïve: Baseline Clinical Characteristics by Exposure Duration, Hospitalized Tuberculosis-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit/TB event; excludes patients with a hospitalized TB within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.122. bDMARD-Experienced: Baseline Healthcare Resource Utilization by Exposure Duration in Pre-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit

Not applicable in CorEvitas RA US data.

COR_US Table 6.123. bDMARD-Naïve: Baseline Healthcare Resource Utilization by Exposure Duration in Pre-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit

Not applicable in CorEvitas RA US data.

COR_US Table 6.124. bDMARD-Experienced: Baseline Healthcare Resource Utilization by Exposure Duration, VTE-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit/VTE event; excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.125. bDMARD-Naïve: Baseline Healthcare Resource Utilization by Exposure Duration, VTE-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit/VTE event; excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.126. bDMARD-Experienced: Baseline Healthcare Resource Utilization by Exposure Duration, MACE-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit/MACE event; excludes patients with a MACE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.127. bDMARD-Naïve: Baseline Healthcare Resource Utilization by Exposure Duration, MACE-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit/MACE event; excludes patients with a MACE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.128. bDMARD-Experienced: Baseline Healthcare Resource Utilization by Exposure Duration, Serious infection-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit/serious infection event; excludes patients with a serious infection within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.129. bDMARD-Naïve: Baseline Healthcare Resource Utilization by Exposure Duration, Serious infection-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit/serious infection event; excludes patients with a serious infection within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.130. bDMARD-Experienced: Baseline Healthcare Resource Utilization by Exposure Duration, Hospitalized Tuberculosis-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit/TB event; excludes patients with a hospitalized TB within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.131. bDMARD-Naïve: Baseline Healthcare Resource Utilization by Exposure Duration, Hospitalized Tuberculosis-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit/TB event; excludes patients with a hospitalized TB within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.132. bDMARD-Experienced: Baseline Clinical Characteristics of Patients with VTE, VTE-matched Population [CorEvitas US] – excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.133. bDMARD-Naïve: Baseline Clinical Characteristics of Patients with VTE, VTE-matched Population [CorEvitas US] – excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.134. bDMARD-Experienced: Pattern of RA Medication Use in Patients with VTE [CorEvitas US] – excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.135. bDMARD-Naïve: Pattern of RA Medication Use in Patients with VTE [CorEvitas US] – excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.136. bDMARD-Experienced: Time to First VTE Event (Days) [CorEvitas US] – excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.137. bDMARD-Naïve: Time to First VTE Event (Days) [CorEvitas US] – excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.138. bDMARD-Experienced: Incidence Rates of First VTE Event [CorEvitas US] – excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.139. bDMARD-Naïve: Incidence Rates of First VTE Event [CorEvitas US] – excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.140. bDMARD-Experienced: Comparative Risk of Incident VTE, Primary Definition [CorEvitas US], VTE-matched population – excludes patients with prior VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.141. bDMARD-Naïve: Comparative Risk of Incident VTE, Primary Definition [CorEvitas US], VTE-matched population – excludes patients with prior VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.142. bDMARD-Experienced: Baseline Clinical Characteristics of Patients with MACE, MACE-matched Population [CorEvitas US] – excludes patients with a MACE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.143. bDMARD-Naïve: Baseline Clinical Characteristics of Patients with MACE, MACE-matched Population [CorEvitas US] – excludes patients with a MACE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.144. bDMARD-Experienced: Pattern of RA Medication Use in Patients with MACE [CorEvitas US] – excludes patients with a MACE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.145. bDMARD-Naïve: Pattern of RA Medication Use in Patients with MACE [CorEvitas US] – excludes patients with a MACE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.146. bDMARD-Experienced: Time to First MACE (Days) [CorEvitas US] – excludes patients with a MACE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.147. bDMARD-Naïve: Time to First MACE (Days) [CorEvitas US] – excludes patients with a MACE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.148. bDMARD-Experienced: Incidence Rates of First MACE [CorEvitas US] – excludes patients with a MACE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.149. bDMARD-Naïve: Incidence Rates of First MACE [CorEvitas US] – excludes patients with a MACE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.150. bDMARD-Experienced: Comparative Risk of Incident MACE, Primary Definition [CorEvitas US], MACE-matched population – excludes patients with prior MACE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.151. bDMARD-Naïve: Comparative Risk of Incident MACE, Primary Definition [CorEvitas US], MACE-matched population – excludes patients with prior MACE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.152. bDMARD-Experienced: Baseline Clinical Characteristics of Patients with Serious Infection, Serious Infection-matched Population [CorEvitas US] – excludes patients with a serious infection within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.153. bDMARD-Naïve: Baseline Clinical Characteristics of Patients with Serious Infection, Serious Infection-matched Population [CorEvitas US] – excludes patients with a serious infection within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.154. bDMARD-Experienced: Pattern of RA Medication Use in Patients with Serious Infection [CorEvitas US] – excludes patients with a Serious Infection within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.155. bDMARD-Naïve: Pattern of RA Medication Use in Patients with Serious Infection [CorEvitas US] – excludes patients with a Serious Infection within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.156. bDMARD-Experienced: Time to First Serious Infection Event (Days) [CorEvitas US] – excludes patients with a Serious Infection within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.157. bDMARD-Naïve: Time to First Serious Infection Event (Days) [CorEvitas US] – excludes patients with a Serious Infection within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.158. bDMARD-Experienced: Incidence Rates of First Serious Infection Event [CorEvitas US] – excludes patients with a Serious Infection within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.159. bDMARD-Naïve: Incidence Rates of First Serious Infection Event [CorEvitas US] – excludes patients with a Serious Infection within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.160. bDMARD-Experienced: Serious Infection Events Per Patient During Baricitinib and TNF Exposure* [CorEvitas US] – excludes patients with a serious infection within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.161. bDMARD-Naïve: Serious Infection Events Per Patient During Baricitinib and TNF Exposure* [CorEvitas US] – excludes patients with a serious infection within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.162. bDMARD-Experienced: Comparative Risk of Incident Serious Infection [CorEvitas US], Serious Infection-matched population – excludes patients with prior serious infection within 6 months prior to index.

Not applicable in CorEvitas RA US data.

COR_US Table 6.163. bDMARD-Naïve: Comparative Risk of Incident Serious Infection [CorEvitas US], Serious Infection-matched population – excludes patients with prior serious infection within 6 months prior to index.

Not applicable in CorEvitas RA US data.

COR_US Table 6.164. bDMARD-Experienced: Incidence Rates of First Hospitalized TB Event [CorEvitas US] – excludes patients with a hospitalized TB within 6 months prior to index date.

Not applicable in CorEvitas RA US data.

COR_US Table 6.165. Class Effect: Baseline Demographics, Pre-matched Population [CorEvitas US].

Not applicable in CorEvitas RA US data.

COR_US Table 6.166. Class Effect: Baseline Demographics, VTE-matched Population [CorEvitas US] – also excludes patients with VTE within 6 months prior to index date or currently taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.167. Class Effect: Clinical history at baseline, Pre-matched Population [CorEvitas US].

Not applicable in CorEvitas RA US data.

COR_US Table 6.168. Class Effect: Clinical history at baseline, VTE-matched Population [CorEvitas US] – also excludes patients with VTE within 6 months prior to index date or currently taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.169. Class Effect: Baseline Healthcare Resource Utilization, Unmatched [CorEvitas US].

Not applicable in CorEvitas RA US data.

COR_US Table 6.170. Class Effect: Baseline Healthcare Resource Utilization, Primary VTE Cohorts, Matched [CorEvitas US].

Not applicable in CorEvitas RA US data.

COR_US Table 6.171. Class Effect: Baseline Prevalence of Outcomes [CorEvitas US].

Not applicable in CorEvitas RA US data.

COR_US Table 6.172. Class Effect: Duration of Exposure (Months*) in Pre-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit.

Not applicable in CorEvitas RA US data.

COR_US Table 6.173. Class Effect: Duration of Exposure (Months*) in VTE-matched Population [CorEvitas US] – exposure ends at discontinuation/last follow-up visit, excludes patients with VTE within 6 months prior to index date or currently taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.174. Class Effect: Baseline Clinical Characteristics by Exposure Duration, Pre-matched Population [CorEvitas US] - exposure ends at discontinuation/last follow-up visit.

Not applicable in CorEvitas RA US data.

COR_US Table 6.175. Class Effect: Baseline Clinical Characteristics by Exposure Duration, VTE-matched Population [CorEvitas US] - exposure ends at discontinuation/last follow-up visit/VTE event; excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.176. Class Effect: Baseline Healthcare Resource Utilization by Exposure Duration, pre-matched.

Not applicable in CorEvitas RA US data.

COR_US Table 6.177. Class Effect: Baseline Healthcare Resource Utilization by Exposure Duration Primary VTE Cohorts, Matched.

Not applicable in CorEvitas RA US data.

COR_US Table 6.178. Class Effect: Baseline Clinical Characteristics of Patients with VTE, VTE-matched Population [CorEvitas US] – excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.179. Class Effect: Pattern of RA Medication Use in Patients with VTE [CorEvitas US] – excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.180. Class Effect: Time to First VTE Event (Months*) [CorEvitas US].

Not applicable in CorEvitas RA US data.

COR_US Table 6.181. Class Effect: Incidence Rates of First VTE Event [CorEvitas US].

Not applicable in CorEvitas RA US data.

COR_US Table 6.182. Class Effect: Comparative Risk of Incident VTE, Primary Definition [CorEvitas US], VTE-matched population – excludes patients with prior VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.183. Any Prior JAKi: Baseline Demographics, Pre-matched Population [CorEvitas US]

	Baricitinib (N=181)	TNFi (N=2015)	Std. Diff.
Age [yrs]			
n	181	2015	0.104
Mean±SD	60.2 ±11.4	58.9 ±13.0	
Median	61.0	60.0	
Min, Max	27.0, 87.0	18.0, 90.0	
≥ 65 years	66 (36.5%)	746 (37.0%)	0.012
Gender			
Male	42 (23.2%)	413 (20.5%)	0.066
Female	139 (76.8%)	1602 (79.5%)	
BMI			
n	176	1975	0.049
Mean±SD	30.2 ± 7.4	30.5 ± 7.4	
Median	28.9	29.5	
Min, Max	16.1, 50.9	15.2, 64.0	
Smoking (current or former)	100 (55.9%)	935 (47.0%)	0.178
Alcohol use	64 (35.4%)	932 (46.3%)	0.225
Education			
College/university	91 (52.9%)	1195 (62.1%)	0.188

Abbreviations: Min = minimum; Max = maximum; SD = standard deviation; Std. Diff = standardized difference; TNFi = tumor necrosis factor inhibitor; JAKi = janus kinase inhibitor.

COR_US Table 6.184. Any Prior JAKi: Baseline Demographics, VTE-matched Population [CorEvitas US]– also excludes patients with VTE within 6 months of index date or currently taking anticoagulant

	Baricitinib (N=167)	TNFi (N=457)	Std. Diff.
Age [yrs]			
n	167	457	0.003
Mean±SD	59.5 ±11.2	59.5 ±12.8	
Median	60.0	61.0	
Min, Max	27.0, 86.0	22.0, 87.0	
≥ 65 years	58 (34.7%)	177 (38.7%)	0.083
Gender			
Male	35 (21.0%)	95 (20.8%)	0.004
Female	132 (79.0%)	362 (79.2%)	
BMI			
n	163	450	0.001
Mean±SD	30.3 ± 7.4	30.3 ± 7.1	
Median	29.0	29.2	
Min, Max	16.1, 50.9	16.3, 58.2	
Smoking (current or former)	89 (53.3%)	230 (50.3%)	0.059
Alcohol use	59 (35.3%)	207 (45.4%)	0.206
Education			
College/university	83 (51.9%)	292 (66.4%)	0.298

Abbreviations: Min = minimum; Max = maximum; SD = standard deviation; Std. Diff = standardized difference; TNFi = tumor necrosis factor inhibitor; JAKi = janus kinase inhibitor.

COR_US Table 6.185. Any Prior JAKi: Clinical history at baseline, Pre-matched Population [CorEvitas US]

	Baricitinib (N=181)	TNFi (N=2015)	Std. Diff.
History of MD-reported comorbidities (ever experienced)			
Cancer, Non-NMSC	10 (5.5%)	145 (7.2%)	0.069
Cancer, NMSC only	20 (11.0%)	115 (5.7%)	0.194
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	22 (12.2%)	206 (10.2%)	0.061
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	8 (4.4%)	62 (3.1%)	0.071
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	16 (8.8%)	129 (6.4%)	0.092
Cardiovascular revascularization	4 (2.2%)	48 (2.4%)	0.011
Congestive heart failure (hospitalized & non-hospitalized)	5 (2.8%)	25 (1.2%)	0.109
Coronary artery disease	9 (5.0%)	73 (3.6%)	0.067
Ischemic heart disease	11 (6.1%)	97 (4.8%)	0.056
TIA	2 (1.1%)	23 (1.1%)	0.003
Unstable angina	1 (0.6%)	11 (0.5%)	0.001
Ventricular arrhythmia	1 (0.6%)	12 (0.6%)	0.006
Diabetes mellitus	18 (9.9%)	230 (11.4%)	0.048
Hyperlipidemia	43 (23.8%)	351 (17.4%)	0.157
Hypertension (hospitalized & non-hospitalized)	73 (40.3%)	708 (35.1%)	0.107
Immune disorders	54 (29.8%)	374 (18.8%)	0.259
Secondary Sjogren Syndrome	54 (29.8%)	374 (18.8%)	0.259
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	13 (7.2%)	57 (2.8%)	0.201
Obesity, current	69 (39.2%)	930 (47.1%)	0.160
Pregnancy, recent (current or since last visit)	0 (0.0%)	11 (0.6%)	0.108
Smoking (current or former)	100 (55.9%)	935 (47.0%)	0.178
RA severity (CDAI)			
n	181	2015	0.167
Mean±SD	18.9 ±11.6	16.8 ±13.0	
Median	16.6	14.0	

	Baricitinib (N=181)	TNFi (N=2015)	Std. Diff.
25th percentile, 75th percentile	10.5, 25.4	6.5, 24.0	
Min, Max	0.8, 51.2	0.0, 72.5	
Prevalent outcomes			
VTE (at any time in the past)	8 (4.4%)	35 (1.7%)	0.156
MACE (at any time in the past)	9 (5.0%)	66 (3.3%)	0.085
Myocardial infarction	5 (2.8%)	33 (1.6%)	0.077
Stroke	4 (2.2%)	35 (1.7%)	0.034
Serious infection (at any time in the past)	23 (12.7%)	191 (9.5%)	0.103
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)	
DMARD history			
Number of cDMARDs used (ever)			
0	3 (1.7%)	81 (4.0%)	0.143
1	53 (29.3%)	887 (44.0%)	0.310
2+	125 (69.1%)	1047 (52.0%)	0.355
Methotrexate (prior use)	170 (93.9%)	1753 (87.0%)	0.237
Number of bDMARDs used (ever)			
0	17 (9.4%)	940 (46.7%)	0.912
1	27 (14.9%)	585 (29.0%)	0.346
2+	137 (75.7%)	490 (24.3%)	1.198
Prior bDMARD use[a]	164 (90.6%)	1075 (53.3%)	0.912
Prior TNFi bDMARD use	160 (88.4%)	983 (48.8%)	0.944
Prior non-TNFi bDMARD use	112 (61.9%)	447 (22.2%)	0.878
DMARD, current (baseline)			
cDMARD, concomitant use at baseline	105 (58.0%)	1408 (69.9%)	0.249
Methotrexate, concomitant use at baseline	76 (42.0%)	1017 (50.5%)	0.171
Prescription medication use, current (baseline)			
Other prescription medications			
Cardiovascular medications			
Anticoagulant (coumadin/warfarin; patient-reported)	6 (3.3%)	30 (1.5%)	0.119
Antihypertensives (blood pressure lowering medication(s); patient-reported)	87 (48.1%)	813 (40.3%)	0.156
Antiplatelet (Plavix; patient-reported)	3 (1.7%)	43 (2.1%)	0.035
Nitrates (angina/nitrate medications; patient-reported)	2 (1.1%)	16 (0.8%)	0.032
Hormonal Medication HRT (in RA US only)	3 (1.7%)	18 (0.9%)	0.068

	Baricitinib (N=181)	TNFi (N=2015)	Std. Diff.
Lipid-lowering agents (cholesterol medication; patient-reported)	40 (22.1%)	416 (20.6%)	0.035
RA-related			
Aspirin (includes non-prescription)	32 (17.7%)	265 (13.2%)	0.126
Celebrex (in RA US only)	17 (9.4%)	116 (5.8%)	0.138
Prednisone	69 (38.1%)	558 (27.7%)	0.223
Vaccinations			
Influenza (baseline) (in RA US only)	61 (40.4%)	742 (41.3%)	0.018
Pneumonia (ever) (in RA US only)	38 (23.9%)	471 (25.4%)	0.034
Shingles (ever)	34 (20.7%)	405 (21.2%)	0.011

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; CDAI = clinical disease activity index; cDMARD = classical disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event (MI (myocardial infarction) and stroke); Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism; SD = standard deviation; Std Diff = absolute value of the standardized difference; JAKi = janus kinase inhibitor.

a. Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

COR_US Table 6.186. Any Prior JAKi: Clinical history at baseline, VTE-matched Population [CorEvitas US]– also excludes patients with VTE within 6 months prior to index date or currently taking anticoagulant.

	Baricitinib (N=167)	TNFi (N=457)	Std. Diff.
History of MD-reported comorbidities (ever experienced)			
Cancer, Non-NMSC	9 (5.4%)	24 (5.3%)	0.006
Cancer, NMSC only	13 (7.8%)	37 (8.1%)	0.012
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	19 (11.4%)	41 (9.0%)	0.080
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	6 (3.6%)	17 (3.7%)	0.007
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	14 (8.4%)	40 (8.8%)	0.013
Cardiovascular revascularization	4 (2.4%)	17 (3.7%)	0.077
Congestive heart failure (hospitalized & non-hospitalized)	3 (1.8%)	10 (2.2%)	0.028
Coronary artery disease	7 (4.2%)	23 (5.0%)	0.040
Ischemic heart disease	9 (5.4%)	27 (5.9%)	0.022
TIA	2 (1.2%)	5 (1.1%)	0.010
Unstable angina	1 (0.6%)	5 (1.1%)	0.054
Ventricular arrhythmia	1 (0.6%)	5 (1.1%)	0.054
Diabetes mellitus	17 (10.2%)	55 (12.0%)	0.059
Hyperlipidemia	38 (22.8%)	74 (16.2%)	0.166
Hypertension (hospitalized & non-hospitalized)	66 (39.5%)	162 (35.4%)	0.084
Immune disorders	49 (29.3%)	127 (27.8%)	0.034
Secondary Sjogren Syndrome	49 (29.3%)	127 (27.8%)	0.034
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	8 (4.8%)	19 (4.2%)	0.031
Obesity, current	66 (40.5%)	198 (44.0%)	0.071
Pregnancy, recent (current or since last visit)	0 (0.0%)	3 (0.7%)	0.119
Smoking (current or former)	89 (53.3%)	230 (50.3%)	0.059
RA severity (CDAI)			
n	167	457	0.077
Mean±SD	18.9 ±11.6	17.9 ±13.8	
Median	16.6	15.0	
25^{th} percentile, 75^{th} percentile	9.9, 25.5	6.5, 26.5	

	Baricitinib (N=167)	TNFi (N=457)	Std. Diff.
Min, Max	0.8, 51.2	0.0, 66.0	
Prevalent outcomes			
VTE (at any time in the past)	5 (3.0%)	9 (2.0%)	0.066
MACE (at any time in the past)	6 (3.6%)	15 (3.3%)	0.017
Myocardial infarction	4 (2.4%)	4 (0.9%)	0.120
Stroke	2 (1.2%)	11 (2.4%)	0.091
Serious infection (at any time in the past)	21 (12.6%)	56 (12.3%)	0.010
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)	
DMARD history			
Number of cDMARDs used (ever)			
0	3 (1.8%)	17 (3.7%)	0.118
1	50 (29.9%)	158 (34.6%)	0.099
2+	114 (68.3%)	282 (61.7%)	0.138
Methotrexate (prior use)	156 (93.4%)	396 (86.7%)	0.227
Number of bDMARDs used (ever)			
0	17 (10.2%)	51 (11.2%)	0.032
1	26 (15.6%)	74 (16.2%)	0.017
2+	124 (74.3%)	332 (72.6%)	0.036
Prior bDMARD use[a]	150 (89.8%)	406 (88.8%)	0.032
Prior TNFi bDMARD use	146 (87.4%)	379 (82.9%)	0.127
Prior non-TNFi bDMARD use	103 (61.7%)	268 (58.6%)	0.062
DMARD, current (baseline)			
cDMARD, concomitant use at baseline	97 (58.1%)	287 (62.8%)	0.097
Methotrexate, concomitant use at baseline	70 (41.9%)	188 (41.1%)	0.016
Prescription medication use, current (baseline)			
Other prescription medications			
Cardiovascular medications			
Anticoagulant (coumadin/warfarin; patient-reported)	0 (0.0%)	0 (0.0%)	
Antihypertensives (blood pressure lowering medication(s); patient-reported)	81 (48.5%)	191 (41.8%)	0.135
Antiplatelet (Plavix; patient-reported)	2 (1.2%)	14 (3.1%)	0.129
Nitrates (angina/nitrate medications; patient-reported)	2 (1.2%)	7 (1.5%)	0.029
Hormonal Medication HRT (in RA US only)	2 (1.2%)	5 (1.1%)	0.010
Lipid-lowering agents (cholesterol medication; patient-reported)	34 (20.4%)	97 (21.2%)	0.021

	Baricitinib (N=167)	TNFi (N=457)	Std. Diff.
RA-related			
Aspirin (includes non-prescription)	28 (16.8%)	73 (16.0%)	0.021
Celebrex (in RA US only)	15 (9.0%)	37 (8.1%)	0.032
Prednisone	62 (37.1%)	161 (35.2%)	0.039
Vaccinations			
Influenza (baseline) (in RA US only)	57 (41.0%)	160 (39.6%)	0.029
Pneumonia (ever) (in RA US only)	35 (24.0%)	115 (27.2%)	0.074
Shingles (ever)	31 (20.4%)	97 (22.2%)	0.045

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; CDAI = clinical disease activity index; cDMARD = classical disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event (MI (myocardial infarction) and stroke); Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism; SD = standard deviation; Std Diff = absolute value of the standardized difference; JAKi = janus kinase inhibitor.

Note: Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 66 for each outcome, e.g., congestive heart failure for VTE. Other factors are included for descriptive purposes only and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., diabetes for VTE.

a. Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

COR_US Table 6.187. Any Prior JAKi Use: Clinical history at baseline, MACE-matched Population [CorEvitas US] – also excludes patients with MACE within 6 months prior to index date or currently taking anticoagulant.

Not applicable in CorEvitas RA US data.

COR_US Table 6.188. Any Prior JAKi Use: Baseline Healthcare Resource Utilization, Unmatched [CorEvitas US]

Not applicable in CorEvitas RA US data.

COR_US Table 6.189. Any Prior JAKi Use: Baseline Healthcare Resource Utilization, Primary VTE Cohorts, Matched [CorEvitas US]

Not applicable in CorEvitas RA US data.

COR_US Table 6.190. Any Prior JAKi: Duration of Exposure (Months*), in Pre-matched Population [CorEvitas US] exposure ends at discontinuation/last follow-up visit.

	Baricitinib (N=181)	TNFi (N=2015)	Std. Diff.
N	181	2015	
Mean±SD	8.1 ± 6.2	9.1 ± 6.3	0.165
Median	6.0	7.0	
Min, Max	1.0, 27.0	1.0, 30.0	

* CorEvitas' RA US Registry collects drug information at the month-level so time is reported in months. A rough conversion to days can be made by multiplying the values in this table by a factor of 30.4375 (the average number of days in a month)
Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std Diff = absolute value of standardized difference; TNFi = tumor necrosis factor inhibitor; JAKi = janus kinase inhibitor.

COR_US Table 6.191. Any Prior JAKi: Duration of Exposure (Months*), in VTE-matched Population [CorEvitas US] exposure ends at discontinuation/last follow-up visit.

	Baricitinib (N=167)	TNFi (N=457)	Std. Diff.
N	167	457	
Mean±SD	8.0 ± 6.1	8.7 ± 6.0	0.125
Median	6.0	7.0	
Min, Max	1.0, 27.0	1.0, 25.0	

* CorEvitas' RA US Registry collects drug information at the month-level so time is reported in months. A rough conversion to days can be made by multiplying the values in this table by a factor of 30.4375 (the average number of days in a month)
Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std Diff = absolute value of standardized difference; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism; JAKi = janus kinase inhibitor.

COR_US Table 6.192. Any Prior JAKi Use: Baseline Clinical Characteristics by Exposure Duration, Pre-matched Population [CorEvitas US] - exposure ends at discontinuation/last follow-up visit.

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 80)	TNFi (N= 738)	Std. Diff.	Baricitinib (N= 57)	TNFi (N= 652)	Std. Diff.	Baricitinib (N= 39)	TNFi (N= 564)	Std. Diff.	Baricitinib (N= 5)	TNFi (N= 61)	Std. Diff.
Age [yrs]												
n	80	738	0.06	57	652	0.10	39	564	0.56	5	61	0.32
Mean±SD	59.3 ± 11.4	58.6 ± 13.4		57.1 ± 11.6	58.4 ± 13.3		65.6 ± 9.5	59.5 ± 12.2		65.4 ± 11.1	62.0 ± 9.7	
Median	61.0	60.0		58.0	59.0		66.0	61.0		59.0	62.0	
Min, Max	27.0, 79.0	19.0, 90.0		31.0, 86.0	18.0, 90.0		40.0, 87.0	20.0, 87.0		56.0, 78.0	37.0, 82.0	
≥ 65 years	27 (33.8%)	260 (35.2%)	0.03	14 (24.6%)	233 (35.7%)	0.25	23 (59.0%)	227 (40.2%)	0.38	2 (40.0%)	26 (42.6%)	0.05
Gender												
Male	17 (21.3%)	147 (19.9%)	0.03	10 (17.5%)	130 (19.9%)	0.06	10 (25.6%)	122 (21.6%)	0.09	5 (100.0%)	14 (23.0%)	2.59
Female	63 (78.8%)	591 (80.1%)		47 (82.5%)	522 (80.1%)		29 (74.4%)	442 (78.4%)		0 (0.0%)	47 (77.0%)	
History of MD-reported comorbidities (ever experienced)												
Cancer, Non-NMSC	5 (6.3%)	49 (6.6%)	0.02	3 (5.3%)	41 (6.3%)	0.04	2 (5.1%)	48 (8.5%)	0.13	0 (0.0%)	7 (11.5%)	0.51
Cancer, NMSC only	7 (8.8%)	40 (5.4%)	0.13	5 (8.8%)	42 (6.4%)	0.09	7 (17.9%)	31 (5.5%)	0.39	1 (20.0%)	2 (3.3%)	0.54
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	7 (8.8%)	60 (8.1%)	0.02	12 (21.1%)	80 (12.3%)	0.24	3 (7.7%)	62 (11.0%)	0.11	0 (0.0%)	4 (6.6%)	0.37
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	4 (5.0%)	22 (3.0%)	0.10	2 (3.5%)	19 (2.9%)	0.03	1 (2.6%)	20 (3.5%)	0.06	1 (20.0%)	1 (1.6%)	0.62
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	9 (11.3%)	50 (6.8%)	0.16	3 (5.3%)	41 (6.3%)	0.04	3 (7.7%)	35 (6.2%)	0.06	1 (20.0%)	3 (4.9%)	0.47
Cardiovascular revascularization	3 (3.8%)	23 (3.1%)	0.03	0 (0.0%)	13 (2.0%)	0.20	1 (2.6%)	12 (2.1%)	0.03	0 (0.0%)	0 (0.0%)	
Congestive heart failure (hospitalized & non-hospitalized)	4 (5.0%)	4 (0.5%)	0.27	1 (1.8%)	9 (1.4%)	0.03	0 (0.0%)	11 (2.0%)	0.20	0 (0.0%)	1 (1.6%)	0.18
Coronary artery disease	5 (6.3%)	32 (4.3%)	0.09	1 (1.8%)	22 (3.4%)	0.10	2 (5.1%)	19 (3.4%)	0.09	1 (20.0%)	0 (0.0%)	0.71
Ischemic heart disease	6 (7.5%)	39 (5.3%)	0.09	2 (3.5%)	34 (5.2%)	0.08	2 (5.1%)	24 (4.3%)	0.04	1 (20.0%)	0 (0.0%)	0.71
TIA	1 (1.3%)	10 (1.4%)	0.01	0 (0.0%)	8 (1.2%)	0.16	1 (2.6%)	3 (0.5%)	0.17	0 (0.0%)	2 (3.3%)	0.26
Unstable angina	0 (0.0%)	1 (0.1%)	0.05	1 (1.8%)	5 (0.8%)	0.09	0 (0.0%)	5 (0.9%)	0.13	0 (0.0%)	0 (0.0%)	
Ventricular arrhythmia	1 (1.3%)	7 (0.9%)	0.03	0 (0.0%)	1 (0.2%)	0.06	0 (0.0%)	4 (0.7%)	0.12	0 (0.0%)	0 (0.0%)	
Diabetes mellitus	12 (15.0%)	88 (11.9%)	0.09	2 (3.5%)	75 (11.5%)	0.31	4 (10.3%)	62 (11.0%)	0.02	0 (0.0%)	5 (8.2%)	0.42
Hyperlipidemia	19 (23.8%)	138 (18.7%)	0.12	15 (26.3%)	111 (17.0%)	0.23	9 (23.1%)	92 (16.3%)	0.17	0 (0.0%)	10 (16.4%)	0.63
Hypertension (hospitalized & non-hospitalized)	32 (40.0%)	269 (36.4%)	0.07	27 (47.4%)	226 (34.7%)	0.26	11 (28.2%)	189 (33.5%)	0.12	3 (60.0%)	24 (39.3%)	0.42
Immune disorders	18 (22.5%)	135 (18.8%)	0.09	21 (36.8%)	130 (20.1%)	0.38	15 (38.5%)	101 (18.0%)	0.47	0 (0.0%)	8 (13.1%)	0.55

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 80)	TNFi (N= 738)	Std. Diff.	Baricitinib (N= 57)	TNFi (N= 652)	Std. Diff.	Baricitinib (N= 39)	TNFi (N= 564)	Std. Diff.	Baricitinib (N= 5)	TNFi (N= 61)	Std. Diff.
Secondary Sjogren Syndrome	18 (22.5%)	135 (18.8%)	0.09	21 (36.8%)	130 (20.1%)	0.38	15 (38.5%)	101 (18.0%)	0.47	0 (0.0%)	8 (13.1%)	0.55
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	5 (6.3%)	22 (3.0%)	0.16	3 (5.3%)	22 (3.4%)	0.09	5 (12.8%)	10 (1.8%)	0.43	0 (0.0%)	3 (4.9%)	0.32
Obesity, current	28 (35.9%)	340 (47.2%)	0.23	25 (46.3%)	293 (46.0%)	0.01	14 (35.9%)	273 (49.0%)	0.27	2 (40.0%)	24 (40.0%)	0.00
Pregnancy, recent (current or since last visit)	0 (0.0%)	4 (0.6%)	0.11	0 (0.0%)	2 (0.3%)	0.08	0 (0.0%)	5 (1.0%)	0.14	0 (0.0%)	0 (0.0%)	
Smoking (current or former)	44 (55.0%)	328 (45.0%)	0.20	27 (49.1%)	315 (49.1%)	0.00	27 (69.2%)	263 (47.0%)	0.46	2 (40.0%)	29 (48.3%)	0.17
RA severity (CDAI)												
n	80	738	0.29	57	652	0.08	39	564	0.12	5	61	0.62
Mean±SD	20.5 ± 11.1	16.9 ± 13.2		18.5 ± 11.9	17.5 ± 13.1		17.6 ± 11.8	16.1 ± 12.9		8.2 ± 8.0	14.5 ± 12.1	
Median	17.3	14.0		15.8	15.2		17.5	13.5		5.1	12.0	
Min, Max	4.0, 51.2	0.0, 70.2		1.0, 49.0	0.0, 66.0		2.1, 48.5	0.0, 72.5		0.8, 20.0	0.0, 48.0	
Prevalent outcomes												
VTE (at any time in the past)	5 (6.3%)	14 (1.9%)	0.22	2 (3.5%)	10 (1.5%)	0.13	1 (2.6%)	11 (2.0%)	0.04	0 (0.0%)	0 (0.0%)	
MACE (at any time in the past)	3 (3.8%)	29 (3.9%)	0.01	3 (5.3%)	18 (2.8%)	0.13	3 (7.7%)	16 (2.8%)	0.22	0 (0.0%)	3 (4.9%)	0.32
Myocardial infarction	3 (3.8%)	16 (2.2%)	0.09	0 (0.0%)	11 (1.7%)	0.19	2 (5.1%)	6 (1.1%)	0.24	0 (0.0%)	0 (0.0%)	
Stroke	0 (0.0%)	14 (1.9%)	0.20	3 (5.3%)	7 (1.1%)	0.24	1 (2.6%)	11 (2.0%)	0.04	0 (0.0%)	3 (4.9%)	0.32
Serious infection (at any time in the past)	9 (11.3%)	76 (10.3%)	0.03	8 (14.0%)	57 (8.7%)	0.17	6 (15.4%)	47 (8.3%)	0.22	0 (0.0%)	11 (18.0%)	0.66
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
DMARD history												
Number of cDMARDs used (ever)												
0	0 (0.0%)	29 (3.9%)	0.29	1 (1.8%)	30 (4.6%)	0.16	1 (2.6%)	19 (3.4%)	0.05	1 (20.0%)	3 (4.9%)	0.47
1	24 (30.0%)	321 (43.5%)	0.28	15 (26.3%)	281 (43.1%)	0.36	12 (30.8%)	255 (45.2%)	0.30	2 (40.0%)	30 (49.2%)	0.19
2+	56 (70.0%)	388 (52.6%)	0.36	41 (71.9%)	341 (52.3%)	0.41	26 (66.7%)	290 (51.4%)	0.31	2 (40.0%)	28 (45.9%)	0.12
Methotrexate (prior use)	76 (95.0%)	645 (87.4%)	0.27	54 (94.7%)	568 (87.1%)	0.27	36 (92.3%)	485 (86.0%)	0.20	4 (80.0%)	55 (90.2%)	0.29
Number of bDMARDs used (ever)												
0	6 (7.5%)	316 (42.8%)	0.89	6 (10.5%)	334 (51.2%)	0.98	4 (10.3%)	260 (46.1%)	0.87	1 (20.0%)	30 (49.2%)	0.64
1	11 (13.8%)	221 (29.9%)	0.40	8 (14.0%)	177 (27.1%)	0.33	8 (20.5%)	166 (29.4%)	0.21	0 (0.0%)	21 (34.4%)	1.02
2+	63 (78.8%)	201 (27.2%)	1.20	43 (75.4%)	141 (21.6%)	1.28	27 (69.2%)	138 (24.5%)	1.00	4 (80.0%)	10 (16.4%)	1.65
Prior bDMARD use[a]	74 (92.5%)	422 (57.2%)	0.89	51 (89.5%)	318 (48.8%)	0.98	35 (89.7%)	304 (53.9%)	0.87	4 (80.0%)	31 (50.8%)	0.64
Prior TNFi bDMARD use	73 (91.3%)	384 (52.0%)	0.97	48 (84.2%)	290 (44.5%)	0.91	35 (89.7%)	282 (50.0%)	0.96	4 (80.0%)	27 (44.3%)	0.79
Prior non-TNFi bDMARD use	54 (67.5%)	184 (24.9%)	0.94	36 (63.2%)	136 (20.9%)	0.95	20 (51.3%)	114 (20.2%)	0.69	2 (40.0%)	13 (21.3%)	0.41
DMARD, current (baseline)												
cDMARD, concomitant use at baseline	42 (52.5%)	505 (68.4%)	0.33	35 (61.4%)	465 (71.3%)	0.21	26 (66.7%)	399 (70.7%)	0.09	2 (40.0%)	39 (63.9%)	0.49
Methotrexate, concomitant use at baseline	28 (35.0%)	359 (48.6%)	0.28	25 (43.9%)	334 (51.2%)	0.15	21 (53.8%)	292 (51.8%)	0.04	2 (40.0%)	32 (52.5%)	0.25
Prescription medication use, current (baseline)												
Other prescription medications												
Cardiovascular medications												

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 80)	TNFi (N= 738)	Std. Diff.	Baricitinib (N= 57)	TNFi (N= 652)	Std. Diff.	Baricitinib (N= 39)	TNFi (N= 564)	Std. Diff.	Baricitinib (N= 5)	TNFi (N= 61)	Std. Diff.
Anticoagulant (coumadin/warfarin; patient-reported)	3 (3.8%)	15 (2.0%)	0.10	1 (1.8%)	8 (1.2%)	0.04	2 (5.1%)	7 (1.2%)	0.22	0 (0.0%)	0 (0.0%)	
Antihypertensives (blood pressure lowering medication(s); patient-reported)	38 (47.5%)	299 (40.5%)	0.14	29 (50.9%)	260 (39.9%)	0.22	19 (48.7%)	230 (40.8%)	0.16	1 (20.0%)	24 (39.3%)	0.43
Antiplatelet (Plavix; patient-reported)	2 (2.5%)	14 (1.9%)	0.04	1 (1.8%)	11 (1.7%)	0.01	0 (0.0%)	17 (3.0%)	0.25	0 (0.0%)	1 (1.6%)	0.18
Nitrates (angina/nitrate medications; patient-reported)	0 (0.0%)	9 (1.2%)	0.16	2 (3.5%)	5 (0.8%)	0.19	0 (0.0%)	2 (0.4%)	0.08	0 (0.0%)	0 (0.0%)	
Hormonal Medication HRT (in RA US only)	1 (1.3%)	6 (0.8%)	0.04	2 (3.5%)	8 (1.2%)	0.15	0 (0.0%)	4 (0.7%)	0.12	0 (0.0%)	0 (0.0%)	
Lipid-lowering agents (cholesterol medication; patient-reported)	20 (25.0%)	155 (21.0%)	0.10	9 (15.8%)	135 (20.7%)	0.13	11 (28.2%)	114 (20.2%)	0.19	0 (0.0%)	12 (19.7%)	0.70
RA-related												
Aspirin (includes non-prescription)	10 (12.5%)	89 (12.1%)	0.01	7 (12.3%)	76 (11.7%)	0.02	12 (30.8%)	95 (16.8%)	0.33	3 (60.0%)	5 (8.2%)	1.30
Celebrex (in RA US only)	10 (12.5%)	47 (6.4%)	0.21	4 (7.0%)	42 (6.4%)	0.02	3 (7.7%)	24 (4.3%)	0.15	0 (0.0%)	3 (4.9%)	0.32
Prednisone	29 (36.3%)	218 (29.5%)	0.14	25 (43.9%)	184 (28.2%)	0.33	14 (35.9%)	145 (25.7%)	0.22	1 (20.0%)	11 (18.0%)	0.05
Vaccinations												
Influenza (baseline) (in RA US only)	28 (43.1%)	279 (42.5%)	0.01	16 (30.8%)	240 (40.7%)	0.21	16 (50.0%)	200 (40.3%)	0.20	1 (50.0%)	23 (41.1%)	0.18
Pneumonia (ever) (in RA US only)	19 (25.7%)	169 (25.0%)	0.02	13 (25.0%)	172 (28.3%)	0.07	6 (19.4%)	119 (23.1%)	0.09	0 (0.0%)	11 (19.3%)	0.69
Shingles (ever)	17 (22.7%)	144 (20.8%)	0.05	4 (7.7%)	138 (22.2%)	0.41	12 (35.3%)	112 (20.9%)	0.32	1 (33.3%)	11 (18.3%)	0.35

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; CDAI = clinical disease activity index; cDMARD = classical disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event (MI (myocardial infarction) and stroke); Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism; SD = standard deviation; Std Diff = absolute value of the standardized difference; JAKi = janus kinase inhibitor.
a. Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

COR_US Table 6.193. Any Prior JAKi Use: Baseline Clinical Characteristics by Exposure Duration, VTE-matched Population [CorEvitas US] - exposure ends at discontinuation/last follow-up visit/VTE event; excludes patients with VTE within 6 months prior to index date or on anticoagulant.

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 75)	TNFi (N= 181)	Std. Diff.	Baricitinib (N= 53)	TNFi (N= 139)	Std. Diff.	Baricitinib (N= 35)	TNFi (N= 128)	Std. Diff.	Baricitinib (N= 4)	TNFi (N= 9)	Std. Diff.
Age [yrs]												
n	75	181	0.08	53	139	0.15	35	128	0.46	4	9	0.10
Mean±SD	58.5 ± 11.1	59.5 ± 13.1		57.4 ± 11.8	59.1 ± 12.6		64.8 ± 9.1	59.8 ± 12.6		62.5 ± 10.4	61.3 ± 13.7	
Median	61.0	61.0		58.0	60.0		66.0	62.5		58.0	57.0	
Min, Max	27.0, 78.0	22.0, 85.0		31.0, 86.0	23.0, 83.0		40.0, 79.0	26.0, 87.0		56.0, 78.0	44.0, 82.0	
≥ 65 years	23 (30.7%)	61 (33.7%)	0.06	14 (26.4%)	56 (40.3%)	0.30	20 (57.1%)	56 (43.8%)	0.27	1 (25.0%)	4 (44.4%)	0.42
Gender												
Male	16 (21.3%)	39 (21.5%)	0.01	8 (15.1%)	24 (17.3%)	0.06	7 (20.0%)	30 (23.4%)	0.08	4 (100.0%)	2 (22.2%)	2.65
Female	59 (78.7%)	142 (78.5%)		45 (84.9%)	115 (82.7%)		28 (80.0%)	98 (76.6%)		0 (0.0%)	7 (77.8%)	
History of MD-reported comorbidities (ever experienced)												
Cancer, Non-NMSC	4 (5.3%)	8 (4.4%)	0.04	3 (5.7%)	8 (5.8%)	0.00	2 (5.7%)	8 (6.3%)	0.02	0 (0.0%)	0 (0.0%)	
Cancer, NMSC only	4 (5.3%)	15 (8.3%)	0.12	5 (9.4%)	11 (7.9%)	0.05	4 (11.4%)	10 (7.8%)	0.12	0 (0.0%)	1 (11.1%)	0.50
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	5 (6.7%)	13 (7.2%)	0.02	12 (22.6%)	16 (11.5%)	0.30	2 (5.7%)	11 (8.6%)	0.11	0 (0.0%)	1 (11.1%)	0.50
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	4 (5.3%)	5 (2.8%)	0.13	2 (3.8%)	6 (4.3%)	0.03	0 (0.0%)	6 (4.7%)	0.31	0 (0.0%)	0 (0.0%)	
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	8 (10.7%)	12 (6.6%)	0.14	3 (5.7%)	15 (10.8%)	0.19	3 (8.6%)	13 (10.2%)	0.05	0 (0.0%)	0 (0.0%)	
Cardiovascular revascularization	3 (4.0%)	7 (3.9%)	0.01	0 (0.0%)	4 (2.9%)	0.24	1 (2.9%)	6 (4.7%)	0.10	0 (0.0%)	0 (0.0%)	
Congestive heart failure (hospitalized & non-hospitalized)	2 (2.7%)	1 (0.6%)	0.17	1 (1.9%)	3 (2.2%)	0.02	0 (0.0%)	6 (4.7%)	0.31	0 (0.0%)	0 (0.0%)	
Coronary artery disease	4 (5.3%)	9 (5.0%)	0.02	1 (1.9%)	7 (5.0%)	0.17	2 (5.7%)	7 (5.5%)	0.01	0 (0.0%)	0 (0.0%)	
Ischemic heart disease	5 (6.7%)	10 (5.5%)	0.05	2 (3.8%)	9 (6.5%)	0.12	2 (5.7%)	8 (6.3%)	0.02	0 (0.0%)	0 (0.0%)	
TIA	1 (1.3%)	1 (0.6%)	0.08	0 (0.0%)	3 (2.2%)	0.21	1 (2.9%)	1 (0.8%)	0.16	0 (0.0%)	0 (0.0%)	
Unstable angina	0 (0.0%)	0 (0.0%)		1 (1.9%)	2 (1.4%)	0.04	0 (0.0%)	3 (2.3%)	0.22	0 (0.0%)	0 (0.0%)	
Ventricular arrhythmia	1 (1.3%)	2 (1.1%)	0.02	0 (0.0%)	1 (0.7%)	0.12	0 (0.0%)	2 (1.6%)	0.18	0 (0.0%)	0 (0.0%)	
Diabetes mellitus	11 (14.7%)	19 (10.6%)	0.13	2 (3.8%)	19 (13.7%)	0.36	4 (11.4%)	16 (12.5%)	0.03	0 (0.0%)	1 (11.1%)	0.50
Hyperlipidemia	17 (22.7%)	23 (12.8%)	0.26	14 (26.4%)	26 (18.7%)	0.19	7 (20.0%)	23 (18.0%)	0.05	0 (0.0%)	2 (22.2%)	0.76
Hypertension (hospitalized & non-hospitalized)	30 (40.0%)	65 (36.1%)	0.08	25 (47.2%)	46 (33.1%)	0.29	9 (25.7%)	46 (35.9%)	0.22	2 (50.0%)	5 (55.6%)	0.11
Immune disorders	16 (21.3%)	51 (28.3%)	0.16	20 (37.7%)	39 (28.1%)	0.21	13 (37.1%)	36 (28.1%)	0.19	0 (0.0%)	1 (11.1%)	0.50

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 75)	TNFi (N= 181)	Std. Diff.	Baricitinib (N= 53)	TNFi (N= 139)	Std. Diff.	Baricitinib (N= 35)	TNFi (N= 128)	Std. Diff.	Baricitinib (N= 4)	TNFi (N= 9)	Std. Diff.
Secondary Sjogren Syndrome	16 (21.3%)	51 (28.3%)	0.16	20 (37.7%)	39 (28.1%)	0.21	13 (37.1%)	36 (28.1%)	0.19	0 (0.0%)	1 (11.1%)	0.50
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	4 (5.3%)	8 (4.4%)	0.04	2 (3.8%)	8 (5.8%)	0.09	2 (5.7%)	3 (2.3%)	0.17	0 (0.0%)	0 (0.0%)	
Obesity, current	28 (38.4%)	70 (39.3%)	0.02	23 (45.1%)	67 (48.9%)	0.08	13 (37.1%)	55 (43.7%)	0.13	2 (50.0%)	6 (66.7%)	0.34
Pregnancy, recent (current or since last visit)	0 (0.0%)	2 (1.2%)	0.15	0 (0.0%)	0 (0.0%)		0 (0.0%)	1 (0.8%)	0.13	0 (0.0%)	0 (0.0%)	
Smoking (current or former)	40 (53.3%)	97 (53.6%)	0.01	25 (47.2%)	71 (51.1%)	0.08	23 (65.7%)	57 (44.5%)	0.44	1 (25.0%)	5 (55.6%)	0.66
RA severity (CDAI)												
n	75	181	0.16	53	139	0.00	35	128	0.05	4	9	0.81
Mean±SD	20.6 ± 11.3	18.6 ± 14.3		19.0 ± 12.1	19.0 ± 14.1		16.4 ± 10.7	15.9 ± 12.6		7.1 ± 8.8	16.8 ± 14.6	
Median	16.6	15.4		17.7	17.5		17.5	12.6		3.8	12.5	
Min, Max	4.0, 51.2	0.0, 62.5		1.0, 49.0	0.0, 66.0		2.1, 44.0	0.0, 52.5		0.8, 20.0	4.4, 42.7	
Prevalent outcomes												
VTE (at any time in the past)	3 (4.0%)	2 (1.1%)	0.18	1 (1.9%)	4 (2.9%)	0.07	1 (2.9%)	3 (2.3%)	0.03	0 (0.0%)	0 (0.0%)	
MACE (at any time in the past)	3 (4.0%)	7 (3.9%)	0.01	2 (3.8%)	2 (1.4%)	0.15	1 (2.9%)	5 (3.9%)	0.06	0 (0.0%)	1 (11.1%)	0.50
Myocardial infarction	3 (4.0%)	3 (1.7%)	0.14	0 (0.0%)	0 (0.0%)		1 (2.9%)	1 (0.8%)	0.16	0 (0.0%)	0 (0.0%)	
Stroke	0 (0.0%)	4 (2.2%)	0.21	2 (3.8%)	2 (1.4%)	0.15	0 (0.0%)	4 (3.1%)	0.25	0 (0.0%)	1 (11.1%)	0.50
Serious infection (at any time in the past)	8 (10.7%)	23 (12.7%)	0.06	8 (15.1%)	18 (12.9%)	0.06	5 (14.3%)	14 (10.9%)	0.10	0 (0.0%)	1 (11.1%)	0.50
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
DMARD history												
Number of cDMARDs used (ever)												
0	0 (0.0%)	7 (3.9%)	0.28	1 (1.9%)	4 (2.9%)	0.07	1 (2.9%)	4 (3.1%)	0.02	1 (25.0%)	2 (22.2%)	0.07
1	22 (29.3%)	67 (37.0%)	0.16	14 (26.4%)	46 (33.1%)	0.15	12 (34.3%)	44 (34.4%)	0.00	2 (50.0%)	1 (11.1%)	0.93
2+	53 (70.7%)	107 (59.1%)	0.24	38 (71.7%)	89 (64.0%)	0.16	22 (62.9%)	80 (62.5%)	0.01	1 (25.0%)	6 (66.7%)	0.92
Methotrexate (prior use)	71 (94.7%)	156 (86.2%)	0.29	50 (94.3%)	121 (87.1%)	0.25	32 (91.4%)	112 (87.5%)	0.13	3 (75.0%)	7 (77.8%)	0.07
Number of bDMARDs used (ever)												
0	6 (8.0%)	19 (10.5%)	0.09	6 (11.3%)	14 (10.1%)	0.04	4 (11.4%)	16 (12.5%)	0.03	1 (25.0%)	2 (22.2%)	0.07
1	11 (14.7%)	30 (16.6%)	0.05	7 (13.2%)	19 (13.7%)	0.01	8 (22.9%)	24 (18.8%)	0.10	0 (0.0%)	1 (11.1%)	0.50
2+	58 (77.3%)	132 (72.9%)	0.10	40 (75.5%)	106 (76.3%)	0.02	23 (65.7%)	88 (68.8%)	0.06	3 (75.0%)	6 (66.7%)	0.18
Prior bDMARD use[a]	69 (92.0%)	162 (89.5%)	0.09	47 (88.7%)	125 (89.9%)	0.04	31 (88.6%)	112 (87.5%)	0.03	3 (75.0%)	7 (77.8%)	0.07
Prior TNFi bDMARD use	68 (90.7%)	151 (83.4%)	0.22	44 (83.0%)	115 (82.7%)	0.01	31 (88.6%)	106 (82.8%)	0.17	3 (75.0%)	7 (77.8%)	0.07
Prior non-TNFi bDMARD use	49 (65.3%)	110 (60.8%)	0.09	36 (67.9%)	92 (66.2%)	0.04	17 (48.6%)	61 (47.7%)	0.02	1 (25.0%)	5 (55.6%)	0.66
DMARD, current (baseline)												
cDMARD, concomitant use at baseline	39 (52.0%)	104 (57.5%)	0.11	33 (62.3%)	92 (66.2%)	0.08	24 (68.6%)	86 (67.2%)	0.03	1 (25.0%)	5 (55.6%)	0.66
Methotrexate, concomitant use at baseline	25 (33.3%)	66 (36.5%)	0.07	24 (45.3%)	58 (41.7%)	0.07	20 (57.1%)	60 (46.9%)	0.21	1 (25.0%)	4 (44.4%)	0.42
Prescription medication use, current (baseline)												
Other prescription medications												
Cardiovascular medications												
Anticoagulant (coumadin/warfarin; patient-reported)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	

	<6mos			6 mos to <12 mos			12 mos to <24 mos			>=24 mos		
	Baricitinib (N= 75)	TNFi (N= 181)	Std. Diff.	Baricitinib (N= 53)	TNFi (N= 139)	Std. Diff.	Baricitinib (N= 35)	TNFi (N= 128)	Std. Diff.	Baricitinib (N= 4)	TNFi (N= 9)	Std. Diff.
Antihypertensives (blood pressure lowering medication(s); patient-reported)	35 (46.7%)	76 (42.0%)	0.09	27 (50.9%)	57 (41.0%)	0.20	18 (51.4%)	55 (43.0%)	0.17	1 (25.0%)	3 (33.3%)	0.18
Antiplatelet (Plavix; patient-reported)	1 (1.3%)	8 (4.4%)	0.19	1 (1.9%)	3 (2.2%)	0.02	0 (0.0%)	3 (2.3%)	0.22	0 (0.0%)	0 (0.0%)	
Nitrates (angina/nitrate medications; patient-reported)	0 (0.0%)	4 (2.2%)	0.21	2 (3.8%)	1 (0.7%)	0.21	0 (0.0%)	2 (1.6%)	0.18	0 (0.0%)	0 (0.0%)	
Hormonal Medication HRT (in RA US only)	0 (0.0%)	0 (0.0%)		2 (3.8%)	4 (2.9%)	0.05	0 (0.0%)	1 (0.8%)	0.13	0 (0.0%)	0 (0.0%)	
Lipid-lowering agents (cholesterol medication; patient-reported)	17 (22.7%)	39 (21.5%)	0.03	8 (15.1%)	26 (18.7%)	0.10	9 (25.7%)	28 (21.9%)	0.09	0 (0.0%)	4 (44.4%)	1.26
RA-related												
Aspirin (includes non-prescription)	9 (12.0%)	27 (14.9%)	0.09	6 (11.3%)	18 (12.9%)	0.05	11 (31.4%)	28 (21.9%)	0.22	2 (50.0%)	0 (0.0%)	1.41
Celebrex (in RA US only)	9 (12.0%)	15 (8.3%)	0.12	3 (5.7%)	15 (10.8%)	0.19	3 (8.6%)	6 (4.7%)	0.16	0 (0.0%)	1 (11.1%)	0.50
Prednisone	26 (34.7%)	65 (36.1%)	0.03	23 (43.4%)	53 (37.9%)	0.11	12 (34.3%)	41 (32.0%)	0.05	1 (25.0%)	2 (22.2%)	0.07
Vaccinations												
Influenza (baseline) (in RA US only)	28 (45.9%)	56 (35.7%)	0.21	15 (31.3%)	59 (48.8%)	0.36	13 (46.4%)	42 (35.9%)	0.22	1 (50.0%)	3 (33.3%)	0.34
Pneumonia (ever) (in RA US only)	18 (26.1%)	45 (26.6%)	0.01	12 (25.0%)	41 (32.5%)	0.17	5 (18.5%)	28 (23.5%)	0.12	0 (0.0%)	1 (11.1%)	0.50
Shingles (ever)	15 (21.4%)	32 (18.8%)	0.07	4 (8.2%)	36 (27.3%)	0.52	11 (36.7%)	29 (23.2%)	0.30	1 (33.3%)	0 (0.0%)	1.00

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; CDAI = clinical disease activity index; cDMARD = classical disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event (MI (myocardial infarction) and stroke); Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism; SD = standard deviation; Std Diff = absolute value of the standardized difference; JAKi = janus kinase inhibitor.

a. Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

COR_US Table 6.194. Any Prior JAKi Use: Baseline Healthcare Resource Utilization by Exposure Duration, Unmatched [CorEvitas US]

Not applicable in CorEvitas RA US data.

COR_US Table 6.195. Any Prior JAKi Use: Baseline Healthcare Resource Utilization by Exposure Duration Primary VTE Cohorts, Matched [CorEvitas US]

Not applicable in CorEvitas RA US data.

COR_US Table 6.196. Any Prior JAKi Use: Baseline Clinical Characteristics of RA Patients with VTE, VTE-matched Population [CorEvitas US]- excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

	Baricitinib (N=0)	TNFi (N=2)	Total (N=2)
Age [yrs]			
n	0	2	2
Mean±SD	0.0 ± 0.0	62.0 ± 0.0	62.0 ± 0.0
Median	0.0	62.0	62.0
Min, Max	0.0, 0.0	62.0, 62.0	62.0, 62.0
Gender			
Male	0 (0.0%)	1 (50.0%)	1 (50.0%)
Female	0 (0.0%)	1 (50.0%)	1 (50.0%)
History of MD-reported comorbidities (ever experienced)			
Cancer, Non-NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cancer, NMSC only	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure (hospitalized & non-hospitalized)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyperlipidemia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertension (hospitalized & non-hospitalized)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Immune disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)
Secondary Sjogren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity, current	0 (0.0%)	1 (50.0%)	1 (50.0%)
Pregnancy, recent (current or since last visit)	0 (0.0%)	0 (0.0%)	0 (0.0%)

	Baricitinib (N=0)	TNFi (N=2)	Total (N=2)
Smoking (current or former)	0 (0.0%)	2 (100.0%)	2 (100.0%)
RA severity (CDAI)			
n	0	2	2
Mean	0.0 ±0.0	12.3 ±14.6	12.3 ±14.6
Median	0.0	12.3	12.3
Min, Max	0.0, 0.0	2.0, 22.7	2.0, 22.7
Prevalent outcomes			
VTE (at any time in the past)	0 (0.0%)	1 (50.0%)	1 (50.0%)
MACE (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Myocardial infarction	0 (0.0%)	0 (0.0%)	0 (0.0%)
Stroke	0 (0.0%)	0 (0.0%)	0 (0.0%)
Serious infection (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prescription medication use, current (baseline)			
Other prescription medications			
Cardiovascular medications			
Anticoagulant (coumadin/warfarin; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antihypertensives (blood pressure lowering medication(s); patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiplatelet (Plavix; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nitrates (angina/nitrate medications; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal Medication HRT (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents (cholesterol medication; patient-reported)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA-related			
Aspirin (includes non-prescription)	0 (0.0%)	1 (50.0%)	1 (50.0%)
Celebrex (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prednisone	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vaccinations			
Influenza (baseline) (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pneumonia (ever) (in RA US only)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Shingles (ever)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Occurrence			
Cancer diagnosis within 90 days after VTE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Concomitant Methotrexate in 1 month prior to VTE	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event (MI (myocardial infarction) and stroke); Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism; SD = standard deviation; Std Diff = absolute value of the standardized difference; JAKi = janus kinase inhibitor.

COR_US Table 6.197. Any prior JAKi Use: Pattern of RA Medication Use in Patients with VTE [CorEvitas US] – excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

	Pre-matched		Matched		
	Baricitinib (N= 0)	TNFi (N= 7)	Baricitinib (N= 0)	TNFi (N= 2)	Total (N= 2)
Baseline Medication					
Number of cDMARDs used (ever)					
0	0 (0.0%)	2 (28.6%)	0 (0.0%)	2 (100.0%)	2 (100.0%)
1	0 (0.0%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2+	0 (0.0%)	2 (28.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate (prior use)	0 (0.0%)	5 (71.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Number of bDMARDs used (ever)					
0	0 (0.0%)	4 (57.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
1	0 (0.0%)	3 (42.9%)	0 (0.0%)	2 (100.0%)	2 (100.0%)
2+	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prior bDMARD use[a]	0 (0.0%)	3 (42.9%)	0 (0.0%)	2 (100.0%)	2 (100.0%)
Prior TNFi bDMARD use	0 (0.0%)	3 (42.9%)	0 (0.0%)	2 (100.0%)	2 (100.0%)
Prior non-TNFi bDMARD use	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DMARD, current (baseline)					
cDMARD (non-methotrexate), concomitant use at baseline	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate, concomitant use at baseline	0 (0.0%)	3 (42.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Medication (Prior to VTE)					
Concomitant methotrexate use during exposure (regardless of use at index date)	0 (0.0%)	4 (57.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Concomitant non-methotrexate cDMARD during exposure (regardless of use at index date)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism; JAKi = janus kinase inhibitor.
a Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

COR_US Table 6.198. Any Prior JAKi Use: Time to First VTE Event (Months*) [CorEvitas US] – excludes patients with a VTE within 6 months prior to index date or on anticoagulant.

	Pre-matched		Matched		
	Baricitinib (N= 0)	TNFi (N= 7)	Baricitinib (N= 0)	TNFi (N= 2)	Total (N= 2)
n	0	7	0	2	2
Mean±SD	n/a	1.5 ± 1.2	n/a	2.5 ± 0.7	2.5 ± 0.7
Median		1.0		2.5	2.5
Min, Max		0.5, 3.0		2.0, 3.0	2.0, 3.0
25th percentile, 75th percentile		0.5, 3.0		2.0, 3.0	2.0, 3.0

Abbreviations: JAKi = janus kinase inhibitor; Max = maximum; Min = minimum; SD = standard deviation; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

* CorEvitas' RA US Registry collects drug information at the month-level so time is reported in months. A rough conversion to days can be made by multiplying the values in this table by a factor of 30.4375 (the average number of days in a month)

COR_US Table 6.199. Any Prior JAKi Use: Incidence Rates of First VTE Event [CorEvitas US] –excludes patients with VTE within 6 months prior to index date or currently taking anticoagulant.

	Pre-matched		Matched		
	Baricitinib (N= 175)	TNFi (N=1,982)	Baricitinib (N= 167)	TNFi (N= 457)	Total (N= 624)
Overall					
N	175	1,982	167	457	624
VTE Events	0	7	0	2	2
Person-Years	118.8	1509.8	111.2	332.8	444.0
VTE Events/100 PY	0.0	0.5	0.0	0.6	0.5
95% CI	0.0, 3.1	0.2, 1.0	0.0, 3.3	0.1, 2.2	0.1, 1.6
Incidence rate difference: baricitinib-TNFi (95% CI)					-0.6 (-1.4, 0.2)
bDMARD-naïve					
N	17	927	17	51	68
VTE Events	0	4	0	0	0
Person-Years	12.8	718.6	12.8	41.6	54.3
VTE Events/100 PY	0.0	0.6	0.0	0.0	0.0
95% CI	0.0, 28.8	0.2, 1.4	0.0, 28.8	0.0, 8.9	0.0, 6.8
Incidence rate difference: baricitinib-TNFi (95% CI)					0.0 (0.0, 0.0)
bDMARD-experienced					
N	158	1,055	150	406	556
VTE Events	0	3	0	2	2
Person-Years	106.1	791.2	98.4	291.2	389.6
VTE Events/100 PY	0.0	0.4	0.0	0.7	0.5
95% CI	0.0, 3.5	0.1, 1.1	0.0, 3.7	0.1, 2.5	0.1, 1.9
Incidence rate difference: baricitinib-TNFi (95% CI)					-0.7 (-1.6, 0.3)
Concomitant MTX Use at Index Date					
N	73	1,001	70	188	258
VTE Events	0	3	0	0	0
Person-Years	54.6	777.5	51.3	145.5	196.9
VTE Events/100 PY	0.0	0.4	0.0	0.0	0.0
95% CI	0.0, 6.8	0.1, 1.1	0.0, 7.2	0.0, 2.5	0.0, 1.9
Incidence rate difference: baricitinib-TNFi (95% CI)					0.0 (0.0, 0.0)
No concomitant MTX Use at Index Date					
N	102	981	97	269	366
VTE Events	0	4	0	2	2
Person-Years	64.3	732.3	59.8	187.2	247.1
VTE Events/100 PY	0.0	0.5	0.0	1.1	0.8
95% CI	0.0, 5.7	0.1, 1.4	0.0, 6.2	0.1, 3.9	0.1, 2.9
Incidence rate difference: baricitinib-TNFi (95% CI)					-1.1 (-2.5, 0.4)

Abbreviations: CI = confidence interval; MTX = methotrexate; PY = person-years; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

COR_US Table 6.200. Any Prior JAKi Use: Any Prior JAKi Use: Comparative Risk of Incident VTE, Primary Definition [CorEvitas US], VTE-matched population – excludes patients with prior VTE within 6 months prior to index date or on anticoagulant.

Not applicable in CorEvitas RA US data.

Appendix COR_US Table 1. Baseline Demographics by TNFi-naïve status, Pre-matched Population [CorEvitas US]

	Baricitinib			TNFi		
	TNFi-naïve (N= 18)	TNFi-experienced (N= 100)	Std. Diff.	TNFi-naïve (N= 991)	TNFi-experienced (N= 906)	Std. Diff.
Age [yrs]						
n	18	100	0.20	991	906	0.11
Mean±SD	58.4 ± 9.4	60.5 ± 11.8		58.4 ± 13.6	59.7 ± 12.1	
Median	58.5	61.0		59.0	61.0	
Min, Max	38.0, 74.0	27.0, 81.0		18.0, 90.0	22.0, 89.0	
≥ 65 years	4 (22.2%)	39 (39.0%)	0.37	355 (35.8%)	361 (39.8%)	0.08
Gender						
Male	5 (27.8%)	24 (24.0%)	0.09	226 (22.8%)	170 (18.8%)	0.10
Female	13 (72.2%)	76 (76.0%)		765 (77.2%)	736 (81.2%)	
BMI						
n	18	98	0.42	970	890	0.01
Mean±SD	32.8 ± 8.2	29.5 ± 7.3		30.5 ± 7.5	30.6 ± 7.3	
Median	31.2	28.7		29.6	29.5	
Min, Max	17.7, 46.0	16.1, 50.9		15.2, 64.0	15.7, 61.6	
Smoking (current or former)	10 (55.6%)	56 (56.0%)	0.01	453 (46.4%)	429 (47.9%)	0.03
Alcohol use	5 (27.8%)	37 (37.0%)	0.20	444 (44.9%)	426 (47.0%)	0.04
Education						
College/university	8 (47.1%)	48 (50.5%)	0.07	562 (60.0%)	561 (64.2%)	0.09

Abbreviations: Max = maximum; Min = minimum; SD = standard deviation; Std Diff = absolute value of the standardized difference; TNFi = tumor necrosis factor inhibitor.

Appendix COR_US Table 2. Baseline Clinical Characteristics by TNF-naïve status, Pre-matched Population [CorEvitas US]

	Baricitinib			TNFi		
	TNFi-naïve (N= 18)	TNFi-experienced (N= 100)	Std. Diff.	TNFi-naïve (N= 991)	TNFi-experienced (N= 906)	Std. Diff.
History of MD-reported comorbidities (ever experienced)						
Cancer, Non-NMSC	1 (5.6%)	6 (6.0%)	0.02	64 (6.5%)	74 (8.2%)	0.07
Cancer, NMSC only	1 (5.6%)	12 (12.0%)	0.23	54 (5.4%)	53 (5.8%)	0.02
Chronic Lung Disease (COPD, pulmonary fibrosis, asthma, interstitial lung disease)	3 (16.7%)	9 (9.0%)	0.23	103 (10.4%)	93 (10.3%)	0.00
CVD-VTE risk (hospitalized congestive heart failure, ventricular or atrial arrhythmia)	1 (5.6%)	4 (4.0%)	0.07	31 (3.1%)	27 (3.0%)	0.01
CVD-MACE risk (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization, coronary artery disease TIA)	1 (5.6%)	9 (9.0%)	0.13	58 (5.9%)	65 (7.2%)	0.05
Cardiovascular revascularization	0 (0.0%)	2 (2.0%)	0.20	19 (1.9%)	25 (2.8%)	0.06
Congestive heart failure (hospitalized & non-hospitalized)	1 (5.6%)	3 (3.0%)	0.13	7 (0.7%)	17 (1.9%)	0.10
Coronary artery disease	0 (0.0%)	6 (6.0%)	0.36	35 (3.5%)	33 (3.6%)	0.01
TIA	0 (0.0%)	1 (1.0%)	0.14	7 (0.7%)	15 (1.7%)	0.09
Unstable angina	0 (0.0%)	0 (0.0%)		5 (0.5%)	6 (0.7%)	0.02
Ischemic heart disease	0 (0.0%)	7 (7.0%)	0.39	47 (4.7%)	45 (5.0%)	0.01
Ventricular arrhythmia	0 (0.0%)	1 (1.0%)	0.14	8 (0.8%)	5 (0.6%)	0.03
Diabetes mellitus	1 (5.6%)	12 (12.0%)	0.23	113 (11.4%)	107 (11.8%)	0.01
Hyperlipidemia	3 (16.7%)	24 (24.0%)	0.18	181 (18.3%)	150 (16.6%)	0.05
Hypertension (hospitalized & non-hospitalized)	8 (44.4%)	40 (40.0%)	0.09	354 (35.7%)	319 (35.2%)	0.01
Immune disorders	3 (16.7%)	28 (28.0%)	0.27	138 (14.2%)	214 (23.8%)	0.25
Secondary Sjogren Syndrome	3 (16.7%)	28 (28.0%)	0.27	138 (14.2%)	214 (23.8%)	0.25
Liver disorder (hepatic event hospitalized & hepatic event non-hospitalized)	0 (0.0%)	5 (5.0%)	0.32	18 (1.8%)	36 (4.0%)	0.13
Obesity, current	10 (55.6%)	32 (32.7%)	0.47	459 (47.3%)	416 (46.7%)	0.01
Pregnancy, recent (current or since last visit)	0 (0.0%)	0 (0.0%)		6 (0.6%)	5 (0.6%)	0.01
Smoking (current or former)	10 (55.6%)	56 (56.0%)	0.01	453 (46.4%)	429 (47.9%)	0.03
RA severity (CDAI)						
n	18	100	0.12	991	906	0.18
Mean±SD	20.1 ± 8.8	18.8 ±12.2		17.8 ± 13.3	15.5 ± 12.7	
Median	20.3	16.5		15.3	12.5	
Min, Max	5.8, 39.5	0.8, 51.2		0.0, 70.2	0.0, 72.5	
Prevalent outcomes						
VTE (at any time in the past)	0 (0.0%)	6 (6.0%)	0.36	14 (1.4%)	20 (2.2%)	0.06
MACE (at any time in the past)	0 (0.0%)	3 (3.0%)	0.25	24 (2.4%)	41 (4.5%)	0.12

	Baricitinib			TNFi		
	TNFi-naïve (N= 18)	TNFi-experienced (N= 100)	Std. Diff.	TNFi-naïve (N= 991)	TNFi-experienced (N= 906)	Std. Diff.
Myocardial infarction	0 (0.0%)	3 (3.0%)	0.25	15 (1.5%)	18 (2.0%)	0.04
Stroke	0 (0.0%)	0 (0.0%)		11 (1.1%)	23 (2.5%)	0.11
Serious infection (at any time in the past)	4 (22.2%)	6 (6.0%)	0.48	72 (7.3%)	102 (11.3%)	0.14
TB, hospitalized (at any time in the past)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
DMARD history						
Number of cDMARDs used (ever)						
0	1 (5.6%)	2 (2.0%)	0.19	35 (3.5%)	38 (4.2%)	0.03
1	12 (66.7%)	28 (28.0%)	0.84	515 (52.0%)	328 (36.2%)	0.32
2+	5 (27.8%)	70 (70.0%)	0.93	441 (44.5%)	540 (59.6%)	0.31
Methotrexate (prior use)	15 (83.3%)	93 (93.0%)	0.30	865 (87.3%)	788 (87.0%)	0.01
Number of bDMARDs used (ever)						
0	15 (83.3%)	0 (0.0%)	3.16	908 (91.6%)	0 (0.0%)	4.68
1	1 (5.6%)	18 (18.0%)	0.39	63 (6.4%)	487 (53.8%)	1.21
2+	2 (11.1%)	82 (82.0%)	2.02	20 (2.0%)	419 (46.2%)	1.21
Prior bDMARD use[a]	3 (16.7%)	100 (100.0%)	3.16	83 (8.4%)	906 (100.0%)	4.68
Prior TNFi bDMARD use	0 (0.0%)	100 (100.0%)	--	0 (0.0%)	906 (100.0%)	--
Prior non-TNFi bDMARD use	3 (16.7%)	69 (69.0%)	1.25	83 (8.4%)	321 (35.4%)	0.69
DMARD, current (baseline)						
cDMARD, concomitant use at baseline	15 (83.3%)	58 (58.0%)	0.58	788 (79.5%)	558 (61.6%)	0.40
Methotrexate, concomitant use at baseline	12 (66.7%)	41 (41.0%)	0.53	613 (61.9%)	367 (40.5%)	0.44
Prescription medication use, current (baseline)						
Other prescription medications						
Cardiovascular medications						
Anticoagulant (coumadin/warfarin; patient-reported)	0 (0.0%)	3 (3.0%)	0.25	15 (1.5%)	15 (1.7%)	0.01
Antihypertensives (blood pressure lowering medication(s); patient-reported)	6 (33.3%)	49 (49.0%)	0.32	384 (38.7%)	384 (42.4%)	0.07
Antiplatelet (Plavix; patient-reported)	0 (0.0%)	2 (2.0%)	0.20	19 (1.9%)	22 (2.4%)	0.04
Nitrates (angina/nitrate medications; patient-reported)	0 (0.0%)	2 (2.0%)	0.20	5 (0.5%)	12 (1.3%)	0.09
Hormonal Medication HRT (in RA US only)	0 (0.0%)	1 (1.0%)	0.14	5 (0.5%)	12 (1.3%)	0.09
Lipid-lowering agents (cholesterol medication; patient-reported)	5 (27.8%)	26 (26.0%)	0.04	196 (19.8%)	199 (22.0%)	0.05
RA-related						
Aspirin (includes non-prescription)	1 (5.6%)	18 (18.0%)	0.39	125 (12.6%)	128 (14.1%)	0.04
Celebrex (in RA US only)	2 (11.1%)	10 (10.0%)	0.04	48 (4.8%)	59 (6.5%)	0.07
Prednisone	2 (11.1%)	41 (41.0%)	0.72	292 (29.5%)	234 (25.8%)	0.08
Vaccinations						
Influenza (baseline) (in RA US only)	4 (26.7%)	41 (48.2%)	0.46	369 (41.3%)	333 (41.6%)	0.01
Pneumonia (ever) (in RA US only)	6 (37.5%)	21 (24.1%)	0.29	246 (27.2%)	196 (23.3%)	0.09

	Baricitinib			TNFi		
	TNFi-naïve (N= 18)	TNFi-experienced (N= 100)	Std. Diff.	TNFi-naïve (N= 991)	TNFi-experienced (N= 906)	Std. Diff.
Shingles (ever)	3 (17.6%)	20 (22.5%)	0.12	195 (21.0%)	191 (22.1%)	0.03

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; CDAI = clinical disease activity index; cDMARD = classical disease-modifying antirheumatic drugs; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MACE = major adverse cardiovascular event (MI (myocardial infarction) and stroke); Max = maximum; Min = minimum; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism; SD = standard deviation; Std Diff = absolute value of the standardized difference.

a. Per CorEvitas' contractual obligations reports on individual drugs are subject to review by individual market authorization holders who are also subscribers to CorEvitas' RA Registry and have therefore not been included in this table.

Annex 5. Humana – Additional Results

This annex includes information about results for the following analyses:

I. Additional analysis
These additional results were not presented in the body of the report. These results, like those included in the report body, are based on 1:1 baricitinib:TNFi propensity score matching. Specifically, this section in the annex includes:
- Descriptive tables for unmatched eligible patients.
- Descriptive tables for matched patient cohorts for the serious infection analyses

II. Variable Ratio Matching
These results were not presented in the body of this report. They are based on matching baricitinib:TNFi using Variable Ratio matching, i.e., as many matched 1:3 as possible, then the maximum number matched 1:2, then the remaining patients matched 1:1.

I. Additional analysis

Table 1_HUM. Baseline Demographics, Unmatched [HUM]

	Baricitinib			TNFi (N=154)	Std. Diff. (Any vs TNFi)
	Any (N=89)	4-mg (N=0)	2-mg (N=89)		
Age [yrs]					
N	89	-	89	154	
Mean (SD)	60.87 (10.06)	-	60.87 (10.06)	60.75 (12.24)	0.01
Median	62.00 [54.00, 67.50]	-	62.00 [54.00, 67.50]	62.00 [52.00, 70.25]	
Min, Max	29.0, 78.0	-	29.0, 78.0	19.0, 83.0	
≥ 65 years	31 (34.8%)	-	31 (34.8%)	65 (42.2%)	0.15
Sex					
Male	12 (13.5%)	-	12 (13.5%)	24 (15.6%)	0.06
Female	77 (86.5%)	-	77 (86.5%)	130 (84.4%)	0.06

Abbreviations: HUM = Humana; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standardised difference; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.1. Baseline Demographics, Unmatched [Humana 1179 Curated (RA) - Rheumatoid Arthritis].docx

Table 4_HUM. Baseline Demographics Incident Serious Infections, Matched [HUM]

	Baricitinib			TNFi (N=53)	Std. Diff. (Any vs TNFi)	Total (N=106)
	Any (N=53)	4-mg (N=0)	2-mg (N=53)			
Age [yrs]						
N	53	-	53	53		106
Mean (SD)	64.17 (11.00)	-	64.17 (11.00)	65.51 (11.30)	0.12	64.84 (11.12)
Median	67.00 [57.00, 73.50]	-	67.00 [57.00, 73.50]	67.00 [55.50, 74.50]		67.00 [56.00, 74.00]
Min, Max	29.0, 78.0	-	29.0, 78.0	44.0, 86.0		29.0, 86.0
≥ 65 years	29 (54.7%)	-	29 (54.7%)	32 (60.4%)	0.12	61 (57.5%)
Sex						
Male	[redacted]	-	[redacted]	[redacted]	0.11	16 (15.1%)
Female	[redacted]	-	[redacted]	[redacted]	0.11	90 (84.9%)

Abbreviations: HUM = Humana; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\(v2) 5. Table 6.4 - Baseline Demographics Incident Serious Infections, Matched [Humana 1179 Curated (RA) - Rheumatoid Arthritis.docx

Table 6_HUM. Clinical History at Baseline, Unmatched Cohorts [HUM]

Characteristic [a,b]	Baricitinib [c] (N=89)	TNFi (N=154)	Std. Diff.
Clinical Conditions during baseline			
Cancer	[redacted]	15 (9.7%)	0.07
NMSC	[redacted]	0 (0.0%)	0.15
Chronic lung disease	15 (16.9%)	35 (22.7%)	0.15
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	[redacted]	[redacted]	0.02
Cardiovascular revascularization	0 (0.0%)	[redacted]	0.11
Congestive heart failure, hospitalized	[redacted]	[redacted]	0.05
Coronary artery disease	[redacted]	15 (9.7%)	0.01
Ischemic heart disease	[redacted]	15 (9.7%)	0.01
Unstable angina	0 (0.0%)	[redacted]	0.11
Ventricular arrhythmia	[redacted]	[redacted]	0.07
Diabetes Mellitus	25 (28.1%)	43 (27.9%)	0.00
Type I	0 (0.0%)	[redacted]	0.16
Type II	24 (27.0%)	43 (27.9%)	0.02
Dyslipidaemia	44 (49.4%)	67 (43.5%)	0.12
Hypertension	49 (55.1%)	87 (56.5%)	0.03
Immune disorders	13 (14.6%)	20 (13.0%)	0.05
AIDS/HIV	0 (0.0%)	0 (0.0%)	-
Antiphospholipid syndrome	0 (0.0%)	[redacted]	0.16
SLE	[redacted]	[redacted]	0.18
Primary Sjögren syndrome	[redacted]	12 (7.8%)	0.09
Liver disorder	[redacted]	[redacted]	0.11
Obesity	38 (42.7%)	47 (30.5%)	0.26
Pregnancy	0 (0.0%)	[redacted]	0.11
RA severity (CIRAS Index), mean (SD)	4.18 (1.17)	4.25 (1.22)	0.05
Smoking	19 (21.3%)	36 (23.4%)	0.05
Surgery, trauma & hospitalization, recent	[redacted]	11 (7.1%)	0.06
TIA	0 (0.0%)	[redacted]	0.20
DMARDs			
cDMARDs, during baseline			
n, total	56 (62.9%)	97 (63.0%)	0.00
Mean (SD)	0.80 (0.74)	0.90 (0.82)	0.13
Median	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-
Min, Max	0.0, 3.0	0.0, 3.0	-
>1 cDMARD concomitantly	11 (12.4%)	34 (22.1%)	0.26
Hydroxychloroquine	16 (18.0%)	33 (21.4%)	0.09
Leflunomide	14 (15.7%)	21 (13.6%)	0.06
Methotrexate	26 (29.2%)	69 (44.8%)	0.33
Minocycline	[redacted]	[redacted]	0.25
Sulfasalazine	[redacted]	[redacted]	0.08
bDMARDs, during baseline[a]			
n, total	41 (46.1%)	147 (95.5%)	1.29

Characteristic [a,b]	Baricitinib [c] (N=89)	TNFi (N=154)	Std. Diff.
Mean (SD)	0.51 (0.59)	1.08 (0.30)	1.24
Median	0.00 [0.00, 1.00]	1.00 [1.00, 1.00]	-
Min, Max	0.0, 2.0	1.0, 3.0	-
cDMARDs, concomitant	21 (23.6%)	82 (53.2%)	0.64
abatacept	[redacted]	[redacted]	0.12
adalimumab[d]	[redacted]	46 (29.9%)	0.81
anakinra	[redacted]	0 (0.0%)	0.21
certolizumab pegol[d]	[redacted]	17 (11.0%)	0.36
etanercept[d]	[redacted]	39 (25.3%)	0.52
golimumab[d]	[redacted]	24 (15.6%)	0.33
infliximab[d]	[redacted]	21 (13.6%)	0.23
rituximab	[redacted]	0 (0.0%)	0.15
sarilumab	[redacted]	[redacted]	0.25
tocilizumab	[redacted]	0 (0.0%)	0.38
Other Prescription Medications			
Antibiotics	56 (62.9%)	72 (46.8%)	0.33
Antidiabetic agents	21 (23.6%)	32 (20.8%)	0.07
Insulins	[redacted]	[redacted]	0.14
Non-insulins	18 (20.2%)	30 (19.5%)	0.02
Aspirin	[redacted]	[redacted]	0.05
Cardiovascular			
Anticoagulant	[redacted]	[redacted]	0.21
Antihypertensives	59 (66.3%)	92 (59.7%)	0.14
Antiplatelet	[redacted]	[redacted]	0.01
Nitrates	[redacted]	[redacted]	0.01
Hormonal			
HRT	[redacted]	12 (7.8%)	0.08
Oral Contraceptives	0 (0.0%)	[redacted]	0.20
SERMs	0 (0.0%)	0 (0.0%)	-
Lipid-lowering agents			
Bile acid binding	[redacted]	[redacted]	0.02
Cholesterol absorption inhibitor	[redacted]	[redacted]	0.02
Fibrates	[redacted]	[redacted]	0.15
Niacin	0 (0.0%)	0 (0.0%)	-
Omega-3 fatty acids	[redacted]	[redacted]	0.02
Statins	31 (34.8%)	54 (35.1%)	0.01
Rheumatoid arthritis-related			
Cox-2 Inhibitor	[redacted]	12 (7.8%)	0.19
Glucocorticosteroid	63 (70.8%)	96 (62.3%)	0.18
Vaccinations	29 (32.6%)	60 (39.0%)	0.13

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = conventional disease-modifying antirheumatic disease; CIRAS = Claims-based Index for Rheumatoid Arthritis Severity ; HIV = human immunodeficiency virus ; HRT = hormone replacement therapy; HUM = Humana; Max = maximum; Min =minimum; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective oestrogen receptor modifier; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics, except for bDMARDs, are measured during the 6 months prior to initiation of study medication including the date at which the qualifying exposure of baricitinib or TNFi occurs (index date). bDMARDs are measured from the 6 months prior to the initiation of study medication until the day prior to baricitinib or the index TNFi exposure, excluding the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d TNF inhibitors.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.6. - Clinical History at Baseline, Unmatched Cohorts [Humana 1179 Curated (RA)]_.docx

Table 9_HUM. Clinical Characteristics Incident Serious Infection Cohorts, Matched [HUM]

Characteristic[a,b]	Baricitinib[c] (N=53)	TNFi (N=53)	Std. Diff.
Clinical Conditions during Baseline			
Cancer	[redacted]	[redacted]	0.13
NMSC	[redacted]	0 (0.0%)	0.20
Chronic lung disease	12 (22.6%)	11 (20.8%)	0.05
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	[redacted]	[redacted]	0.14
Cardiovascular revascularization	0 (0.0%)	[redacted]	0.20
Congestive heart failure, hospitalized	[redacted]	0 (0.0%)	0.20
Coronary artery disease	[redacted]	[redacted]	0.06
Ischemic heart disease	[redacted]	[redacted]	0.06
Unstable angina	0 (0.0%)	[redacted]	0.20
Ventricular arrhythmia	[redacted]	[redacted]	0.08
Diabetes Mellitus	19 (35.8%)	17 (32.1%)	0.08
Type I	0 (0.0%)	0 (0.0%)	-
Type II	19 (35.8%)	17 (32.1%)	0.08
Dyslipidaemia	28 (52.8%)	24 (45.3%)	0.15
Hypertension	34 (64.2%)	32 (60.4%)	0.08
Immune disorders	[redacted]	[redacted]	0.19
AIDS/HIV	0 (0.0%)	0 (0.0%)	-
Antiphospholipid syndrome	0 (0.0%)	[redacted]	0.20
SLE	[redacted]	[redacted]	0.33
Primary Sjögren syndrome	[redacted]	[redacted]	0.00
Liver disorder	0 (0.0%)	0 (0.0%)	-
Obesity	18 (34.0%)	19 (35.8%)	0.04
Pregnancy	0 (0.0%)	0 (0.0%)	-
RA severity (CIRAS Index), mean (SD)	3.97 (1.25)	3.98 (1.18)	0.01
Smoking	[redacted]	12 (22.6%)	0.14
Surgery, trauma & hospitalization, recent	[redacted]	[redacted]	0.08
TIA	0 (0.0%)	[redacted]	0.20
DMARDs			
cDMARDs, during baseline			
n, total	34 (64.2%)	35 (66.0%)	0.04
Mean (SD)	0.75 (0.68)	0.98 (0.87)	0.29
Median	1.00 [0.00, 1.00]	1.00 [0.00, 1.50]	-
Min, Max	0.0, 3.0	0.0, 3.0	-
>1 cDMARD concomitantly	[redacted]	13 (24.5%)	0.41
Hydroxychloroquine	[redacted]	[redacted]	0.11
Leflunomide	[redacted]	[redacted]	0.06
Methotrexate	16 (30.2%)	25 (47.2%)	0.35
Minocycline	[redacted]	[redacted]	0.20
Sulfasalazine	[redacted]	[redacted]	0.12
bDMARDs, during baseline[a]			
n, total	[redacted]	51 (96.2%)	2.83

Characteristic[a,b]	Baricitinib[c] (N=53)	TNFi (N=53)	Std. Diff.
Mean (SD)	0.15 (0.36)	1.17 (0.38)	2.75
Median	0.00 [0.00, 0.00]	1.00 [1.00, 1.00]	-
Min, Max	0.0, 1.0	1.0, 2.0	-
cDMARDs, concomitant	[redacted]	33 (62.3%)	1.49
abatacept	[redacted]	[redacted]	0.23
adalimumab[d]	0 (0.0%)	17 (32.1%)	0.97
anakinra	0 (0.0%)	0 (0.0%)	-
certolizumab pegol[d]	[redacted]	[redacted]	0.39
etanercept[d]	[redacted]	[redacted]	0.58
golimumab[d]	[redacted]	11 (20.8%)	0.62
infliximab[d]	[redacted]	[redacted]	0.39
rituximab	0 (0.0%)	0 (0.0%)	-
sarilumab	0 (0.0%)	[redacted]	0.40
tocilizumab	[redacted]	0 (0.0%)	0.28
Other Prescription Medications			
Antibiotics	30 (56.6%)	28 (52.8%)	0.08
Antidiabetic agents	17 (32.1%)	15 (28.3%)	0.08
Insulins	[redacted]	[redacted]	0.20
Non-insulins	14 (26.4%)	14 (26.4%)	0.00
Aspirin	0 (0.0%)	0 (0.0%)	-
Cardiovascular			
Anticoagulant	[redacted]	[redacted]	0.31
Antihypertensives	38 (71.7%)	32 (60.4%)	0.24
Antiplatelet	[redacted]	[redacted]	0.16
Nitrates	[redacted]	[redacted]	0.11
Hormonal			
HRT	[redacted]	[redacted]	0.08
Oral Contraceptives	0 (0.0%)	[redacted]	0.20
SERMs	0 (0.0%)	0 (0.0%)	-
Lipid-lowering agents			
Bile acid binding	[redacted]	[redacted]	0.09
Cholesterol absorption inhibitor	[redacted]	0 (0.0%)	0.20
Fibrates	[redacted]	[redacted]	0.11
Niacin	0 (0.0%)	0 (0.0%)	-
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	-
Statins	17 (32.1%)	22 (41.5%)	0.20
Rheumatoid arthritis-related			
Cox-2 Inhibitor	[redacted]	[redacted]	0.00
Glucocorticosteroid	33 (62.3%)	38 (71.7%)	0.20
Vaccinations	16 (30.2%)	22 (41.5%)	0.24

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = conventional disease-modifying antirheumatic drug; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; HUM = Humana; Max = maximum; Min =minimum; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modifier; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics, except for bDMARDs, are measured during the 6 months prior to initiation of study medication including the date at which the qualifying exposure of baricitinib or TNFi occurs (index date). bDMARDs are measured from the 6 months prior to the initiation of study medication until the day prior to baricitinib or the index TNFi exposure, excluding the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d TNF inhibitors.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.9. - Clinical Characteristics Incident Serious Infection Cohorts, Matched [Humana 1179 Curated (RA)].docx

Table 11A_HUM. Baseline Healthcare Resource Utilization, Unmatched [HUM]

Type of Resource Use	Baricitinib (N=89)	TNFi (N=154)	Std. Diff.
Physician Office Visits			
n, patients	82 (92.1%)	145 (94.2%)	0.08
n, events	2160.0	2613	
Mean (SD)	24.27 (26.28)	16.97 (19.31)	0.32
Median	14.00 [5.00, 35.50]	11.50 [4.00, 20.50]	
Min, Max	0.0, 126.0	0.0, 104.0	
Rheumatologist Visits			
n, patients	74 (83.1%)	131 (85.1%)	0.05
n, events	626	1425	
Mean (SD)	7.03 (9.51)	9.25 (14.55)	0.18
Median	4.00 [2.00, 8.50]	4.00 [2.00, 12.00]	
Min, Max	0.0, 67.0	0.0, 139.0	
Other Outpatient Visits			
n, patients	88 (98.9%)	150 (97.4%)	0.11
n, events	2962	5167	
Mean (SD)	33.28 (30.46)	33.55 (32.30)	0.01
Median	24.00 [11.50, 44.00]	27.00 [11.00, 45.25]	
Min, Max	0.0, 172.0	0.0, 294.0	
Inpatient Visits			
n, patients	[redacted] (CCI %)	18 (11.7%)	0.17
n, events	368	653	
Mean (SD)	4.13 (19.79)	4.24 (17.69)	0.01
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 145.0	0.0, 148.0	
ED Visits			
n, patients	23 (25.8%)	38 (24.7%)	0.03
n, events	369	835	
Mean (SD)	4.15 (12.03)	5.42 (18.15)	0.08
Median	0.00 [0.00, 1.00]	0.00 [0.00, 0.25]	
Min, Max	0.0, 89.0	0.0, 167.0	

Abbreviations: ED = emergency department; HUM = Humana; Max = maximum; Min = minimum; N = number of patients in the specified category; RA = rheumatoid arthritis; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.11A. Baseline Healthcare Resource Utilization, Unmatched [Humana 1179 Curated (RA) - Rheumatoid Arthritis].docx

Table 11B_HUM. Baseline Healthcare Resource Utilization, Unmatched [HUM], count at most one visit per day[1]

Type of Resource Use	Baricitinib (N=89)	TNFi (N=154)	Std. Diff.
Physician Office Visits[1]			
n, patients	82 (92.1%)	145 (94.2%)	0.08
n, events	800	1,154	
Mean (SD)	8.99 (7.95)	7.49 (7.63)	0.19
Median	7.00 [3.00, 13.50]	6.00 [2.00, 10.00]	
Min, Max	0.0, 33.0	0.0, 50.0	
Rheumatologist Visits[1]			
n, patients	74 (83.1%)	131 (85.1%)	0.05
n, events	262	453	
Mean (SD)	2.94 (3.24)	2.94 (2.30)	0.00
Median	3.00 [2.00, 4.00]	2.00 [1.00, 4.00]	
Min, Max	0.0, 28.0	0.0, 10.0	
Other Outpatient Visits[1]			
n, patients	88 (98.9%)	150 (97.4%)	0.11
n, events	637	1,257	
Mean (SD)	7.16 (7.48)	8.16 (8.19)	0.13
Median	5.00 [3.00, 9.00]	6.00 [3.00, 10.00]	
Min, Max	0.0, 55.0	0.0, 57.0	
Inpatient Visits[1]			
n, patients	[redacted] (CCI %)	18 (11.7%)	0.17
n, events	58	128	
Mean (SD)	0.65 (3.02)	0.83 (3.28)	0.06
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 17.0	0.0, 24.0	
ED Visits[1]			
n, patients	23 (25.8%)	38 (24.7%)	0.03
n, events	41	91	
Mean (SD)	0.46 (1.02)	0.59 (1.48)	0.10
Median	0.00 [0.00, 1.00]	0.00 [0.00, 0.25]	
Min, Max	0.0, 6.0	0.0, 10.0	

Abbreviations: ED = emergency department; HUM = Humana; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

[1] In this table, results describe utilization of healthcare where a maximum of one event was allowed per day. In the PS matching analyses, multiple claims on the same day were allowed to capture additional information on the amount of services received in a given visit. These results are presented in table 6.11A.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.11B (count at most one visit per day). Baseline Healthcare Resource Utilization, Unmatched [Humana 1179 Curated (RA) - Rheumatoid Arthritis].docx

Table 12A_HUM. - Baseline Healthcare Resource Utilization Primary VTE Cohorts, Matched [HUM]

Type of Resource Use	Baricitinib (N=49)	TNFi (N=49)	Std. Diff.
Physician Office Visits			
n, patients	43 (87.8%)	46 (93.9%)	0.21
n, events	789	877	
Mean (SD)	16.10 (20.01)	17.90 (19.32)	0.09
Median	7.00 [3.00, 21.50]	13.00 [4.50, 19.50]	
Min, Max	0.0, 93.0	0.0, 87.0	
Rheumatologist Visits			
n, patients	39 (79.6%)	41 (83.7%)	0.11
n, events	338	371	
Mean (SD)	6.90 (7.99)	7.57 (8.16)	0.08
Median	4.00 [1.50, 10.50]	6.00 [2.00, 9.50]	
Min, Max	0.0, 34.0	0.0, 39.0	
Other Outpatient Visits			
n, patients	48 (98.0%)	49 (100.0%)	0.20
n, events	1508	1574	
Mean (SD)	30.78 (32.78)	32.12 (21.60)	0.05
Median	22.00 [9.00, 40.00]	28.00 [14.00, 45.00]	
Min, Max	0.0, 172.0	1.0, 111.0	
Inpatient Visits			
n, patients	[redacted] (CCI %)	[redacted] (CCI %)	0.17
n, events	214	12	
Mean (SD)	4.37 (21.91)	0.24 (1.27)	0.27
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 145.0	0.0, 8.0	
ED Visits			
n, patients	[redacted] (CCI %)	[redacted] (CCI %)	0.00
n, events	172	123	
Mean (SD)	3.51 (13.67)	2.51 (7.22)	0.09
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 89.0	0.0, 37.0	

Abbreviations: ED = emergency department; HUM = Humana; Max = maximum; Min = minimum; N = number of patients in the specified category; RA = rheumatoid arthritis; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\ 5. Table 6.12A. Baseline Healthcare Resource Utilization, Primary VTE Cohorts, Matched [Humana 1179 Curated (RA) - Rheumatoid Arthritis].docx

Table 13A_HUM. Baseline Healthcare Resource Utilization MACE Cohorts, Matched [HUM]

Type of Resource Use	Baricitinib (N=51)	TNFi (N=51)	Std. Diff.
Physician Office Visits			
n, patients	45 (88.2%)	48 (94.1%)	0.21
n, events	939	975	
Mean (SD)	18.41 (21.10)	19.12 (21.57)	0.03
Median	11.00 [3.00, 24.00]	11.00 [5.00, 23.00]	
Min, Max	0.0, 77.0	0.0, 87.0	
Rheumatologist Visits			
n, patients	40 (78.4%)	42 (82.4%)	0.10
n, events	137	147	
Mean (SD)	2.69 (4.00)	2.88 (2.27)	0.06
Median	2.00 [1.00, 3.00]	3.00 [1.00, 4.00]	
Min, Max	0.0, 28.0	0.0, 10.0	
Other Outpatient Visits			
n, patients	50 (98.0%)	49 (96.1%)	0.12
n, events	1927	1473	
Mean (SD)	31.78 (34.64)	28.88 (22.41)	0.10
Median	22.00 [8.00, 41.00]	25.00 [11.00, 40.00]	
Min, Max	0.0, 172.0	0.0, 93.0	
Inpatient Visits			
n, patients	[redacted] (CCI [redacted]%)	[redacted] (CCI [redacted]%)	0.00
n, events	214	267	
Mean (SD)	4.20 (21.49)	5.24 (22.96)	0.05
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 145.0	0.0, 148.0	
ED Visits			
n, patients	12 (23.5%)	[redacted] (CCI [redacted]%)	0.15
n, events	227	97	
Mean (SD)	4.45 (13.99)	1.90 (7.18)	0.23
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 89.0	0.0, 46.0	

Abbreviations: ED = emergency department; HUM = Humana; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.13A. Baseline Healthcare Resource Utilization MACE Cohorts, Matched [Humana 1179 Curated (RA) - Rheumatoid Arthritis].docx

Table 14A_HUM. Baseline Healthcare Resource Utilization Serous Infection Cohorts, Matched [HUM]

Type of Resource Use	Baricitinib (N=53)	TNFi (N=53)	Std. Diff.
Physician Office Visits			
n, patients	48 (90.6%)	50 (94.3%)	0.14
n, events	1108	933	
Mean (SD)	20.91 (21.91)	17.60 (18.50)	0.16
Median	13.00 [4.50, 32.50]	12.00 [5.00, 23.50]	
Min, Max	0.0, 76.0	0.0, 76.0	
Rheumatologist Visits			
n, patients	42 (79.2%)	42 (79.2%)	0.00
n, events	354	430	
Mean (SD)	6.68 (7.28)	8.11 (9.82)	0.17
Median	4.00 [1.00, 10.50]	4.00 [2.00, 10.00]	
Min, Max	0.0, 34.0	0.0, 41.0	
Other Outpatient Visits			
n, patients	52 (98.1%)	53 (100.0%)	0.20
n, events	1980	1961	
Mean (SD)	37.36 (36.47)	37.00 (22.62)	0.01
Median	23.00 [10.50, 53.50]	34.00 [15.50, 52.50]	
Min, Max	0.0, 172.0	7.0, 88.0	
Inpatient Visits			
n, patients	[redacted] (CCI%)	[redacted] (CCI%)	0.06
n, events	303	174	
Mean (SD)	5.72 (23.82)	3.28 (20.39)	0.11
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 145.0	0.0, 148.0	
ED Visits			
n, patients	12 (22.6%)	11 (20.8%)	0.05
n, events	256	255	
Mean (SD)	4.83 (15.64)	4.81 (14.22)	0.00
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 89.0	0.0, 70.0	

Abbreviations: ED = emergency department; HUM = Humana; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.14A. Baseline Healthcare Resource Utilization Incident Serious Infection Cohorts, Matched [Humana 1179 Curated (RA) - Rheumatoid Arthritis].docx

Table 14B_HUM. Baseline Healthcare Resource Utilization Serious Infection Cohorts, Matched [HUM], count at most one visit per day[1]

Type of Resource Use	Baricitinib (N=53)	TNFi (N=53)	Std. Diff.
Physician Office Visits[1]			
n, patients	48 (90.6%)	50 (94.3%)	0.14
n, events	451	421	
Mean (SD)	8.51 (7.96)	7.94 (7.84)	0.07
Median	7.00 [3.00, 13.00]	6.00 [3.00, 11.00]	
Min, Max	0.0, 31.0	0.0, 32.0	
Rheumatologist Visits[1]			
n, patients	42 (79.2%)	42 (79.2%)	0.00
n, events	144	164	
Mean (SD)	2.72 (2.15)	3.09 (2.47)	0.16
Median	3.00 [1.00, 4.00]	3.00 [1.00, 5.00]	
Min, Max	0.0, 8.0	0.0, 10.0	
Other Outpatient Visits[1]			
n, patients	52 (98.1%)	53 (100.0%)	0.20
n, events	428	443	
Mean (SD)	8.08 (9.46)	8.36 (5.23)	0.04
Median	5.00 [3.00, 9.00]	7.00 [4.50, 11.00]	
Min, Max	0.0, 55.0	1.0, 26.0	
Inpatient Visits[1]			
n, patients	[redacted] (CCI%)	[redacted] (CCI%)	0.06
n, events	58	24	
Mean (SD)	1.09 (3.86)	0.45 (2.09)	0.21
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 17.0	0.0, 13.0	
ED Visits[1]			
n, patients	12 (22.6%)	11 (20.8%)	0.05
n, events	30	29	
Mean (SD)	0.57 (1.29)	0.55 (1.56)	0.01
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 6.0	0.0, 8.0	

Abbreviations: ED = emergency department; HUM = Humana; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

1 In this table, results describe utilization of healthcare where a maximum of one event was allowed per day. In the PS matching analyses, multiple claims on the same day were allowed to capture additional information on the amount of services received in a given visit. These results are presented in table 6.14A.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.14B (count at most one visit per day). Baseline HCRU Serious Infection Cohorts, Matched [Humana 1179 Curated (RA)].docx

Table 16_HUM. Baseline Prevalence of Outcomes [HUM]

Outcome in Each Matched Cohort[a,c,d]	Unmatched			Matched			
	Baricitinib[b]	TNFi	Std. Diff	Baricitinib[b]	TNFi	Std. Diff	Total
VTE	N=90	N=154	-	N=53	N=53	-	N=106
Main case definition in baseline	CCI (CCI%)	0 (0.0%)	0.15	CCI (CCI%)	0 (0.0%)	0.20	CCI (CCI%)
Alternate case definition I in baseline	CCI (CCI%)	0 (0.0%)	0.15	CCI (CCI%)	0 (0.0%)	0.20	CCI (CCI%)
Alternative case definition II in baseline	CCI (CCI%)	CCI (CCI%)	0.07	CCI (CCI%)	CCI (CCI%)	0.00	CCI (CCI%)
MACE	N=90	N=154	-	N=51	N=51	-	N=102
MACE in baseline	CCI (CCI%)	CCI (CCI%)	0.05	0 (0.0%)	CCI (CCI%)	0.20	CCI (CCI%)
Serious Infection	N=97	N=169	-	N=54	N=54	-	N=108
Serious Infection in baseline	CCI (CCI%)	CCI (CCI%)	0.12	CCI (CCI%)	CCI (CCI%)	0.11	CCI (CCI%)
Hospitalized Tuberculosis	N=97	N=169	-	N=54	N=54	-	N=108
Hospitalized Tuberculosis in baseline	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)	-	0 (0.0%)

Abbreviations: HUM = Humana; MACE = major adverse cardiovascular event, defined as hospital primary discharge diagnosis code of acute MI or hospital primary discharge diagnosis code of ischemic or hemorrhagic stroke; N = number of patients in specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism, defined based on the case definitions.

a Baseline prevalence was calculated for each distinct matched cohort for VTE, MACE, serious infection and hospitalized tuberculosis.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c Patients with the prevalent outcomes enumerated in this table are those excluded from the main analyses of each outcome, except for VTE alternative case definitions I and II. Only the VTE main case definition was used as an exclusion criterion in the main analyses.

d In the VTE and MACE analyses, cohorts additionally excluded the use of anticoagulants at the time of cohort entry (see protocol Section 8.7.7), resulting in a different N compared to the Serious Infection and Hospitalized Tuberculosis cohorts.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.16. Baseline Prevalence of Outcomes [Humana 1179 Curated (RA) - Rheumatoid Arthritis]_.docx

Table 17_HUM. Duration of Follow-up Period (Days), Unmatched [HUM]

	Baricitinib[a] (N=89)	TNFi (N=154)	Std. Diff.
N	89	154	
Mean (SD)	166.90 (154.02)	166.02 (161.16)	0.01
Median	92.00 [59.00, 264.00]	114.00 [58.00, 210.00]	
Min, Max	5.0, 670.0	5.0, 724.0	

Abbreviations: HUM = Humana ; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be reported for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.17. Duration of Follow-up Period (Days), Unmatched [Humana 1179 Curated (RA)].docx

Table 18_HUM. Duration of Follow-up Period (Days) Primary VTE Cohorts, Matched [HUM]

	Baricitinib[a,b] (N=49)	TNFi (N=49)	Std. Diff.
N	49	49	0
Mean (SD)	147.73 (134.15)	153.20 (138.88)	0.04
Median	85.00 [59.00, 236.00]	114.00 [58.00, 203.50]	
Min, Max	5.0, 523.0	6.0, 542.0	
Reasons for censoring [c]			
Incident event	0	0	-
Medication discontinued	33 (67.3%)	25 (51.0%)	-
Initiated b/tsDMARD	[redacted]	0 (0.0%)	-
End of patient record	14 (28.6%)	17 (34.7%)	-
Death (where available)	0 (0.0%)	0 (0.0%)	-
End of study period (12/31/2020)	[redacted]	[redacted]	-

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; HUM = Humana; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be reported for each dose where numbers of patients are sufficient to warrant separate reporting.

b There were 0 patients with a baricitinib dose of 4 mg. Hence, 100% of the patients presented in this column have a baricitinib dose of 2 mg.

c A single patient can be censored on the same day for multiple reasons, e.g., medication discontinued could also be the same day as initiated b/tsDMARD. Further, additional censoring criteria (e.g., switching medication) were specified in the SAP. For these reasons, the total number of reasons for censoring may be less than or greater than the total number of patients.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.18. Duration of Follow-up Period (Days) Primary VTE Cohorts, Matched [Humana].docx

Table 21_HUM. Duration of Follow-up Period (Days) MACE Cohorts, Matched [HUM]

	Baricitinib[a,b] (N=51)	TNFi (N=51)	Std. Diff.
N	51	51	
Mean (SD)	153.08 (144.31)	182.31 (168.37)	0.19
Median	85.00 [59.00, 243.00]	125.00 [65.00, 225.00]	
Min, Max	5.0, 525.0	4.0, 688.0	
Reasons for censoring			
Incident event	0	2	-
Medication discontinued	34 (66.7%)	19 (37.3%)	-
Initiated b/tsDMARD	0 (0.0%)	[redacted] (%)	-
End of patient record	15 (29.4%)	22 (43.1%)	-
Death (where available)	0 (0.0%)	0 (0.0%)	-
End of study period (12/31/2020)	[redacted] (%)	[redacted] (%)	-

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; HUM = Humana; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = Standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be reported for each dose where numbers of patients are sufficient to warrant separate reporting.

b There were 0 patients with a baricitinib dose of 4 mg. Hence, 100% of the patients presented in this column have a baricitinib dose of 2 mg.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.21. Duration of Follow-up Period (Days) MACE Cohorts, Matched [Humana].docx

Table 22_HUM. Duration of Follow-up Period (Days) Incident Serious Infection Cohorts, Matched [HUM]

	Baricitinib[a,b] (N=53)	TNFi (N=53)	Std. Diff.
N	53	53	
Mean (SD)	136.17 (130.44)	188.02 (150.95)	0.37
Median	59.00 [59.00, 169.50]	140.00 [69.00, 253.50]	
Min, Max	5.0, 523.0	6.0, 628.0	
Reasons for censoring			
Incident event	2	1	-
Medication discontinued	30 (56.6%)	23 (43.4%)	-
Initiated b/tsDMARD	[redacted] (CCI %)	[redacted] (CCI %)	-
End of patient record	18 (34.0%)	20 (37.7%)	-
Death (where available)	0 (0.0%)	0 (0.0%)	-
End of study period (07/05/2021)	[redacted] (CCI %)	[redacted] (CCI %)	-

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; HUM = Humana; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b There were 0 patients with a baricitinib dose of 4 mg. Hence, 100% of the patients presented in this column have a baricitinib dose of 2 mg.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.22. Duration of Follow-up Period (Days) Incident Serious Infection Cohorts, Matched [Humana].docx

Table 39_HUM. Pattern of VTE and Related Diagnostic Codes in Patients with RA [HUM]

Code	Total Patients (CCI)
Pulmonary Embolism	
I26.0 - Pulmonary embolism with acute cor pulmonale	0 (0.0%)
I26.02 - Saddle embolus of pulmonary artery with acute cor pulmonale	0 (0.0%)
I26.09 - Other pulmonary embolism with acute cor pulmonale	0 (0.0%)
I26.9 - Pulmonary embolism without acute cor pulmonale	0 (0.0%)
I26.92 - Saddle embolus of pulmonary artery without acute cor pulmonale	0 (0.0%)
I26.99 - Other pulmonary embolism without acute cor pulmonale	[redacted] (CCI)
Deep Vein Thrombosis, lower	
I80.10 - Phlebitis and thrombophlebitis of unspecified femoral vein	0 (0.0%)
I80.11 - Phlebitis and thrombophlebitis of right femoral vein	0 (0.0%)
I80.13 - Phlebitis and thrombophlebitis of femoral vein, bilateral	0 (0.0%)
I80.211 - Phlebitis and thrombophlebitis of right iliac vein	0 (0.0%)
I80.221 - Phlebitis and thrombophlebitis of right popliteal vein	0 (0.0%)
I80.223 - Phlebitis and thrombophlebitis of popliteal vein, bilateral	0 (0.0%)
I80.232 - Phlebitis and thrombophlebitis of left tibial vein	0 (0.0%)
I80.233 - Phlebitis and thrombophlebitis of tibial vein, bilateral	0 (0.0%)
I80.292 - Phlebitis and thrombophlebitis of other deep vessels of left lower extremity	0 (0.0%)
I80.293 - Phlebitis and thrombophlebitis of other deep vessels of lower extremity, bilateral	0 (0.0%)
I80.3 - Phlebitis and thrombophlebitis of lower extremities, unspecified	0 (0.0%)
I82.419 - Acute embolism and thrombosis of unspecified femoral vein	0 (0.0%)
I82.423 - Acute embolism and thrombosis of iliac vein, bilateral	0 (0.0%)
I82.431 - Acute embolism and thrombosis of right popliteal vein	0 (0.0%)
I82.432 - Acute embolism and thrombosis of left popliteal vein	0 (0.0%)
I82.433 - Acute embolism and thrombosis of popliteal vein, bilateral	0 (0.0%)
I82.441 - Acute embolism and thrombosis of right tibial vein	0 (0.0%)
I82.442 - Acute embolism and thrombosis of left tibial vein	0 (0.0%)
I82.443 - Acute embolism and thrombosis of tibial vein, bilateral	0 (0.0%)
I82.449 - Acute embolism and thrombosis of unspecified tibial vein	0 (0.0%)

Code	Total Patients (CCI)
I82.491 - Acute embolism and thrombosis of other specified deep vein of right lower extremity	0 (0.0%)
I82.4Y1 - Acute embolism and thrombosis of unspecified deep veins of right proximal lower extremity	0 (0.0%)
I82.4Y3 - Acute embolism and thrombosis of unspecified deep veins of proximal lower extremity, bilateral	0 (0.0%)
I82.4Y9 - Acute embolism and thrombosis of unspecified deep veins of unspecified proximal lower extremity	0 (0.0%)
I82.4Z1 - Acute embolism and thrombosis of unspecified deep veins of right distal lower extremity	0 (0.0%)
I82.4Z2 - Acute embolism and thrombosis of unspecified deep veins of left distal lower extremity	0 (0.0%)
I82.4Z3 - Acute embolism and thrombosis of unspecified deep veins of distal lower extremity, bilateral	0 (0.0%)
I80.12 - Phlebitis and thrombophlebitis of left femoral vein	0 (0.0%)
I80.201 - Phlebitis and thrombophlebitis of unspecified deep vessels of right lower extremity	0 (0.0%)
I80.202 - Phlebitis and thrombophlebitis of unspecified deep vessels of left lower extremity	0 (0.0%)
I80.203 - Phlebitis and thrombophlebitis of unspecified deep vessels of lower extremities, bilateral	0 (0.0%)
I80.209 - Phlebitis and thrombophlebitis of unspecified deep vessels of unspecified lower extremity	0 (0.0%)
I80.212 - Phlebitis and thrombophlebitis of left iliac vein	0 (0.0%)
I80.213 - Phlebitis and thrombophlebitis of iliac vein, bilateral	0 (0.0%)
I80.219 - Phlebitis and thrombophlebitis of unspecified iliac vein	0 (0.0%)
I80.222 - Phlebitis and thrombophlebitis of left popliteal vein	0 (0.0%)
I80.229 - Phlebitis and thrombophlebitis of unspecified popliteal vein	0 (0.0%)
I80.231 - Phlebitis and thrombophlebitis of right tibial vein	0 (0.0%)
I80.291 - Phlebitis and thrombophlebitis of other deep vessels of right lower extremity	0 (0.0%)
I80.299 - Phlebitis and thrombophlebitis of other deep vessels of unspecified lower extremity	0 (0.0%)
I82.401 - Acute embolism and thrombosis of unspecified deep veins of right lower extremity	[redacted] (CCI %)
I82.402 - Acute embolism and thrombosis of unspecified deep veins of left lower extremity	0 (0.0%)

Code	Total Patients (CCI)
I82.403 - Acute embolism and thrombosis of unspecified deep veins of lower extremity, bilateral	0 (0.0%)
I82.409 - Acute embolism and thrombosis of unspecified deep veins of unspecified lower extremity	0 (0.0%)
I82.411 - Acute embolism and thrombosis of right femoral vein	0 (0.0%)
I82.412 - Acute embolism and thrombosis of left femoral vein	0 (0.0%)
I82.413 - Acute embolism and thrombosis of femoral vein, bilateral	0 (0.0%)
I82.421 - Acute embolism and thrombosis of right iliac vein	0 (0.0%)
I82.422 - Acute embolism and thrombosis of left iliac vein	0 (0.0%)
I82.429 - Acute embolism and thrombosis of unspecified iliac vein	0 (0.0%)
I82.439 - Acute embolism and thrombosis of unspecified popliteal vein	0 (0.0%)
I82.492 - Acute embolism and thrombosis of other specified deep vein of left lower extremity	0 (0.0%)
I82.493 - Acute embolism and thrombosis of other specified deep vein of lower extremity, bilateral	0 (0.0%)
I82.499 - Acute embolism and thrombosis of other specified deep vein of unspecified lower extremity	0 (0.0%)
I82.4Y2 - Acute embolism and thrombosis of unspecified deep veins of left proximal lower extremity	0 (0.0%)
Deep Vein Thrombosis, upper	
I82.210 - Acute embolism and thrombosis of superior vena cava	0 (0.0%)
I82.601 - Acute embolism and thrombosis of unspecified veins of right upper extremity	0 (0.0%)
I82.621 - Acute embolism and thrombosis of deep veins of right upper extremity	0 (0.0%)
I82.622 - Acute embolism and thrombosis of deep veins of left upper extremity	0 (0.0%)
I82.623 - Acute embolism and thrombosis of deep veins of upper extremity, bilateral	0 (0.0%)
I82.A12 - Acute embolism and thrombosis of left axillary vein	0 (0.0%)
I82.C11 - Acute embolism and thrombosis of right internal jugular vein	0 (0.0%)
I82.C13 - Acute embolism and thrombosis of internal jugular vein, bilateral	0 (0.0%)
I82.C19 - Acute embolism and thrombosis of unspecified internal jugular vein	0 (0.0%)
I82.602 - Acute embolism and thrombosis of unspecified veins of left upper extremity	0 (0.0%)
I82.603 - Acute embolism and thrombosis of unspecified veins of upper extremity, bilateral	0 (0.0%)

Code	Total Patients (CCI)
I82.609 - Acute embolism and thrombosis of unspecified veins of unspecified upper extremity	0 (0.0%)
I82.629 - Acute embolism and thrombosis of deep veins of unspecified upper extremity	0 (0.0%)
I82.A11 - Acute embolism and thrombosis of right axillary vein	0 (0.0%)
I82.A13 - Acute embolism and thrombosis of axillary vein, bilateral	0 (0.0%)
I82.A19 - Acute embolism and thrombosis of unspecified axillary vein	0 (0.0%)
I82.C12 - Acute embolism and thrombosis of left internal jugular vein	0 (0.0%)
Other Venous Thrombosis	
I81 - Portal vein thrombosis	0 (0.0%)
I82.0 - Budd-Chiari syndrome	0 (0.0%)
I82.1 - Thrombophlebitis migrans	0 (0.0%)
I82.3 - Embolism and thrombosis of renal vein	0 (0.0%)
I82.90 - Acute embolism and thrombosis of unspecified vein	0 (0.0%)
I82.B13 - Acute embolism and thrombosis of subclavian vein, bilateral	0 (0.0%)
I80.8 - Phlebitis and thrombophlebitis of other sites	0 (0.0%)
I80.9 - Phlebitis and thrombophlebitis of unspecified site	0 (0.0%)
I82.220 - Acute embolism and thrombosis of inferior vena cava	0 (0.0%)
I82.890 - Acute embolism and thrombosis of other specified veins	0 (0.0%)
I82.B11 - Acute embolism and thrombosis of right subclavian vein	0 (0.0%)
I82.B12 - Acute embolism and thrombosis of left subclavian vein	0 (0.0%)

Abbreviations: ICD-10 = International Classification of Disease, 10th Revision; N = number of patients in the specified category; RA = rheumatoid arthritis; VTE = venous thromboembolism

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.39. Pattern of VTE and Related Diagnostic Codes in Patients with RA [Humana 1179 Curated (RA) - Rheumatoid Arthritis].docx

Table 40_HUM. Clinical Characteristics of RA Patients with VTE, Primary Definition [HUM]

Characteristic[a,b]	Baricitinibc (N=0)	TNFi (N=0)	Total (N=0)
Age (mean) [SD]	- (-)	- (-)	- (-)
Sex			
Female	0 (0.0%)	0 (0.0%)	0 (0.0%)
Male	0 (0.0%)	0 (0.0%)	0 (0.0%)
Clinical Conditions during baseline			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic Lung disease Disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular conditions			
Atrial arrhythmia/ fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dyslipidaemia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertension	0 (0.0%)	0 (0.0%)	0 (0.0%)
Immune disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Primary Sjögren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	- (-)	- (-)	- (-)
Smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)
Surgery, trauma, & hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medication			
Antibiotics	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antidiabetic agents	0 (0.0%)	0 (0.0%)	0 (0.0%)
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			
Antihypertensives	0 (0.0%)	0 (0.0%)	0 (0.0%)

Characteristic[a,b]	Baricitinibc (N=0)	TNFi (N=0)	Total (N=0)
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anticoagulant	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiplatelet	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			
Oral contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERM	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucocorticosteroid	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vaccinations	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post index Occurrence[d]			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hospitalization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Surgery	0 (0.0%)	0 (0.0%)	0 (0.0%)
Trauma	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; Chronic lung disease = asthma, chronic obstructive lung disease, interstitial lung disease, pulmonary fibrosis; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modifier; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = Venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d Except for cancer diagnosed within 90 days of VTE diagnosis, events in this category must have occurred in the 4 weeks immediately prior to VTE (Kline et al. 2017).

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.40. - Clinical Characteristics of RA Patients with VTE, Primary Definition [Humana 1179 Curated (RA) - Rheumatoid Arthritis].docx

Table 41_HUM. Pattern of RA Medication Use in Patients with VTE, Primary Definition [HUM]

Characteristic[a]	Unmatched		Matched		
	Baricitinib[b] (N=CCI)	TNFi (N=CCI)	Baricitinib[b] (N=0)	TNFi (N=0)	Total (N=0)
Baseline Medication					
cDMARDs, during baseline					
n, total	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	0.00 (0.00)	CCI	- (-)	- (-)	- (-)
Median	0.00 [0.00, 0.00]	CCI	- [-, -]	- [-, -]	- [-, -]
Min, Max	0.0, 0.0	CCI	-, -	-, -	-, -
>1 cDMARD concomitantly	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hydroxychloroquine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Leflunomide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Minocycline	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
bDMARDs, during baseline					
n, total	CCI	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	CCI	CCI	- (-)	- (-)	- (-)
Median	CCI	CCI	- [-, -]	- [-, -]	- [-, -]
Min, Max	CCI	CCI	-, -	-, -	-, -
cDMARDs, concomitant	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abatacept	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adalimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Etanercept[c]	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Golimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infliximab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Medication[d]					
Methotrexate, concomitant	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Concomitant cDMARD	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dose change, baricitinib	NA[d]	0 (0.0%)	NA[d]	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; HUM = Humana; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c TNF inhibitors.

d Only baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked 'NA' as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.41. - Pattern of RA Medication Use in Patients with VTE, Primary Definition [Humana].docx

Table 42_HUM. Time to First Event Outcome (days) - VTE, Primary Definition [HUM)]

Time	Unmatched		Matched		
	Baricitinib[a,b] (N=89)	TNFi (N=154)	Baricitinib[a,b] (N=49)	TNFi (N=49)	Total (N=98)
n	89	154	49	49	98
Mean (SD)	59.00 (0.00)	41.00 (0.00)	- (-)	- (-)	- (-)
Median	59.00 [59.00, 59.00]	41.00 [41.00, 41.00]	- [-, -]	- [-, -]	- [-, -]
Min, Max	59.0, 59.0	41.0, 41.0	-,-	-,-	-,-

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Only baricitinib 2-mg dose is available in the US

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.42. Time to First Event Outcome (days) - VTE, Primary Definition [Humana].docx

Table 48_HUM. Comparative Risk of Incident VTE, Primary Definition [HUM]

	TNFi	Baricitinib		p-value
		HR	95%CI	
Base Model[1,2]	Ref	-	-	-

Abbreviations: cDMARD = conventional disease-modifying antirheumatic drug; CI = confidence interval; HR = Cox proportional hazard ratio; Ref = referent group; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

1 Base model - propensity score-matched model with confounders, outcome and baricitinib exposure.

2 Zero events in both the baricitinib exposure and TNFi referent groups preclude analyzing models with additional parameters. The model did not converge.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.48. Comparative Risk of Incident VTE, Primary Definition [Humana 1179 Curated (RA) - Rheumatoid Arthritis], updated base model = PS matched.docx

Table 51_HUM. Clinical Characteristics of RA Patients with MACE [HUM]

Characteristic[a,b]	Baricitinib[c] (N=0)	TNFi (N=CCI	Total (N=CCI
Age (mean) [SD]	- (-)	66.50 (7.78)	66.50 (7.78)
Sex			
Female	0 (0.0%)	CCI	CCI
Male	0 (0.0%)	CCI	CCI
Clinical Conditions during baseline			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic lung disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	0 (0.0%)	CCI	CCI
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	0 (0.0%)	CCI	CCI
Dyslipidaemia	0 (0.0%)	CCI	CCI
Hypertension	0 (0.0%)	CCI	CCI
Immune disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Primary Sjögren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	- (-)	4.69 (1.13)	4.69 (1.13)
Smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)
Surgery, Trauma, & Hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medications			
Antibiotics	0 (0.0%)	CCI	CCI
Antidiabetic agents	0 (0.0%)	CCI	CCI
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-insulins	0 (0.0%)	CCI	CCI
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			
Anticoagulant	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antihypertensives	0 (0.0%)	CCI	CCI
Antiplatelet	0 (0.0%)	CCI	CCI

Characteristic[a,b]	Baricitinib[c] (N=0)	TNFi (N=CCI	Total (N=CCI
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			
Oral contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERM	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	0 (0.0%)	CCI	CCI
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	CCI	CCI
Glucocorticosteroid	0 (0.0%)	CCI	CCI
Vaccinations	0 (0.0%)	CCI	CCI
Post-index Occurrence[d]			
Methotrexate, concomitant	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modifier; SLE = systemic lupus erythematosus; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d Events in this category must have occurred in the 7 days immediately prior to MACE.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.51. - Clinical Characteristics of RA Patients with MACE [Humana 1179 Curated (RA) - Rheumatoid Arthritis]_.docx

Table 52_HUM. Pattern of RA Medication Use in Patients with MACE [HUM]

Characteristic[a]	Unmatched		Matched		
	Baricitinib[b] (N=0)	TNFi (N=CCI	Baricitinib[b] (N=0)	TNFi (N=CCI	Total (N=CCI
Baseline Medication					
cDMARDs, during baseline					
n, total	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	- (-)	0.00 (0.00)	- (-)	0.00 (0.00)	0.00 (0.00)
Median	- [-, -]	0.00 [0.00, 0.00]	- [-, -]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]
Min, Max	-, -	0.0, 0.0	-, -	0.0, 0.0	0.0, 0.0
>1 cDMARD concomitantly	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hydroxychloroquine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Leflunomide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
bDMARDs, during baseline					
n, total	0 (0.0%)	CCI (CCI	0 (0.0%)	CCI (CCI	CCI (CCI
Mean (SD)	- (-)	2.00 (0.00)	- (-)	2.00 (0.00)	2.00 (0.00)
Median	- [-, -]	2.00 [2.00, 2.00]	- [-, -]	2.00 [2.00, 2.00]	2.00 [2.00, 2.00]
Min, Max	-, -	2.0, 2.0	-, -	2.0, 2.0	2.0, 2.0
cDMARDs, concomitant	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abatacept	0 (0.0%)	CCI (CCI	0 (0.0%)	CCI (CCI	CCI (CCI
Adalimumab[c]	0 (0.0%)	CCI (CCI	0 (0.0%)	CCI (CCI	CCI (CCI
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	CCI (CCI	0 (0.0%)	CCI (CCI	CCI (CCI
Etanercept[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Golimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infliximab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Medication[d]					
Methotrexate, concomitant	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Concomitant cDMARD	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dose change, baricitinib	NA[d]	0 (0.0%)	NA[d]	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis code of acute myocardial infarction or ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c TNF inhibitors.

d Only baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked 'NA' as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.52. - Pattern of RA Medication Use in Patients with MACE [Humana].docx

Table 53_HUM. Time to First MACE (Days) [HUM]

	Unmatched		Matched		
	Baricitinib[a,b] (N=89)	TNFi (N=153)	Baricitinib[a,b] (N=51)	TNFi (N=51)	Total (N=102)
n	89	153	51	51	102
Mean (SD)	- (-)	60.50 (79.90)	- (-)	60.50 (79.90)	60.50 (79.90)
Median	- [-, -]	60.50 [4.00, 117.00]	- [-, -]	60.50 [4.00, 117.00]	60.50 [4.00, 117.00]
Min, Max	-,-	4.0, 117.0	-,-	4.0, 117.0	4.0, 117.0

Abbreviations: HUM = Humana; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis code of acute myocardial infarction or ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Only baricitinib 2-mg dose is available in the US

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.53. - Time to First MACE (Days) [Humana].docx

Table 55_HUM. Comparative Risk of MACE [HUM]

	TNFi	Baricitinib HR	95%CI	p-value
Base Model[1,2]	Ref	<0.001	<0.001, >999.999	0.90

Abbreviations: cDMARD = conventional disease-modifying antirheumatic drug; CI = confidence interval; HR = Cox proportional hazard ratio; Ref = referent group; VTE = venous thromboembolism.

1 Base model - propensity score-matched model with confounders, outcome and baricitinib exposure.

2 Zero outcome events in the Baricitinib exposed group preclude the interpretation of the HR.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.55. - Comparative Risk of MACE [Humana 1179 Curated (RA) - Rheumatoid Arthritis].docx

Table 56_HUM. Clinical Characteristics of RA Patients with Incident Serious Infections [HUM]

Characteristics[a,b]	Baricitinib[c] (N=CCI	TNFi (N=CCI	Total (N=CCI
Age (mean) [SD]	69.50 (7.78)	72.00 (0.00)	70.33 (5.69)
Sex			
Female	CCI (CCI	0 (0.0%)	CCI (CCI
Male	0 (0.0%)	CCI (CCI	CCI (CCI
Clinical Conditions during baseline			
Cancer	CCI (50.0%)	0 (0.0%)	CCI (CCI
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic Lung disease	CCI (50.0%)	CCI (CCI	CCI (CCI
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive Heart Failure, hospitalized	CCI (CCI	0 (0.0%)	CCI (CCI
Coronary artery disease	CCI (CCI	0 (0.0%)	CCI (CCI
Ischemic heart disease	CCI (CCI	0 (0.0%)	CCI (CCI
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	CCI (CCI	CCI (CCI
Diabetes Mellitus	CCI (CCI	CCI (CCI	CCI (CCI
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	CCI (CCI	CCI (CCI	CCI (CCI
Dyslipidaemia	CCI (CCI	0 (0.0%)	CCI (CCI
Hypertension	CCI (CCI	CCI (CCI	CCI (CCI
Immune disorders	CCI (CCI	0 (0.0%)	CCI (CCI
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	CCI (CCI	0 (0.0%)	CCI (CCI
Primary Sjögren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	CCI (CCI	CCI (CCI	CCI (CCI
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	4.30 (1.43)	3.26 (0.00)	3.95 (1.18)
Smoking	0 (0.0%)	CCI (CCI	CCI (CCI
Surgery, Trauma, & Hospitalization, recent	CCI (CCI	CCI (CCI	CCI (CCI
TIA	0 (0.0%)	CCI (CCI	CCI (CCI
Other Prescription Medications			
Antibiotics	CCI (CCI	CCI (CCI	CCI (CCI
Antidiabetic agents	CCI (CCI	CCI (CCI	CCI (CCI
Insulins	CCI (CCI	CCI (CCI	CCI (CCI
Non-insulins	CCI (CCI	CCI (CCI	CCI (CCI
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			

Characteristics[a,b]	Baricitinib[c] (N=CCI	TNFi (N=CCI	Total (N=CCI
Anticoagulant	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antihypertensives	CCI	CCI	CCI
Antiplatelet	0 (0.0%)	CCI	CCI
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oral Contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERMs	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	CCI	0 (0.0%)	CCI
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	CCI	CCI	CCI
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucocorticosteroid	CCI	CCI	CCI
Vaccinations	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; HUM = Humana; N = number of patients in the analysis in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modifier; SLE = systemic lupus erythematosus; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.56. Clinical Characteristics of RA Patients with Incident Serious Infections [Humana 1179 Curated (RA) - Rheumatoid Arthritis].docx

Table 57_HUM. Pattern of RA Medication Use in Patients with Serious Infection Event [HUM]

Characteristic[a]	Unmatched		Matched		
	Baricitinib[b] (N=CCI)	TNFi (N=CCI)	Baricitinib[b] (N=CCI)	TNFi (N=CCI)	Total (N=CCI)
Baseline Medication DMARDS					
cDMARDs, during baseline					
n, total	0 (0.0%)	CCI	0 (0.0%)	CCI	CCI
Mean (SD)	0.00 (0.00)	CCI	0.00 (0.00)	CCI	CCI
Median	0.00 [0.00, 0.00]	CCI	0.00 [0.00, 0.00]	CCI	CCI
Min, Max	0.0, 0.0	CCI	0.0, 0.0	CCI	CCI
>1 cDMARD concomitantly	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hydroxychloroquine	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Leflunomide	0 (0.0%)	CCI	0 (0.0%)	CCI	CCI
Methotrexate	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
bDMARDs, during baseline					
n, total	CCI	CCI	CCI	CCI	CCI
Mean (SD)	CCI	CCI	0.50 (0.71)	CCI	CCI
Median	CCI	CCI	CCI	CCI	CCI
Min, Max	CCI	CCI	CCI	CCI	CCI
cDMARDs, concomitant	0 (0.0%)	CCI	0 (0.0%)	CCI	CCI
Abatacept	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adalimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Etanercept[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Golimumab[c]	0 (0.0%)	CCI	0 (0.0%)	CCI	CCI
Infliximab[c]	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	CCI	0 (0.0%)	CCI	0 (0.0%)	CCI
Post-index Medication					
Methotrexate, concomitant	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Concomitant cDMARD	0 (0.0%)	CCI	0 (0.0%)	CCI	CCI
Dose change, baricitinib	NA	0 (0.0%)	NA	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c TNF inhibitors.

d Only baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked 'NA' as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.57. Pattern of RA Medication Use in Patients with Serious Infection Event [Humana].docx

Table 58_HUM. Time to First Serious Infection (Days) [HUM)]

	Unmatched		Matched		
	Baricitinib[a,b] (N=95)	**TNFi (N=162)**	**Baricitinib[a,b] (N=53)**	**TNFi (N=53)**	**Total (N=106)**
n	95	162	53	53	106
Mean (SD)	53.50 (0.71)	155.67 (108.35)	53.50 (0.71)	140.00 (0.00)	82.33 (49.94)
Median	53.50 [53.00, 54.00]	140.00 [56.00, 271.00]	53.50 [53.00, 54.00]	140.00 [140.00, 140.00]	54.00 [53.00, 140.00]
Min, Max	53.0, 54.0	56.0, 271.0	53.0, 54.0	140.0, 140.0	53.0, 140.0

Abbreviations: HUM = Humana; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Only baricitinib 2-mg dose is available in the US

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.58. Time to First Seroius Infection (Days) [Humana 1179 Curated (RA)].docx

Table 60_HUM. Serious Infection Events Per Patient During All Available Follow-up [HUM]

Number of Infections per Person	Unmatched		Matched		
	Baricitinib (N=95)	TNFi (N=162)	Baricitinib (N=53)	TNFi (N=53)	Total (N=106)
0	88 (92.6%)	154 (95.1%)	49 (92.5%)	50 (94.3%)	99 (93.4%)
1	[redacted]	0 (0.0%)	[redacted]	0 (0.0%)	[redacted]
2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
5	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
6	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
>6	[redacted]	[redacted]	[redacted]	[redacted] (5.7%)	[redacted]

Abbreviations: HUM = Humana; N = number of patients in the specified category; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.60. Serious Infection Events Per Patient During All Available Follow-up [Humana 1179 Curated (RA) - Rheumatoid Arthritis].docx

Table 64_HUM. Incidence Rate of Hospitalized TB Event [HUM]

	Unmatched		Matched		
	Baricitinib (N=97)	**TNFi (N=169)**	**Baricitinib (N=54)**	**TNFi (N=54)**	**Total (N=108)**
Overall					
Person-Years	45.45	78.76	18.91	27.61	46.52
TB Events	0.0	0.0	0.0	0.0	0.0
TB Events/100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 8.12	0.00, 4.68	0.00, 19.51	0.00, 13.36	0.00, 7.93

Abbreviations: CI = confidence interval; HUM = Humana; N = number of patients in the specified category; PY = person-years; TB = tuberculosis; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.64. Incidence Rate of Hospitalized TB Event [Humana].docx

II. Variable Ratio Matching

All prior tables presented were based on propensity score matched baricitinib:TNFi cohorts using a 1:1 matching strategy. In this section, the tables include results that are based on a variable ratio matching (VRM) approach as described in Section 9.9.6.1 of the final study report.

The main analysis was modified to use 1:1 matching, as this allows the results in the meta-analysis to be directly proportional to the amount of baricitinib exposure in each data source. For transparency, comparative results generated using VRM prior to the adoption of the 1:1 matching are included here.

Table 6.45_HUM_VRM. Incidence Rate of Event - VTE, Primary Definition [HUM]

	Unmatched		Matched		
	Baricitinib[a] (N=89)	**TNFi (N=154)**	**Baricitinib[a] (N=46)**	**TNFi (N=98)**	**Total (N=144)**
Overall					
Person-Years	CCI	CCI	17.09	41.91	59.00
VTE Events	CCI	CCI	0	0	0
VTE Events/100 PY	2.46	1.43	0.00	0.00	0.00
95% CI	0.06, 13.69	0.04, 7.95	0.00, 21.59	0.00, 8.80	0.00, 6.25
Concomitant MTX Use[b]					
Total, n	13 (14.6%)	29 (18.8%)	8 (17.4%)	16 (16.3%)	24 (16.7%)
Person-Years	9.30	CCI	3.78	13.32	17.09
VTE Events	0	CCI	0	0	0
VTE Events/100 PY	0.00	4.23	0.00	0.00	0.00
95% CI	0.00, 39.67	0.11, 23.57	0.00, 97.71	0.00, 27.70	0.00, 21.58
No Concomitant MTX Use[b]					
Total, n	76 (85.4%)	125 (81.2%)	38 (82.6%)	82 (83.7%)	120 (83.3%)
Person-Years	CCI	46.41	13.31	28.59	41.91
VTE Events	CCI	0	0	0	0
VTE Events/100 PY	3.18	0.00	0.00	0.00	0.00
95% CI	0.08, 17.75	0.00, 7.95	0.00, 27.71	0.00, 12.90	0.00, 8.80

Abbreviations: CI = confidence intervals; MTX = methotrexate; N = number of patients in the specified category; PY = person-year; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available.

b Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period

c N (%) of subgroups may not always sum precisely to total group N (%) due to rounding

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.45. Incidence Rate of Event - VTE, Primary Definition [Humana 1179 Curated (RA) - Rheumatoid Arthritis]_vrm.docx

Table 6.48_HUM_VRM. Comparative Risk of Incident VTE, Primary Definition [HUM]

	TNFi	Baricitinib		p-value
		HR	95%CI	
Base Model	Ref	1.52	0.09, 24.35	0.77
Adjusted – Model [1][1,2]	Ref	-	-	-
Adjusted – Model [n][3]	Ref	-	-	-

Abbreviations: CI = confidence interval; HR = Cox proportional hazard ratio; Ref = referent group; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[1]Model [1] = propensity score-matched model with outcome and baricitinib exposure, adjusted for any variables that remain unbalanced after PS matching.

[2]Zero events in both the baricitinib exposure group and TNFi referent group preclude analyzing models with additional parameters. The model did not converge.

[3]Models [n] may include additional variables that remain unbalanced after propensity-score matching. Overall, rare outcome events in the exposure and/or referent groups preclude analyzing models with additional parameter

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.48. Comparative Risk of Incident VTE, Primary Definition [Humana 1179 Curated (RA) - Rheumatoid Arthritis]_vrm.docx

Table 6.54__HUM_VRM. Incidence Rate of Event - MACE [HUM]

Model	Unmatched		Matched		
	Baricitinib[a] (N=89)	TNFi (N=153)	Baricitinib[a] (N=48)	TNFi (N=92)	Total (N=140)
Overall					
Person-Years	41.29	CCI	17.81	CCI	CCI
MACE	0	CCI	0	CCI	CCI
MACE/100 PY	0.00	2.84	0.00	4.91	3.41
95% CI	0.00, 8.93	0.34, 10.24	0.00, 20.71	0.59, 17.72	0.41, 12.33
MI					
MI	0	CCI	0	CCI	CCI
Person-Years	41.29	CCI	17.81	CCI	CCI
IR per100 PY	0.00	1.42	0.00	2.45	1.71
95% CI	0.00, 8.93	0.04, 7.90	0.00, 20.71	0.06, 13.67	0.04, 9.51
Stroke, any					
Stroke	0	CCI	0	CCI	CCI

Person-Years	41.29	70.96	17.81	41.19	59.01
IR per 100 PY	0.00	1.41	0.00	2.43	1.69
95% CI	0.00, 8.93	0.04, 7.85	0.00, 20.71	0.06, 13.53	0.04, 9.44
Concomitant MTX Use[b]					
MACE	0	0	0	0	0
Person-Years	9.30	24.67	3.24	13.56	16.80
IR per 100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 39.67	0.00, 14.95	0.00, 113.91	0.00, 27.21	0.00, 21.96
No Concomitant MTX Use[b]					
MACE	0	CCI	0	CCI	CCI
Person-Years	31.99	CCI	14.58	CCI	CCI
IR per 100 PY	0.00	4.36	0.00	7.35	4.79
95% CI	0.00, 11.53	0.53, 15.76	0.00, 25.31	0.89, 26.55	0.58, 17.29

Abbreviations: CI = confidence interval; IR = incidence rate; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; MI = myocardial infarction; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

c N in subgroups may not always sum precisely to total group N due to rounding.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.54. Incidence Rate of Event - MACE [Humana 1179 Curated (RA) - Rheumatoid Arthritis]_vrm.docx

Table 6.59_HUM_VRM. Incidence Rate of Event - First Serious Infection [HUM]

	Unmatched		**Matched**		
	Baricitinib[a] (N=95)	**TNFi (N=162)**	**Baricitinib[a] (N=49)**	**TNFi (N=104)**	**Total (N=153)**
SI Events	CCI	CCI	CCI	0	CCI
Person-years	CCI	CCI	CCI	52.31	CCI
IR per 100 PY	4.52	3.98	9.86	0.00	2.76
95% CI	0.55, 16.32	0.82, 11.64	1.19, 35.61	0.00, 7.05	0.33, 9.95

Abbreviations: CI = confidence interval; IR = incidence rate; N = number of patients in the specified category; PY = person-years; SI = serious infection; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\humana_HUM\5. Table 6.59. Incidence Rate of Event - First Serious Infection [Humana 1179 Curated RA]_vrm.docx

Annex 6. Marketscan – Additional Results

This annex includes information about results for the following analyses:

I. Additional analysis
These additional results were not presented in the body of the report. These results, like those included in the report body, are based on 1:1 baricitinib:TNFi propensity score matching. Specifically, this section in the annex includes:
- Descriptive tables for unmatched eligible patients.
- Descriptive tables for matched patient cohorts for the serious infection analyses

II. Variable Ratio Matching
These results were not presented in the body of this report. They are based on matching baricitinib:TNFi using Variable Ratio matching, i.e., as many matched 1:3 as possible, then the maximum number matched 1:2, then the remaining patients matched 1:1.

I. Additional analysis

Table 1_MTSCN. Baseline Demographics, Unmatched [MTSCN]

	Baricitinib			TNFi (N=1,599)	Std. Diff. (Any vs TNFi)
	Any (N=257)	4-mg (N=0)	2-mg (N=257)		
Age [yrs]					
N	257	-	257	1,599	
Mean (SD)	51.76 (9.80)	-	51.76 (9.80)	50.47 (11.65)	0.12
Median	53.00 [45.50, 60.00]	-	53.00 [45.50, 60.00]	52.00 [43.00, 59.00]	
Min, Max	18.0, 70.0	-	18.0, 70.0	19.0, 88.0	
≥ 65 years	13 (5.1%)	-	13 (5.1%)	79 (4.9%)	0.01
Sex					
Male	40 (15.6%)	-	40 (15.6%)	323 (20.2%)	0.12
Female	217 (84.4%)	-	217 (84.4%)	1,276 (79.8%)	0.12

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = Standardised difference; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1.Table 6.1. Baseline Demographics, Unmatched [IBM MarketScan RA].docx

Table 4_MTSCN. Baseline Demographics Incident Serious Infections, Matched [MTSCN]

	Baricitinib			TNFi (N=194)	Std. Diff. (Any vs TNFi)	Total (N=388)
	Any (N=194)	4-mg (N=0)	2-mg (N=194)			

Age [yrs]						
N	194	-	194	194		388
Mean (SD)	51.85 (9.91)	-	51.85 (9.91)	51.43 (11.50)	0.04	51.64 (10.72)
Median	54.00 [46.75, 60.00]	-	54.00 [46.75, 60.00]	52.00 [44.00, 60.00]		53.00 [45.00, 60.00]
Min, Max	18.0, 72.0	-	18.0, 72.0	20.0, 85.0		18.0, 85.0
≥ 65 years	9 (4.6%)	-	9 (4.6%)	15 (7.7%)	0.13	24 (6.2%)
Sex						
Male	33 (17.0%)	-	33 (17.0%)	37 (19.1%)	0.05	70 (18.0%)
Female	161 (83.0%)	-	161 (83.0%)	157 (80.9%)	0.05	318 (82.0%)

Abbreviations: N = number of patients in the specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.4. - Baseline Demographics Incident Serious Infections, Matched [IBM MarketScan RA].docx

Table 6_MTSCN. Clinical History at Baseline, Unmatched Cohorts [MTSCN]

Characteristic[a,b]	Baricitinib[c] (N=257)	TNFi (N=1,599)	Std. Diff.
Clinical Conditions during baseline			
Cancer	24 (9.3%)	115 (7.2%)	0.08
NMSC	2 (0.8%)	13 (0.8%)	0.00
Chronic lung disease	21 (8.2%)	188 (11.8%)	0.12
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	3 (1.2%)	25 (1.6%)	0.03
Cardiovascular revascularization	1 (0.4%)	1 (0.1%)	0.07
Congestive heart failure, hospitalized	0 (0.0%)	6 (0.4%)	0.09
Coronary artery disease	10 (3.9%)	73 (4.6%)	0.03
Ischemic heart disease	10 (3.9%)	73 (4.6%)	0.03
Unstable angina	1 (0.4%)	8 (0.5%)	0.02
Ventricular arrhythmia	1 (0.4%)	44 (2.8%)	0.19
Diabetes Mellitus	36 (14.0%)	192 (12.0%)	0.06
Type I	2 (0.8%)	17 (1.1%)	0.03
Type II	35 (13.6%)	182 (11.4%)	0.07
Dyslipidaemia	79 (30.7%)	387 (24.2%)	0.15
Hypertension	85 (33.1%)	536 (33.5%)	0.01
Immune disorders	29 (11.3%)	101 (6.3%)	0.18
AIDS/HIV	0 (0.0%)	2 (0.1%)	0.05
Antiphospholipid syndrome	1 (0.4%)	2 (0.1%)	0.05
SLE	18 (7.0%)	35 (2.2%)	0.23
Primary Sjögren syndrome	12 (4.7%)	69 (4.3%)	0.02
Liver disorder	5 (1.9%)	17 (1.1%)	0.07
Obesity	60 (23.3%)	363 (22.7%)	0.02
Pregnancy	0 (0.0%)	14 (0.9%)	0.13
RA severity (CIRAS Index), mean (SD)	4.83 (1.24)	4.90 (1.22)	0.06
Smoking	13 (5.1%)	128 (8.0%)	0.12
Surgery, trauma & hospitalization, recent	6 (2.3%)	58 (3.6%)	0.08
TIA	0 (0.0%)	4 (0.3%)	0.07
DMARDs			
cDMARDs, during baseline			
n, total	145 (56.4%)	959 (60.0%)	0.07
Mean (SD)	0.81 (0.80)	0.79 (0.74)	0.03
Median	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-
Min, Max	0.0, 3.0	0.0, 3.0	-
>1 cDMARD concomitantly	51 (19.8%)	224 (14.0%)	0.16
Hydroxychloroquine	60 (23.3%)	255 (15.9%)	0.19
Leflunomide	25 (9.7%)	180 (11.3%)	0.05
Methotrexate	89 (34.6%)	605 (37.8%)	0.07
Minocycline	0 (0.0%)	6 (0.4%)	0.09
Sulfasalazine	12 (4.7%)	115 (7.2%)	0.11
bDMARDs, during baseline[a]			
n, total	155 (60.3%)	1,599 (100.0%)	1.15

Characteristic[a,b]	Baricitinib[c] (N=257)	TNFi (N=1,599)	Std. Diff.
Mean (SD)	0.77 (0.68)	1.08 (0.30)	0.60
Median	1.00 [0.00, 1.00]	1.00 [1.00, 1.00]	-
Min, Max	0.0, 3.0	1.0, 3.0	-
cDMARDs, concomitant	85 (33.1%)	794 (49.7%)	0.34
abatacept	23 (8.9%)	53 (3.3%)	0.24
adalimumab[d]	21 (8.2%)	513 (32.1%)	0.63
anakinra	2 (0.8%)	0 (0.0%)	0.13
certolizumab pegol[d]	16 (6.2%)	141 (8.8%)	0.10
etanercept[d]	19 (7.4%)	459 (28.7%)	0.58
golimumab[d]	13 (5.1%)	203 (12.7%)	0.27
infliximab[d]	8 (3.1%)	304 (19.0%)	0.52
rituximab	13 (5.1%)	5 (0.3%)	0.30
sarilumab	31 (12.1%)	19 (1.2%)	0.45
tocilizumab	33 (12.8%)	13 (0.8%)	0.49
Other Prescription Medications			
Antibiotics	130 (50.6%)	779 (48.7%)	0.04
Antidiabetic agents	35 (13.6%)	188 (11.8%)	0.06
Insulins	12 (4.7%)	61 (3.8%)	0.04
Non-insulins	32 (12.5%)	163 (10.2%)	0.07
Aspirin	2 (0.8%)	19 (1.2%)	0.04
Cardiovascular			
Anticoagulant	4 (1.6%)	42 (2.6%)	0.08
Antihypertensives	120 (46.7%)	690 (43.2%)	0.07
Antiplatelet	4 (1.6%)	33 (2.1%)	0.04
Nitrates	4 (1.6%)	17 (1.1%)	0.04
Hormonal			
HRT	21 (8.2%)	122 (7.6%)	0.02
Oral Contraceptives	21 (8.2%)	110 (6.9%)	0.05
SERMs	4 (1.6%)	10 (0.6%)	0.09
Lipid-lowering agents			
Bile acid binding	2 (0.8%)	15 (0.9%)	0.02
Cholesterol absorption inhibitor	6 (2.3%)	23 (1.4%)	0.07
Fibrates	5 (1.9%)	23 (1.4%)	0.04
Niacin	1 (0.4%)	0 (0.0%)	0.09
Omega-3 fatty acids	3 (1.2%)	8 (0.5%)	0.07
Statins	63 (24.5%)	307 (19.2%)	0.13
Rheumatoid arthritis-related			
Cox-2 Inhibitor	22 (8.6%)	125 (7.8%)	0.03
Glucocorticosteroid	163 (63.4%)	981 (61.4%)	0.04
Vaccinations	71 (27.6%)	421 (26.3%)	0.03

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = conventional disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modulator; SLE = systemic lupus erythematosus; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics, except for bDMARDs, are measured during the 6 months prior to initiation of study medication including the date at which the qualifying exposure of baricitinib or TNFi occurs (index date). bDMARDs are measured from the 6 months prior to the initiation of study medication until the day prior to baricitinib or the index TNFi exposure, excluding the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d TNF inhibitors.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.6. - Clinical History at Baseline, Unmatched Cohorts [IBM MarketScan]_.docx

Table 9_MTSCN. Clinical Characteristics Incident Serious Infection Cohorts, Matched [MTSCN]

Characteristic[a,b]	Baricitinib[c] (N=194)	TNFi (N=194)	Std. Diff.
Clinical Conditions during baseline			
Cancer	19 (9.8%)	16 (8.2%)	0.05
NMSC	2 (1.0%)	3 (1.5%)	0.05
Chronic lung disease	18 (9.3%)	15 (7.7%)	0.06
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	5 (2.6%)	2 (1.0%)	0.12
Cardiovascular revascularization	1 (0.5%)	0 (0.0%)	0.10
Congestive heart failure, hospitalized	0 (0.0%)	1 (0.5%)	0.10
Coronary artery disease	10 (5.2%)	4 (2.1%)	0.17
Ischemic heart disease	10 (5.2%)	4 (2.1%)	0.17
Unstable angina	1 (0.5%)	1 (0.5%)	0.0
Ventricular arrhythmia	2 (1.0%)	8 (4.1%)	0.20
Diabetes Mellitus	29 (14.9%)	30 (15.5%)	0.01
Type I	2 (1.0%)	1 (0.5%)	0.06
Type II	28 (14.4%)	29 (14.9%)	0.02
Dyslipidaemia	63 (32.5%)	52 (26.8%)	0.12
Hypertension	67 (34.5%)	70 (36.1%)	0.03
Immune disorders	16 (8.2%)	18 (9.3%)	0.04
AIDS/HIV	0 (0.0%)	0 (0.0%)	-
Antiphospholipid syndrome	1 (0.5%)	0 (0.0%)	0.10
SLE	12 (6.2%)	8 (4.1%)	0.09
Primary Sjögren syndrome	5 (2.6%)	12 (6.2%)	0.18
Liver disorder	2 (1.0%)	3 (1.5%)	0.05
Obesity	51 (26.3%)	49 (25.3%)	0.02
Pregnancy	0 (0.0%)	2 (1.0%)	0.14
RA severity (CIRAS Index), mean (SD)	4.77 (1.21)	4.78 (1.30)	0.01
Smoking	13 (6.7%)	14 (7.2%)	0.02
Surgery, trauma & hospitalization, recent	7 (3.6%)	2 (1.0%)	0.17
TIA	0 (0.0%)	1 (0.5%)	0.10
DMARDs			
cDMARDs, during baseline			
n, total	106 (54.6%)	118 (60.8%)	0.13
Mean (SD)	0.78 (0.79)	0.86 (0.78)	0.10
Median	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-
Min, Max	0.0, 3.0	0.0, 3.0	-
>1 cDMARD concomitantly	38 (19.6%)	32 (16.5%)	0.08
Hydroxychloroquine	43 (22.2%)	40 (20.6%)	0.04
Leflunomide	19 (9.8%)	29 (14.9%)	0.16
Methotrexate	66 (34.0%)	68 (35.1%)	0.02
Minocycline	0 (0.0%)	1 (0.5%)	0.10
Sulfasalazine	8 (4.1%)	15 (7.7%)	0.15
bDMARDs, during baseline[a]			

Characteristic[a,b]	Baricitinib[c] (N=194)	TNFi (N=194)	Std. Diff.
n, total	92 (47.4%)	194 (100.0%)	1.49
Mean (SD)	0.54 (0.57)	1.53 (0.57)	1.75
Median	0.50 [0.00, 1.00]	1.00 [1.00, 2.00]	-
Min, Max	0.0, 2.0	1.0, 3.0	-
cDMARDs, concomitant	47 (24.2%)	100 (51.5%)	0.59
abatacept	12 (6.2%)	44 (22.7%)	0.48
adalimumab[d]	14 (7.2%)	64 (33.0%)	0.68
anakinra	0 (0.0%)	0 (0.0%)	-
certolizumab pegol[d]	6 (3.1%)	23 (11.9%)	0.34
etanercept[d]	12 (6.2%)	64 (33.0%)	0.72
golimumab[d]	9 (4.6%)	22 (11.3%)	0.25
infliximab[d]	5 (2.6%)	32 (16.5%)	0.49
rituximab	8 (4.1%)	3 (1.5%)	0.16
sarilumab	15 (7.7%)	18 (9.3%)	0.06
tocilizumab	16 (8.2%)	9 (4.6%)	0.15
Other Prescription Medications			
Antibiotics	97 (50.0%)	97 (50.0%)	0.00
Antidiabetic agents	30 (15.5%)	29 (14.9%)	0.01
Insulins	9 (4.6%)	10 (5.2%)	0.02
Non-insulins	28 (14.4%)	27 (13.9%)	0.02
Aspirin	3 (1.5%)	0 (0.0%)	0.18
Cardiovascular			
Anticoagulant	9 (4.6%)	8 (4.1%)	0.03
Antihypertensives	93 (47.9%)	83 (42.8%)	0.10
Antiplatelet	4 (2.1%)	1 (0.5%)	0.14
Nitrates	4 (2.1%)	1 (0.5%)	0.14
Hormonal			
HRT	13 (6.7%)	15 (7.7%)	0.04
Oral Contraceptives	17 (8.8%)	10 (5.2%)	0.14
SERMs	2 (1.0%)	2 (1.0%)	0.00
Lipid-lowering agents			
Bile acid binding	2 (1.0%)	1 (0.5%)	0.06
Cholesterol absorption inhibitor	4 (2.1%)	1 (0.5%)	0.14
Fibrates	5 (2.6%)	4 (2.1%)	0.03
Niacin	1 (0.5%)	0 (0.0%)	0.10
Omega-3 fatty acids	3 (1.5%)	1 (0.5%)	0.10
Statins	49 (25.3%)	46 (23.7%)	0.04
Rheumatoid arthritis-related			
Cox-2 Inhibitor	16 (8.2%)	20 (10.3%)	0.07
Glucocorticosteroid	124 (63.9%)	128 (66.0%)	0.04
Vaccinations	51 (26.3%)	61 (31.4%)	0.11

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = conventional disease-modifying antirheumatic drug; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modulator; SLE = systemic lupus erythematosus; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics, except for bDMARDs, are measured during the 6 months prior to initiation of study medication including the date at which the qualifying exposure of baricitinib or TNFi occurs (index date). bDMARDs are measured from the 6 months prior to the initiation of study medication until the day prior to baricitinib or the index TNFi exposure, excluding the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d TNF inhibitors.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.9. - Clinical Characteristics Incident Serious Infection Cohorts, Matched [IBM Marketscan RA].docx

Table 11A_MTSCN. Baseline Healthcare Resource Utilization, Unmatched [MTSCN]

Type of Resource Use	Baricitinib (N=257)	TNFi (N=1,599)	Std. Diff.
Physician Office Visits			
n, patients	242 (94.2%)	1,507 (94.2%)	0.00
n, events	5695	30461	
Mean (SD)	22.16 (27.36)	19.05 (20.78)	0.13
Median	13.00 [5.00, 28.00]	13.00 [6.00, 25.00]	
Min, Max	0.0, 218.0	0.0, 159.0	
Rheumatologist Visits			
n, patients	192 (74.7%)	1,184 (74.0%)	0.02
n, events	1375	14231	
Mean (SD)	5.35 (6.94)	8.90 (11.27)	0.38
Median	3.00 [0.00, 7.00]	4.00 [0.00, 14.00]	
Min, Max	0.0, 35.0	0.0, 107.0	
Other Outpatient Visits			
n, patients	234 (91.1%)	1,460 (91.3%)	0.01
n, events	6081	40567	
Mean (SD)	23.66 (29.73)	25.37 (32.76)	0.06
Median	16.00 [7.00, 27.00]	16.00 [7.00, 33.00]	
Min, Max	0.0, 239.0	0.0, 508.0	
Inpatient Visits			
n, patients	9 (3.5%)	89 (5.6%)	0.10
n, events	10	112	
Mean (SD)	0.04 (0.21)	0.07 (0.34)	0.12
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 2.0	0.0, 5.0	
ED Visits			
n, patients	35 (13.6%)	310 (19.4%)	0.16
n, events	249	2686	
Mean (SD)	0.97 (3.40)	1.68 (6.41)	0.14
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 22.0	0.0, 130.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.11A.Baseline Healthcare Resource Utilization, Unmatched [IBM MarketScan RA].docx

Table 11B_MTSCN. Baseline Healthcare Resource Utilization, Unmatched [MTSCN], count at most one visit per day1

Type of Resource Use	Baricitinib (N=257)	TNFi (N=1,599)	Std. Diff.
Physician Office Visits[1]			
n, patients	242 (94.2%)	1,507 (94.2%)	0.00
n, events	2,303	12,600	
Mean (SD)	8.96 (8.96)	7.88 (7.50)	0.13
Median	7.00 [3.00, 11.00]	6.00 [3.00, 11.00]	
Min, Max	0.0, 70.0	0.0, 70.0	
Rheumatologist Visits[1]			
n, patients	192 (74.7%)	1,184 (74.0%)	0.02
n, events	547	4,173	
Mean (SD)	2.13 (2.00)	2.61 (2.52)	0.21
Median	2.00 [0.00, 3.00]	2.00 [0.00, 4.00]	
Min, Max	0.0, 16.0	0.0, 23.0	
Other Outpatient Visits[1]			
n, patients	234 (91.1%)	1,460 (91.3%)	0.01
n, events	1,375	8,363	
Mean (SD)	5.35 (11.91)	5.23 (6.69)	0.01
Median	3.00 [2.00, 6.00]	4.00 [2.00, 7.00]	
Min, Max	0.0, 179.0	0.0, 107.0	
Inpatient Visits[1]			
n, patients	9 (3.5%)	89 (5.6%)	0.10
n, events	10	112	
Mean (SD)	0.04 (0.21)	0.07 (0.34)	0.12
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 2.0	0.0, 5.0	
ED Visits[1]			
n, patients	35 (13.6%)	310 (19.4%)	0.16
n, events	46	496	
Mean (SD)	0.18 (0.57)	0.31 (0.83)	0.19
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 5.0	0.0, 9.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

[1] In this table, results describe utilization of healthcare where a maximum of one event was allowed per day. In the PS matching analyses, multiple claims on the same day were allowed to capture additional information on the amount of services received in a given visit. These results are presented in table 6.11A.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.11B (count at most one visit per day). Baseline Healthcare Resource Utilization, Unmatched [IBM MarketScan RA].docx

Table 12A_MTSCN. Baseline Healthcare Resource Utilization Primary VTE Cohorts, Matched [MTSCN]

Type of Resource Use	Baricitinib (N=185)	TNFi (N=185)	Std. Diff.
Physician Office Visits			
n, patients	174 (94.1%)	174 (94.1%)	0.00
n, events	3469	3687	
Mean (SD)	18.75 (19.40)	19.93 (20.24)	0.06
Median	13.00 [5.00, 26.00]	13.00 [6.00, 27.50]	
Min, Max	0.0, 101.0	0.0, 123.0	
Rheumatologist Visits			
n, patients	139 (75.1%)	128 (69.2%)	0.13
n, events	1075	1025	
Mean (SD)	5.81 (7.34)	5.54 (7.34)	0.04
Median	3.00 [0.50, 8.00]	2.00 [0.00, 8.00]	
Min, Max	0.0, 35.0	0.0, 38.0	
Other Outpatient Visits			
n, patients	167 (90.3%)	167 (90.3%)	0.00
n, events	4207	3781	
Mean (SD)	22.74 (29.14)	20.44 (20.59)	0.09
Median	16.00 [7.50, 26.00]	15.00 [6.50, 28.00]	
Min, Max	0.0, 239.0	0.0, 128.0	
Inpatient Visits			
n, patients	6 (3.2%)	5 (2.7%)	0.03
n, events	6	6	
Mean (SD)	0.03 (0.18)	0.03 (0.16)	0.03
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 1.0	0.0, 1.0	
ED Visits			
n, patients	26 (14.1%)	26 (14.1%)	0.00
n, events	192	189	
Mean (SD)	1.04 (3.68)	1.02 (4.51)	0.01
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 22.0	0.0, 46.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.12A. - Baseline Healthcare Resource Utilization Primary VTE Cohorts, Matched [IBM Marketscan RA].docx

Table 13A_MTSCN. Baseline Healthcare Resource Utilization MACE Cohorts, Matched [MTSCN]

Type of Resource Use	Baricitinib (N=192)	TNFi (N=192)	Std. Diff.
Physician Office Visits			
n, patients	179 (93.2%)	183 (95.3%)	0.09
n, events	3740	3921	
Mean (SD)	19.48 (20.13)	20.42 (21.81)	0.05
Median	13.00 [5.00, 28.00]	14.00 [6.00, 27.00]	
Min, Max	0.0, 102.0	0.0, 123.0	
Rheumatologist Visits			
n, patients	147 (76.6%)	136 (70.8%)	0.13
n, events	1123	1094	
Mean (SD)	5.85 (7.28)	5.70 (7.35)	0.02
Median	3.00 [1.00, 9.00]	3.00 [0.00, 9.75]	
Min, Max	0.0, 35.0	0.0, 54.0	
Other Outpatient Visits			
n, patients	174 (90.6%)	178 (92.7%)	0.08
n, events	4702	4034	
Mean (SD)	24.49 (32.38)	21.01 (19.59)	0.13
Median	16.50 [6.25, 28.50]	16.00 [8.00, 28.00]	
Min, Max	0.0, 239.0	0.0, 132.0	
Inpatient Visits			
n, patients	5 (2.6%)	5 (2.6%)	0.00
n, events	6	6	
Mean (SD)	0.03 (0.16)	0.03 (0.16)	0.00
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 1.0	0.0, 1.0	
ED Visits			
n, patients	31 (16.1%)	29 (15.1%)	0.03
n, events	219	190	
Mean (SD)	1.14 (3.68)	0.99 (3.65)	0.04
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 22.0	0.0, 39.0	

Abbreviations: ED = emergency department; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.13A. - Baseline Healthcare Resource Utilization MACE Cohorts, Matched [IBM Marketscan RA].docx

Table 14A_MTSCN. Baseline Healthcare Resource Utilization Serious Infection Cohorts, Matched [MTSCN]

Type of Resource Use	Baricitinib (N=194)	TNFi (N=194)	Std. Diff.
Physician Office Visits			
n, patients	182 (93.8%)	185 (95.4%)	0.07
n, events	4146	4029	
Mean (SD)	21.37 (25.54)	20.77 (20.40)	0.03
Median	13.00 [5.00, 28.25]	15.00 [7.00, 29.00]	
Min, Max	0.0, 218.0	0.0, 115.0	
Rheumatologist Visits			
n, patients	148 (76.3%)	134 (69.1%)	0.16
n, events	1073	1079	
Mean (SD)	5.53 (6.76)	5.56 (7.77)	0.00
Median	3.00 [1.00, 8.00]	2.00 [0.00, 8.25]	
Min, Max	0.0, 28.0	0.0, 54.0	
Other Outpatient Visits			
n, patients	177 (91.2%)	176 (90.7%)	0.02
n, events	4875	4485	
Mean (SD)	25.13 (32.85)	23.12 (24.27)	0.07
Median	16.00 [7.00, 29.25]	16.00 [8.00, 30.25]	
Min, Max	0.0, 239.0	0.0, 188.0	
Inpatient Visits			
n, patients	7 (3.6%)	3 (1.5%)	0.13
n, events	8	4	
Mean (SD)	0.04 (0.19)	0.02 (0.18)	0.09
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 1.0	0.0, 2.0	
ED Visits			
n, patients	31 (16.0%)	23 (11.9%)	0.12
n, events	215	99	
Mean (SD)	1.11 (3.65)	0.51 (1.90)	0.21
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 22.0	0.0, 17.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.14A. - Baseline Healthcare Resource Utilization Serious Infection Cohorts, Matched [IBM Marketscan RA].docx

Table 14B_MTSCN. Baseline Healthcare Resource Utilization Serious Infection Cohorts, Matched [MTSCN], count at most one visit per day[1]

Type of Resource Use	Baricitinib (N=194)	TNFi (N=194)	Std. Diff.
Physician Office Visits[1]			
n, patients	182 (93.8%)	185 (95.4%)	0.07
n, events	1736	1569	
Mean (SD)	8.95 (8.98)	8.09 (6.60)	0.11
Median	7.00 [3.00, 12.00]	6.50 [3.00, 11.25]	
Min, Max	0.0, 70.0	0.0, 39.0	
Rheumatologist Visits[1]			
n, patients	148 (76.3%)	134 (69.1%)	0.16
n, events	411	419	
Mean (SD)	2.12 (1.79)	2.16 (2.15)	0.02
Median	2.00 [1.00, 3.00]	2.00 [0.00, 3.00]	
Min, Max	0.0, 8.0	0.0, 10.0	
Other Outpatient Visits[1]			
n, patients	177 (91.2%)	176 (90.7%)	0.02
n, events	1125	935	
Mean (SD)	5.80 (13.52)	4.82 (5.04)	0.10
Median	3.50 [2.00, 6.00]	4.00 [2.00, 6.00]	
Min, Max	0.0, 179.0	0.0, 37.0	
Inpatient Visits[1]			
n, patients	7 (3.6%)	3 (1.5%)	0.13
n, events	8	4	
Mean (SD)	0.04 (0.19)	0.02 (0.18)	0.09
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 1.0	0.0, 2.0	
ED Visits[1]			
n, patients	31 (16.0%)	23 (11.9%)	0.12
n, events	46	25	
Mean (SD)	0.24 (0.72)	0.13 (0.38)	0.20
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 5.0	0.0, 3.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

[1] In this table, results describe utilization of healthcare where a maximum of one event was allowed per day. In the PS matching analyses, multiple claims on the same day were allowed to capture additional information on the amount of services received in a given visit. These results are presented in table 6.14A.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.14B (count at most one visit per day). Baseline Healthcare Resource Utilization Serious Infection Cohorts, Matched [IBM Marketscan RA].docx

Table 16_MTSCN. Baseline Prevalence of Outcomes [MTSCN]

Outcome in Each Matched Cohort[a,c,d]	Unmatched			Matched			
	Baricitinib[b]	TNFi	Std. Diff	Baricitinib[b]	TNFi	Std. Diff	Total
VTE	N=260	N=1,605	-	N=187	N=187	-	N=374
Main case definition in baseline	3 (1.2%)	6 (0.4%)	0.09	2 (1.1%)	0 (0.0%)	0.15	2 (0.5%)
Alternate case definition I in baseline	3 (1.2%)	6 (0.4%)	0.09	2 (1.1%)	0 (0.0%)	0.15	2 (0.5%)
Alternative case definition II in baseline	3 (1.2%)	10 (0.6%)	0.06	2 (1.1%)	0 (0.0%)	0.15	2 (0.5%)
MACE	N=260	N=1,605	-	N=188	N=188	-	N=376
MACE in baseline	1 (0.4%)	1 (0.1%)	0.07	1 (0.5%)	0 (0.0%)	0.10	1 (0.3%)
Serious Infection	N=265	N=1,642	-	N=193	N=193	-	N=386
Serious Infection in baseline	2 (0.8%)	15 (0.9%)	0.02	1 (0.5%)	1 (0.5%)	0.00	2 (0.5%)
Hospitalized Tuberculosis	N=265	N=1,642	-	N=193	N=193	-	N=386
Hospitalized Tuberculosis in baseline	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)	-	0 (0.0%)

Abbreviations: MACE = major adverse cardiovascular event, defined as hospital primary discharge diagnosis code of acute MI or hospital primary discharge diagnosis code of ischemic or hemorrhagic stroke; N = number of patients in specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism, defined based on the case definitions.

a Baseline prevalence was calculated for each distinct matched cohort for VTE, MACE, serious infection and hospitalized tuberculosis.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c Patients with the prevalent outcomes enumerated in this table are those excluded from the main analyses of each outcome, except for VTE alternative case definitions I and II. Only the VTE main case definition was used as an exclusion criterion in the main analyses.

d In the VTE and MACE analyses, cohorts additionally excluded the use of anticoagulants at the time of cohort entry (see protocol Section 8.7.7), resulting in a different N compared to the Serious Infection and Hospitalized Tuberculosis cohorts.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.16. Baseline Prevalence of Outcomes [IBM Marketscan RA].docx

Table 17_MTSCN. Duration of Follow-up Period (Days), Unmatched [MTSCN]

	Baricitinib[a] (N=257)	TNFi (N=1,599)	Std. Diff.
N	257	1,599	
Mean (SD)	171.30 (141.68)	174.29 (157.31)	0.02
Median	121.00 [58.00, 240.00]	121.00 [58.00, 226.00]	
Min, Max	4.0, 718.0	1.0, 876.0	

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = standardised difference; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be reported for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.17. Duration of Follow-up Period (Days), Unmatched [IBM Marketscan RA].docx

Table 18_MTSCN. Duration of Follow-up Period (Days) Primary VTE Cohorts, Matched [MTSCN]

	Baricitinib[a,b] (N=185)	TNFi (N=185)	Std. Diff.
N	185	185	0
Mean (SD)	166.55 (140.46)	153.10 (141.13)	0.10
Median	117.00 [58.00, 229.50]	112.00 [57.00, 201.00]	
Min, Max	6.0, 718.0	2.0, 707.0	
Reasons for censoring [c]			
Incident event	1	1	-
Medication discontinued	9 (4.9%)	7 (3.8%)	-
Initiated b/tsDMARD	83 (44.9%)	100 (54.1%)	-
End of patient record	72 (38.9%)	60 (32.4%)	-
Death (where available)	0 (0.0%)	0 (0.0%)	-
End of study period (07/05/2021)	0 (0.0%)	0 (0.0%)	-

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = standardised difference ; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be reported for each dose where numbers of patients are sufficient to warrant separate reporting.

b There were 0 patients with a baricitinib dose of 4 mg. Hence, 100% of the patients presented in this column have a baricitinib dose of 2 mg.

c A single patient can be censored on the same day for multiple reasons, e.g., medication discontinued could also be the same day as initiated b/tsDMARD. Further, additional censoring criteria (e.g., switching medication) were specified in the SAP. For these reasons, the total number of reasons for censoring may be less than or greater than the total number of patients.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.18. Duration of Follow-up Period (Days) Primary VTE Cohorts, Matched [IBM Marketscan RA].docx

Table 21_MTSCN. Duration of Follow-up Period (Days) MACE Cohorts, Matched [MTSCN]

	Baricitinib[a,b] (N=192)	TNFi (N=192)	Std. Diff.
N	192	192	
Mean (SD)	164.65 (143.43)	148.91 (125.12)	0.12
Median	117.00 [58.00, 221.75]	116.00 [58.25, 194.25]	
Min, Max	4.0, 764.0	1.0, 707.0	
Reasons for censoring			
Incident event	1	0	-
Medication discontinued	86 (44.8%)	94 (49.0%)	-
Initiated b/tsDMARD	8 (4.2%)	6 (3.1%)	-
End of patient record	75 (39.1%)	74 (38.5%)	-
Death (where available)	0 (0.0%)	0 (0.0%)	-
End of study period (07/05/2021)	0 (0.0%)	0 (0.0%)	-

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = standardised difference; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be reported for each dose where numbers of patients are sufficient to warrant separate reporting.

b There were 0 patients with a baricitinib dose of 4 mg. Hence, 100% of the patients presented in this column have a baricitinib dose of 2 mg.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.21. Duration of Follow-up Period (Days) MACE Cohorts, Matched [IBM Marketscan RA].docx

Table 22_MTSCN. Duration of Follow-up Period (Days) Incident Serious Infection Cohorts, Matched [MTSCN]

	Baricitinib[a,b] (N=194)	TNFi (N=194)	Std. Diff.
N	194	194	
Mean (SD)	164.11 (144.01)	157.16 (139.41)	0.05
Median	117.00 [58.00, 227.50]	113.00 [57.00, 204.50]	
Min, Max	4.0, 764.0	2.0, 747.0	
Reasons for censoring			
Incident event	1	0	-
Medication discontinued	90 (46.4%)	88 (45.4%)	-
Initiated b/tsDMARD	13 (6.7%)	6 (3.1%)	-
End of patient record	74 (38.1%)	77 (39.7%)	-
Death (where available)	0 (0.0%)	0 (0.0%)	-
End of study period (07/05/2021)	0 (0.0%)	0 (0.0%)	-

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = standardised difference; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b There were 0 patients with a baricitinib dose of 4 mg. Hence, 100% of the patients presented in this column have a baricitinib dose of 2 mg.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.22. Duration of Follow-up Period (Days) Incident Serious Infection Cohorts, Matched [IBM Marketscan RA].docx

Table 39_MTSCN. Pattern of VTE and Related Diagnostic Codes in Patients with RA [MTSCN]

Code	Total Patients (N=7)
Pulmonary Embolism	
I26.0 - Pulmonary embolism with acute cor pulmonale	0 (0.0%)
I26.02 - Saddle embolus of pulmonary artery with acute cor pulmonale	0 (0.0%)
I26.09 - Other pulmonary embolism with acute cor pulmonale	0 (0.0%)
I26.9 - Pulmonary embolism without acute cor pulmonale	0 (0.0%)
I26.92 - Saddle embolus of pulmonary artery without acute cor pulmonale	0 (0.0%)
I26.99 - Other pulmonary embolism without acute cor pulmonale	5 (71.4%)
Deep Vein Thrombosis, lower	
I80.10 - Phlebitis and thrombophlebitis of unspecified femoral vein	0 (0.0%)
I80.11 - Phlebitis and thrombophlebitis of right femoral vein	0 (0.0%)
I80.13 - Phlebitis and thrombophlebitis of femoral vein, bilateral	0 (0.0%)
I80.211 - Phlebitis and thrombophlebitis of right iliac vein	0 (0.0%)
I80.221 - Phlebitis and thrombophlebitis of right popliteal vein	0 (0.0%)
I80.223 - Phlebitis and thrombophlebitis of popliteal vein, bilateral	0 (0.0%)
I80.232 - Phlebitis and thrombophlebitis of left tibial vein	0 (0.0%)
I80.233 - Phlebitis and thrombophlebitis of tibial vein, bilateral	0 (0.0%)
I80.292 - Phlebitis and thrombophlebitis of other deep vessels of left lower extremity	0 (0.0%)
I80.293 - Phlebitis and thrombophlebitis of other deep vessels of lower extremity, bilateral	0 (0.0%)
I80.3 - Phlebitis and thrombophlebitis of lower extremities, unspecified	0 (0.0%)
I82.419 - Acute embolism and thrombosis of unspecified femoral vein	0 (0.0%)
I82.423 - Acute embolism and thrombosis of iliac vein, bilateral	0 (0.0%)
I82.431 - Acute embolism and thrombosis of right popliteal vein	1 (14.3%)
I82.432 - Acute embolism and thrombosis of left popliteal vein	0 (0.0%)
I82.433 - Acute embolism and thrombosis of popliteal vein, bilateral	0 (0.0%)
I82.441 - Acute embolism and thrombosis of right tibial vein	0 (0.0%)
I82.442 - Acute embolism and thrombosis of left tibial vein	0 (0.0%)
I82.443 - Acute embolism and thrombosis of tibial vein, bilateral	0 (0.0%)

Code	Total Patients (N=7)
I82.449 - Acute embolism and thrombosis of unspecified tibial vein	0 (0.0%)
I82.491 - Acute embolism and thrombosis of other specified deep vein of right lower extremity	0 (0.0%)
I82.4Y1 - Acute embolism and thrombosis of unspecified deep veins of right proximal lower extremity	0 (0.0%)
I82.4Y3 - Acute embolism and thrombosis of unspecified deep veins of proximal lower extremity, bilateral	0 (0.0%)
I82.4Y9 - Acute embolism and thrombosis of unspecified deep veins of unspecified proximal lower extremity	0 (0.0%)
I82.4Z1 - Acute embolism and thrombosis of unspecified deep veins of right distal lower extremity	0 (0.0%)
I82.4Z2 - Acute embolism and thrombosis of unspecified deep veins of left distal lower extremity	1 (14.3%)
I82.4Z3 - Acute embolism and thrombosis of unspecified deep veins of distal lower extremity, bilateral	0 (0.0%)
I80.12 - Phlebitis and thrombophlebitis of left femoral vein	0 (0.0%)
I80.201 - Phlebitis and thrombophlebitis of unspecified deep vessels of right lower extremity	0 (0.0%)
I80.202 - Phlebitis and thrombophlebitis of unspecified deep vessels of left lower extremity	0 (0.0%)
I80.203 - Phlebitis and thrombophlebitis of unspecified deep vessels of lower extremities, bilateral	0 (0.0%)
I80.209 - Phlebitis and thrombophlebitis of unspecified deep vessels of unspecified lower extremity	0 (0.0%)
I80.212 - Phlebitis and thrombophlebitis of left iliac vein	0 (0.0%)
I80.213 - Phlebitis and thrombophlebitis of iliac vein, bilateral	0 (0.0%)
I80.219 - Phlebitis and thrombophlebitis of unspecified iliac vein	0 (0.0%)
I80.222 - Phlebitis and thrombophlebitis of left popliteal vein	0 (0.0%)
I80.229 - Phlebitis and thrombophlebitis of unspecified popliteal vein	0 (0.0%)
I80.231 - Phlebitis and thrombophlebitis of right tibial vein	0 (0.0%)
I80.291 - Phlebitis and thrombophlebitis of other deep vessels of right lower extremity	0 (0.0%)
I80.299 - Phlebitis and thrombophlebitis of other deep vessels of unspecified lower extremity	0 (0.0%)
I82.401 - Acute embolism and thrombosis of unspecified deep veins of right lower extremity	2 (28.6%)

Code	Total Patients (N=7)
I82.402 - Acute embolism and thrombosis of unspecified deep veins of left lower extremity	1 (14.3%)
I82.403 - Acute embolism and thrombosis of unspecified deep veins of lower extremity, bilateral	0 (0.0%)
I82.409 - Acute embolism and thrombosis of unspecified deep veins of unspecified lower extremity	1 (14.3%)
I82.411 - Acute embolism and thrombosis of right femoral vein	0 (0.0%)
I82.412 - Acute embolism and thrombosis of left femoral vein	0 (0.0%)
I82.413 - Acute embolism and thrombosis of femoral vein, bilateral	0 (0.0%)
I82.421 - Acute embolism and thrombosis of right iliac vein	0 (0.0%)
I82.422 - Acute embolism and thrombosis of left iliac vein	0 (0.0%)
I82.429 - Acute embolism and thrombosis of unspecified iliac vein	0 (0.0%)
I82.439 - Acute embolism and thrombosis of unspecified popliteal vein	0 (0.0%)
I82.492 - Acute embolism and thrombosis of other specified deep vein of left lower extremity	0 (0.0%)
I82.493 - Acute embolism and thrombosis of other specified deep vein of lower extremity, bilateral	0 (0.0%)
I82.499 - Acute embolism and thrombosis of other specified deep vein of unspecified lower extremity	0 (0.0%)
I82.4Y2 - Acute embolism and thrombosis of unspecified deep veins of left proximal lower extremity	0 (0.0%)
Deep Vein Thrombosis, upper	
I82.210 - Acute embolism and thrombosis of superior vena cava	0 (0.0%)
I82.601 - Acute embolism and thrombosis of unspecified veins of right upper extremity	0 (0.0%)
I82.621 - Acute embolism and thrombosis of deep veins of right upper extremity	0 (0.0%)
I82.622 - Acute embolism and thrombosis of deep veins of left upper extremity	0 (0.0%)
I82.623 - Acute embolism and thrombosis of deep veins of upper extremity, bilateral	0 (0.0%)
I82.A12 - Acute embolism and thrombosis of left axillary vein	0 (0.0%)
I82.C11 - Acute embolism and thrombosis of right internal jugular vein	0 (0.0%)
I82.C13 - Acute embolism and thrombosis of internal jugular vein, bilateral	0 (0.0%)
I82.C19 - Acute embolism and thrombosis of unspecified internal jugular vein	0 (0.0%)
I82.602 - Acute embolism and thrombosis of unspecified veins of left upper extremity	0 (0.0%)

Code	Total Patients (N=7)
I82.603 - Acute embolism and thrombosis of unspecified veins of upper extremity, bilateral	0 (0.0%)
I82.609 - Acute embolism and thrombosis of unspecified veins of unspecified upper extremity	0 (0.0%)
I82.629 - Acute embolism and thrombosis of deep veins of unspecified upper extremity	0 (0.0%)
I82.A11 - Acute embolism and thrombosis of right axillary vein	0 (0.0%)
I82.A13 - Acute embolism and thrombosis of axillary vein, bilateral	0 (0.0%)
I82.A19 - Acute embolism and thrombosis of unspecified axillary vein	0 (0.0%)
I82.C12 - Acute embolism and thrombosis of left internal jugular vein	0 (0.0%)
Other Venous Thrombosis	
I81 - Portal vein thrombosis	0 (0.0%)
I82.0 - Budd-Chiari syndrome	0 (0.0%)
I82.1 - Thrombophlebitis migrans	0 (0.0%)
I82.3 - Embolism and thrombosis of renal vein	0 (0.0%)
I82.90 - Acute embolism and thrombosis of unspecified vein	0 (0.0%)
I82.B13 - Acute embolism and thrombosis of subclavian vein, bilateral	0 (0.0%)
I80.8 - Phlebitis and thrombophlebitis of other sites	0 (0.0%)
I80.9 - Phlebitis and thrombophlebitis of unspecified site	0 (0.0%)
I82.220 - Acute embolism and thrombosis of inferior vena cava	0 (0.0%)
I82.890 - Acute embolism and thrombosis of other specified veins	0 (0.0%)
I82.B11 - Acute embolism and thrombosis of right subclavian vein	0 (0.0%)
I82.B12 - Acute embolism and thrombosis of left subclavian vein	0 (0.0%)

Abbreviations: ICD-10 = International Classification of Disease, 10th Revision; N = number of patients in the specified category; RA = rheumatoid arthritis;
VTE = venous thromboembolism

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.39. Pattern of VTE and Related Diagnostic Codes in Patients with RA [IBM Marketscan RA].docx

Table 40_MTSCN. Clinical Characteristics of RA Patients with VTE, Primary Definition [MTSCN]

Characteristic[a,b]	Baricitinib[c] (N=1)	TNFi (N=1)	Total (N=2)
Age (mean) [SD]	62.00 (0.00)	52.00 (0.00)	57.00 (7.07)
Sex			
Female	1 (100.0%)	1 (100.0%)	2 (100.0%)
Male	0 (0.0%)	0 (0.0%)	0 (0.0%)
Clinical Conditions during baseline			
Cancer	1 (100.0%)	0 (0.0%)	1 (50.0%)
NMSC	1 (100.0%)	0 (0.0%)	1 (50.0%)
Chronic Lung disease Disease	0 (0.0%)	1 (100.0%)	1 (50.0%)
Cardiovascular conditions			
Atrial arrhythmia/ fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	1 (100.0%)	1 (100.0%)	2 (100.0%)
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	1 (100.0%)	1 (100.0%)	2 (100.0%)
Dyslipidaemia	1 (100.0%)	1 (100.0%)	2 (100.0%)
Hypertension	1 (100.0%)	1 (100.0%)	2 (100.0%)
Immune disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Primary Sjögren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	1 (100.0%)	1 (100.0%)	2 (100.0%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	3.25 (0.00)	7.05 (0.00)	5.15 (2.69)
Smoking	0 (0.0%)	1 (100.0%)	1 (50.0%)
Surgery, trauma, & hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)

Characteristic[a,b]	Baricitinib[c] (N=1)	TNFi (N=1)	Total (N=2)
Other Prescription Medication			
Antibiotics	1 (100.0%)	1 (100.0%)	2 (100.0%)
Antidiabetic agents	1 (100.0%)	0 (0.0%)	1 (50.0%)
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-insulins	1 (100.0%)	0 (0.0%)	1 (50.0%)
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			
Antihypertensives	1 (100.0%)	1 (100.0%)	2 (100.0%)
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anticoagulant	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiplatelet	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			
Oral contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERM	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	1 (100.0%)	1 (50.0%)
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	1 (100.0%)	1 (100.0%)	2 (100.0%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucocorticosteroid	1 (100.0%)	0 (0.0%)	1 (50.0%)
Vaccinations	1 (100.0%)	0 (0.0%)	1 (50.0%)
Post-index Occurrence[d]			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hospitalization	1 (100.0%)	0 (0.0%)	1 (50.0%)
Surgery	0 (0.0%)	0 (0.0%)	0 (0.0%)
Trauma	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modifier; SLE = systemic lupus erythematosus; TIA = transient ischemic attack;TNFi = tumour necrosis factor inhibitor; VTE = Venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d Except for cancer diagnosed within 90 days of VTE diagnosis, events in this category must have occurred in the 4 weeks immediately prior to VTE (Kline et al. 2017).

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.40. - Clinical Characteristics of RA Patients with VTE, Primary Definition [IBM Marketscan RA].docx

Table 41_MTSCN. Pattern of RA Medication Use in Patients with VTE, Primary Definition [MTSCN]

Characteristic[a]	Unmatched		Matched		
	Baricitinib[b] (N=1)	TNFi (N=6)	Baricitinib[b] (N=1)	TNFi (N=1)	Total (N=2)
Baseline Medication					
cDMARDs, during baseline					
n, total	0 (0.0%)	3 (50.0%)	0 (0.0%)	1 (100.0%)	1 (50.0%)
Mean (SD)	0.00 (0.00)	0.83 (0.75)	0.00 (0.00)	1.00 (0.00)	0.50 (0.71)
Median	0.00 [0.00, 0.00]	1.00 [0.00, 1.25]	0.00 [0.00, 0.00]	1.00 [1.00, 1.00]	0.50 [0.00, 1.00]
Min, Max	0.0, 0.0	0.0, 2.0	0.0, 0.0	1.0, 1.0	0.0, 1.0
>1 cDMARD concomitantly	0 (0.0%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hydroxychloroquine	0 (0.0%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Leflunomide	0 (0.0%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate	0 (0.0%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	1 (16.7%)	0 (0.0%)	1 (100.0%)	1 (50.0%)
bDMARDs, during baseline					
n, total	0 (0.0%)	6 (100.0%)	0 (0.0%)	1 (100.0%)	1 (50.0%)
Mean (SD)	0.00 (0.00)	1.17 (0.41)	0.00 (0.00)	2.00 (0.00)	1.00 (1.41)
Median	0.00 [0.00, 0.00]	1.00 [1.00, 1.25]	0.00 [0.00, 0.00]	2.00 [2.00, 2.00]	1.00 [0.00, 2.00]
Min, Max	0.0, 0.0	1.0, 2.0	0.0, 0.0	2.0, 2.0	0.0, 2.0
cDMARDs, concomitant	0 (0.0%)	2 (33.3%)	0 (0.0%)	1 (100.0%)	1 (50.0%)
Abatacept	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adalimumab[c]	0 (0.0%)	2 (33.3%)	0 (0.0%)	1 (100.0%)	1 (50.0%)
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Etanercept[c]	0 (0.0%)	2 (33.3%)	0 (0.0%)	1 (100.0%)	1 (50.0%)
Golimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infliximab[c]	0 (0.0%)	2 (33.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Medication[d]					
Methotrexate, concomitant	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Concomitant cDMARD	0 (0.0%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dose change, baricitinib	NA[d]	0 (0.0%)	NA[d]	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c TNF inhibitors.

d Only baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked 'NA' as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.41. - Pattern of RA Medication Use in Patients with VTE, Primary Definition [IBM MarketScan RA].docx

Table 42_MTSCN. Time to First Event Outcome (days) - VTE, Primary Definition [MTSCN]

Time	Unmatched		Matched		
	Baricitinib[a,b] (N=257)	TNFi (N=1,599)	Baricitinib[a,b] (N=185)	TNFi (N=185)	Total (N=370)
n	257	1,599	185	185	370
Mean (SD)	402.00 (0.00)	150.17 (193.19)	402.00 (0.00)	248.00 (0.00)	325.00 (108.89)
Median	402.00 [402.00, 402.00]	63.00 [16.25, 311.50]	402.00 [402.00, 402.00]	248.00 [248.00, 248.00]	325.00 [248.00, 402.00]
Min, Max	402.0, 402.0	5.0, 502.0	402.0, 402.0	248.0, 248.0	248.0, 402.0

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Only baricitinib 2-mg dose is available in the US.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.42. Time to First Event Outcome (days) - VTE, Primary Definition [IBM Marketscan RA].docx

Table 51_MTSCN. Clinical Characteristics of RA Patients with MACE [MKSCN]

Characteristic[a,b]	Baricitinib[c] (N=1)	TNFi (N=0)	Total (N=1)
Age (mean) [SD]	60.00 (0.00)	- (-)	60.00 (0.00)
Sex			
Female	0 (0.0%)	0 (0.0%)	0 (0.0%)
Male	1 (100.0%)	0 (0.0%)	1 (100.0%)
Clinical Conditions during baseline			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic lung disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	1 (100.0%)	0 (0.0%)	1 (100.0%)
Ischemic heart disease	1 (100.0%)	0 (0.0%)	1 (100.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dyslipidaemia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertension	1 (100.0%)	0 (0.0%)	1 (100.0%)
Immune disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	0 (0.0%)	0 (0.0%)	0 (0.0%)

Characteristic[a,b]	Baricitinib[c] (N=1)	TNFi (N=0)	Total (N=1)
Primary Sjögren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	1 (100.0%)	0 (0.0%)	1 (100.0%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	3.95 (0.00)	- (-)	3.95 (0.00)
Smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)
Surgery, Trauma, & Hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medications			
Antibiotics	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antidiabetic agents	0 (0.0%)	0 (0.0%)	0 (0.0%)
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			
Anticoagulant	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antihypertensives	1 (100.0%)	0 (0.0%)	1 (100.0%)
Antiplatelet	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			
Oral contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERM	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	1 (100.0%)	0 (0.0%)	1 (100.0%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucocorticosteroid	1 (100.0%)	0 (0.0%)	1 (100.0%)
Vaccinations	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Occurrence[d]			
Methotrexate, concomitant	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modifier; SLE = systemic lupus erythematosus; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d Events in this category must have occurred in the 7 days immediately prior to MACE.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\ 1. Table 6.51. - Clinical Characteristics of RA Patients with MACE [IBM Marketscan RA]_.docx

Table 52_MTSCN. - Pattern of RA Medication Use in Patients with MACE [MKSCN]

Characteristic[a]	Unmatched		Matched		
	Baricitinib[b] (N=2)	TNFi (N=1)	Baricitinib[b] (N=1)	TNFi (N=0)	Total (N=1)
Baseline Medication					
cDMARDs, during baseline					
n, total	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	0.50 (0.71)	0.00 (0.00)	0.00 (0.00)	- (-)	0.00 (0.00)
Median	0.50 [0.00, 1.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	- [-, -]	0.00 [0.00, 0.00]
Min, Max	0.0, 1.0	0.0, 0.0	0.0, 0.0	-, -	0.0, 0.0
>1 cDMARD concomitantly	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hydroxychloroquine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Leflunomide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
bDMARDs, during baseline					
n, total	2 (100.0%)	1 (100.0%)	1 (100.0%)	0 (0.0%)	1 (100.0%)
Mean (SD)	1.50 (0.71)	1.00 (0.00)	1.00 (0.00)	- (-)	1.00 (0.00)
Median	1.50 [1.00, 2.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	- [-, -]	1.00 [1.00, 1.00]
Min, Max	1.0, 2.0	1.0, 1.0	1.0, 1.0	-, -	1.0, 1.0
cDMARDs, concomitant	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abatacept	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adalimumab[c]	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Etanercept[c]	2 (100.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	1 (100.0%)
Golimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infliximab[c]	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Medication[d]					
Methotrexate, concomitant	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Concomitant cDMARD	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dose change, baricitinib	NA	0 (0.0%)	NA	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c TNF inhibitors.

d Only baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked 'NA' as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\ 1. Table 6.52. - Pattern of RA Medication Use in Patients with MACE [IBM].docx

Table 53_MTSCN. Time to First MACE (Days) [MKSCN]

	Unmatched		Matched		
	Baricitinibᵃ,ᵇ (N=259)	**TNFi (N=1,604)**	**Baricitinibᵃ,ᵇ (N=192)**	**TNFi (N=192)**	**Total (N=384)**
n	259	1,604	192	192	384
Mean (SD)	85.50 (16.26)	3.00 (0.00)	97.00 (0.00)	- (-)	97.00 (0.00)
Median	85.50 [74.00, 97.00]	3.00 [3.00, 3.00]	97.00 [97.00, 97.00]	- [-, -]	97.00 [97.00, 97.00]
Min, Max	74.0, 97.0	3.0, 3.0	97.0, 97.0	-,-	97.0, 97.0

Abbreviations: MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis code of acute myocardial infarction or ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Only baricitinib 2-mg dose is available in the US

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.53. - Time to First MACE (Days) [IBM].docx

Table 55_MTSCN. Comparative Risk of MACE [MTSCN]

		TNFi	Baricitinib HR	95%CI	p-value
Base Model[1,2]	Ref	-	-	-	

Abbreviations: cDMARD = conventional disease-modifying antirheumatic drug; CI = confidence interval; HR = Cox proportional hazard ratio; Ref = referent group; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

1 Base model - propensity score-matched model with confounders, outcome and baricitinib exposure.

2 Zero events in the TNFi group preclude analyzing models with additional parameters. The model did not converge.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.55. - Comparative Risk of MACE [IBM MarketScan RA].docx

Table 56_MTSCN. Clinical Characteristics of RA Patients with Incident Serious Infections [MTSCN]

Characteristics[a,b]	Baricitinib[c] (N=1)	TNFi (N=0)	Total (N=1)
Age (mean) [SD]	51.00 (0.00)	- (-)	51.00 (0.00)
Sex			
Female	1 (100.0%)	0 (0.0%)	1 (100.0%)
Male	0 (0.0%)	0 (0.0%)	0 (0.0%)
Clinical Conditions during baseline			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic Lung disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive Heart Failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dyslipidaemia	1 (100.0%)	0 (0.0%)	1 (100.0%)
Hypertension	1 (100.0%)	0 (0.0%)	1 (100.0%)
Immune disorders	1 (100.0%)	0 (0.0%)	1 (100.0%)
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	1 (100.0%)	0 (0.0%)	1 (100.0%)
Primary Sjögren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	4.25 (0.00)	- (-)	4.25 (0.00)
Smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)
Surgery, Trauma, & Hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medications			
Antibiotics	1 (100.0%)	0 (0.0%)	1 (100.0%)
Antidiabetic agents	0 (0.0%)	0 (0.0%)	0 (0.0%)
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			
Anticoagulant	1 (100.0%)	0 (0.0%)	1 (100.0%)

Characteristics[a,b]	Baricitinib[c] (N=1)	TNFi (N=0)	Total (N=1)
Antihypertensives	1 (100.0%)	0 (0.0%)	1 (100.0%)
Antiplatelet	1 (100.0%)	0 (0.0%)	1 (100.0%)
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oral Contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERMs	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucocorticosteroid	1 (100.0%)	0 (0.0%)	1 (100.0%)
Vaccinations	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; CIRAS = claims-based index for RA severity; HRT = hormone replacement therapy; HIV = human immunodeficiency virus; N = number of patients in the analysis in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modifier; SLE = systemic lupus erythematosus; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.56. Clinical Characteristics of RA Patients with Incident Serious Infections [IBM Marketscan RA].docx

Table 57_MTSCN. Pattern of RA Medication Use in Patients with Serious Infection Event [MTSCN]

Characteristic[a]	Unmatched		Matched		
	Baricitinib[b] (N=2)	TNFi (N=8)	Baricitinib[b] (N=1)	TNFi (N=0)	Total (N=1)
Baseline Medication DMARDS					
cDMARDs, during baseline					
n, total	1 (50.0%)	6 (75.0%)	1 (100.0%)	0 (0.0%)	1 (100.0%)
Mean (SD)	1.00 (0.00)	0.88 (0.64)	1.00 (0.00)	- (-)	1.00 (0.00)
Median	1.00 [1.00, 1.00]	1.00 [0.25, 1.00]	1.00 [1.00, 1.00]	- [-, -]	1.00 [1.00, 1.00]
Min, Max	1.0, 1.0	0.0, 2.0	1.0, 1.0	-, -	0.0, 1.0
>1 cDMARD concomitantly	0 (0.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hydroxychloroquine	1 (50.0%)	1 (12.5%)	1 (100.0%)	0 (0.0%)	1 (100.0%)
Leflunomide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate	0 (0.0%)	5 (62.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
bDMARDs, during baseline					
n, total	1 (50.0%)	8 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	0.50 (0.71)	1.00 (0.00)	0.00 (0.00)	- (-)	0.00 (0.00)
Median	0.50 [0.00, 1.00]	1.00 [1.00, 1.00]	0.00 [0.00, 0.00]	- [-, -]	0.00 [0.00, 0.00]
Min, Max	0.0, 1.0	1.0, 1.0	0.0, 0.0	-, -	0.0, 0.0
cDMARDs, concomitant	1 (50.0%)	5 (62.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abatacept	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adalimumab[c]	0 (0.0%)	6 (75.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	3 (37.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Etanercept[c]	0 (0.0%)	4 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Golimumab[c]	0 (0.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infliximab[c]	0 (0.0%)	2 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Medication					
Methotrexate, concomitant	0 (0.0%)	3 (37.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Concomitant cDMARD	2 (100.0%)	4 (50.0%)	1 (100.0%)	0 (0.0%)	1 (100.0%)
Dose change, baricitinib	NA	0 (0.0%)	NA	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c TNF inhibitors.

d Only baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked 'NA' as necessarySource: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.57. Pattern of RA Medication Use in Patients with Serious Infection Event [IBM MarketScan RA].docx

Table 58_MTSCN. Time to First Serious Infection (Days) [MTSCN]

	Unmatched		Matched		
	Baricitinib[a,b] (N=263)	**TNFi (N=1,627)**	**Baricitinib[a,b] (N=194)**	**TNFi (N=194)**	**Total (N=388)**
n	263	1,627	194	194	388
Mean (SD)	201.50 (248.19)	156.38 (164.76)	26.00 (0.00)	- (-)	26.00 (0.00)
Median	201.50 [26.00, 377.00]	69.50 [33.00, 323.50]	26.00 [26.00, 26.00]	- [-, -]	26.00 [26.00, 26.00]
Min, Max	26.00, 377.00	20.0, 444.0	26.0, 26.0	-,-	26.0, 26.0

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Only baricitinib 2-mg dose is available in the US

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.58. Time to First Seroius Infection (Days) [IBM].docx

Table 60_MTSCN. Serious Infection Events Per Patient During All Available Follow-up [MTSCN]

Number of Infections per Person	Unmatched		Matched		
	Baricitinib (N=263)	TNFi (N=1,627)	Baricitinib (N=194)	TNFi (N=194)	Total (N=388)
0	258 (98.1%)	1,606 (98.7%)	191 (98.5%)	194 (100.0%)	385 (99.2%)
1	4 (1.5%)	14 (0.9%)	2 (1.0%)	0 (0.0%)	2 (1.0%)
2	0 (0.0%)	6 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
3	0 (0.0%)	1 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
4	1 (0.4%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	1 (0.3%)
5	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
6	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
>6	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: N = number of patients in the specified category; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.60. Serious Infection Events Per Patient During All Available Follow-up [IBM Marketscan RA].docx

Table 61_MTSCN. Comparative Risk of First Serious Infection Event [MTSCN]

	TNFi	Baricitinib		p-value
		HR	95%CI	
Base Model[1,2]	Ref	-	-	-

Abbreviations: CI = confidence interval; HR = Cox proportional hazard ratio; Ref = referent group; TNFi = tumour necrosis factor inhibitor.

[1] Base model - propensity score-matched model with confounders, outcome and baricitinib exposure.

[2] Zero outcome events in the TNFi group preclude the interpretation of the HR.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\ Table 6.61. Comparative Risk of First Serious Infection Event [IBM Marketscan RA].docx

Table 64_MTSCN. Incidence Rate of Hospitalized TB Event [MTSCN]

	Unmatched		Matched		
	Baricitinib (N=265)	**TNFi (N=1,642)**	**Baricitinib (N=193)**	**TNFi (N=193)**	**Total (N=386)**
Overall					
Person-Years	123.81	784.23	87.95	80.88	168.83
TB Events	0.0	0.0	0.0	0.0	0.0
TB Events/100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 2.98	0.00, 0.47	0.00, 4.20	0.00, 4.56	0.00, 2.19

Abbreviations: CI = confidence interval; N = number of patients in the specified category; PY = person-years; TB = tuberculosis; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.64. Incidence Rate of Hospitalized TB Event [IBM MarketScan].docx

II. Variable Ratio Matching

All prior tables presented were based on propensity score matched baricitinib:TNFi cohorts using a 1:1 matching strategy. In this section, the tables include results that are based on a variable ratio matching (VRM) approach as described in Section 9.9.6.1 of the final study report.

The main analysis was modified to use 1:1 matching, as this allows the results in the meta-analysis to be directly proportional to the amount of baricitinib exposure in each data source. For transparency, comparative results generated using VRM prior to the adoption of the 1:1 matching are included here.

Table 6.45_MTSCN_VRM. Incidence Rate of Event - VTE, Primary Definition [MTSCN]

	Unmatched		Matched		
	Baricitinib[a] (N=257)	**TNFi (N=1,599)**	**Baricitinib[a] (N=159)**	**TNFi (N=386)**	**Total (N=545)**
Overall					
Person-Years	120.93	765.76	69.45	172.21	241.67
VTE Events	1	6	1	1	2
VTE Events/100 PY	0.83	0.78	1.44	0.58	0.83
95% CI	0.02, 4.61	0.29, 1.71	0.04, 8.02	0.02, 3.24	0.10, 2.99
Concomitant MTX Use[b]					
Total, n	44 (17.1%)	339 (21.2%)	20 (12.6%)	65 (16.8%)	85 (15.6%)
Person-Years	29.53	233.58	13.65	36.01	49.65
VTE Events	0	0	0	0	0
VTE Events/100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 12.49	0.00, 1.58	0.00, 27.03	0.00, 10.25	0.00, 7.43
No Concomitant MTX Use[b]					
Total, n	213 (82.9%)	1,260 (78.8%)	139 (87.4%)	321 (83.2%)	460 (84.4%)
Person-Years	91.39	532.19	55.80	136.21	192.01
VTE Events	1	6	1	1	2
VTE Events/100 PY	1.09	1.13	1.79	0.73	1.04
95% CI	0.03, 6.10	0.41, 2.45	0.05, 9.99	0.02, 4.09	0.13, 3.76

Abbreviations: CI = confidence intervals; MTX = methotrexate; N = number of patients in the specified category; PY = person-year; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available.

b Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period

c N (%) of subgroups may not always sum precisely to total group N (%) due to rounding

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.45. Incidence Rate of Event - VTE, Primary Definition [IBM MarketScan RA]_vrm.docx

Table 48_MTSCN_VRM. Comparative Risk of Incident VTE, Primary Definition [MTSCN]

	TNFi	Baricitinib		p-value
		HR	95%CI	
Base Model	Ref	1.06	0.13, 8.83	0.96
Adjusted – Model [1][1]	Ref	3.88	0.24, 62.29	0.34

Abbreviations: CI = confidence interval; HR = Cox proportional hazard ratio; Ref = referent group; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

1Model [1] - propensity score-matched model with outcome and baricitinib exposure, adjusted for any variables that remain unbalanced after PS matching.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.48. Comparative Risk of Incident VTE, Primary Definition [IBM MarketScan RA]_vrm.docx

Table 54_MTSCN_VRM. Incidence Rate of Event - MACE [MTSCN]

Model	Unmatched		Matched		
	Baricitinib[a] (N=259)	TNFi (N=1,604)	Baricitinib[a] (N=163)	TNFi (N=386)	Total (N=549)
Overall					
Person-Years	121.01	769.46	74.25	184.60	258.85
MACE	2	1	0	0	0
MACE/100 PY	1.65	0.13	0.00	0.00	0.00
95% CI	0.20, 5.97	0.00, 0.72	0.00, 4.97	0.00, 2.00	0.00, 1.43
MI					
MI	1	1	0	0	0
Person-Years	121.43	769.46	74.25	184.60	258.85
IR per100 PY	0.82	0.13	0.00	0.00	0.00
95% CI	0.02, 4.59	0.00, 0.72	0.00, 4.97	0.00, 2.00	0.00, 1.43
Stroke, any					
Stroke	1	0	0	0	0
Person-Years	121.18	769.70	74.25	184.60	258.85
IR per 100 PY	0.83	0.00	0.00	0.00	0.00
95% CI	0.02, 4.60	0.00, 0.48	0.00, 4.97	0.00, 2.00	0.00, 1.43
Concomitant MTX Use[b]					

Model	Unmatched		Matched		
	Baricitinib[a] (N=259)	TNFi (N=1,604)	Baricitinib[a] (N=163)	TNFi (N=386)	Total (N=549)
MACE	0	0	0	0	0
Person-Years	28.91	233.58	18.17	51.04	69.21
IR per 100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 12.76	0.00, 1.58	0.00, 20.30	0.00, 7.23	0.00, 5.33
No Concomitant MTX Use[b]					
MACE	2	1	0	0	0
Person-Years	92.10	535.88	56.08	133.56	189.64
IR per 100 PY	2.17	0.19	0.00	0.00	0.00
95% CI	0.26, 7.85	0.01, 1.04	0.00, 6.58	0.00, 2.76	0.00, 1.95

Abbreviations: CI = confidence interval; IR = incidence rate; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; MI = myocardial infarction; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

c N in subgroups may not always sum precisely to total group N due to rounding.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.54. Incidence Rate of Event - MACE [IBM MarketScan RA]_vrm.docx

Table 59_MTSCN_VRM. Incidence Rate of Event - First Serious Infection [MTSCN]

	Unmatched		Matched		
	Baricitinib (N=263)	TNFi (N=1,627)	Baricitinib (N=167)	TNFi (N=401)	Total (N=568)
SI Events	2	8	1	1	2
Person-years	123.28	775.56	77.00	185.76	262.76
IR per 100 PY	1.62	1.03	1.30	0.54	0.76
95% CI	0.20, 5.86	0.45, 2.03	0.03, 7.24	0.01, 3.00	0.09, 2.75

Abbreviations: CI = confidence interval; IR = incidence rate; N = number of patients in the specified category; PY = person-years; SI = serious infection; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\marketscan_MKTSN\1. Table 6.59. Incidence Rate of Event - Serious Infections [IBM MarketScan RA]_vrm.docx

Annex 7. MDR – Additional Results

This annex includes information about results for the following analyses:

I. Additional analysis

These are the additional results that were not presented in the body of this report. Like the results in the body, they are based on 1:1 baricitinib:TNFi propensity-score matching. Specifically, this includes the following:

a. Descriptive tables for unmatched eligible patients.
b. Descriptive tables for matched patient cohorts for the serious infection analyses

I. Additional analysis

Table 1_MDR. Baseline Demographics, Unmatched [MDR]

	Baricitinib			TNFi	Std. Diff.
	Any	4-mg	2-mg	(N=1686)	(Any vs TNFi)
	(N=188)	(n=1)	(n=187)		
Age [yrs]					
N	188	1	187	1686	0.2
Mean (SD)	60.5 (12)	68.0 (NA)	60.5 (12)	57.5 (15)	
Median	60.0	68.0	60.0	59.0	
Min, Max	25.0, 85.0	68.0, 68.0	25.0, 85.0	18.0, 85.0	
≥ 65 years	71 (38%)	1 (100%)	70 (37%)	623 (37%)	
Sex					
Male	24 (13%)	0 (0%)	24 (13%)	352 (21%)	-0.2
Female	164 (87%)	1 (100%)	163 (87%)	1334 (79%)	

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\military health_MDR\Lilly Baricitinib Results_Top-Line_Military Health_v2.0.docx -page 2

Table 4_MDR. Baseline Demographics Incident Serious Infections, Matched [MDR]

	Baricitinib			TNFi	Std. Diff.	Total
	Any	4-mg	2-mg	(N=115)	(Any vs TNFi)	(N=230)
	(N=115)	(n=0)	(n=115)			
Age [yrs]						
N	115	0	115	115	0.0	230
Mean (SD)	59.2 (12)	NA	59.2 (12)	59.0 (14)		59.1 (13)
Median	58.0	NA	58.0	59.0		58.0
Min, Max	25.0, 85.0	NA	25.0, 85.0	28.0, 85.0		25.0, 85.0
≥ 65 years	36 (31%)	0 (0%)	36 (31%)	41 (36%)		77 (33%)
Sex						
Male	17 (15%)	0 (0%)	17 (15%)	16 (14%)	0.0	33 (14%)
Female	98 (85%)	0 (0%)	98 (85%)	99 (86%)		197 (86%)

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\military health_MDR\Lilly Baricitinib Results_Top-Line_Military Health_v2.0.docx -page 5

Table 5_MDR. Baseline Demographics Hospitalized Tuberculosis, Matched [MDR]

	Baricitinib			TNFi	Std. Diff.	Total
	Any	4-mg	2-mg	(N=118)	(Any vs TNFi)	(N=236)
	(N=118)	(n=0)	(n=118)			
Age [yrs]						
N	118	0	118	118	0.0	236
Mean (SD)	59.4 (12)	NA	59.4 (12)	58.7 (16)		59.1 (14)
Median	58.0	NA	58.0	60.0		59.0
Min, Max	25.0, 85.0	NA	25.0, 85.0	18.0, 85.0		18.0, 85.0
≥ 65 years	37 (31%)	0 (0%)	37 (31%)	43 (36%)		80 (34%)
Sex						
Male	17 (14%)	0 (0%)	17 (14%)	14 (12%)	0.1	31 (13%)
Female	101 (86%)	0 (0%)	101 (86%)	104 (88%)		205 (87%)

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

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Table 6_MDR. Clinical History at Baseline, Unmatched Cohorts [MDR]

Characteristic[a,b]	Baricitinib[c] (N=188)	TNFi (N=1686)	Std. Diff.
Clinical Conditions during baseline			
Cancer	16 (9%)	105 (6%)	0.1
NMSC	5 (3%)	28 (2%)	0.1
Chronic lung disease	52 (28%)	279 (17%)	0.3
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	4 (2%)	41 (2%)	0.0
Cardiovascular revascularization	0 (0%)	3 (0%)	-0.1
Congestive Heart Failure, hospitalized	1 (1%)	18 (1%)	-0.1
Coronary artery disease	18 (10%)	147 (9%)	0.0
Ischemic heart disease	19 (10%)	162 (10%)	0.0
Unstable angina	1 (1%)	4 (0%)	0.0
Ventricular arrhythmia	7 (4%)	64 (4%)	0.0
Diabetes Mellitus	30 (16%)	294 (17%)	0.0
Type I	3 (2%)	11 (1%)	0.1
Type II	30 (16%)	291 (17%)	0.0
Dyslipidaemia	80 (43%)	577 (34%)	0.2
Hypertension	101 (54%)	733 (43%)	0.2
Immune disorders	31 (16%)	184 (11%)	0.2
AIDS/HIV	0 (0%)	1 (0%)	0.0
Antiphospholipid syndrome	0 (0%)	5 (0%)	-0.1
SLE	10 (5%)	49 (3%)	0.1
Primary Sjögren Syndrome	27 (14%)	142 (8%)	0.2
Liver Disorder	4 (2%)	18 (1%)	0.1
Obesity	40 (21%)	381 (23%)	0.0
Pregnancy	0 (0%)	5 (0%)	-0.1
RA Severity (CIRAS Index), mean (SD)	3.9 (1)	4.2 (2)	-0.2
Smoking	28 (15%)	238 (14%)	0.0
Surgery, trauma & hospitalization, recent	8 (4%)	86 (5%)	0.0
TIA	1 (1%)	16 (1%)	0.0
Genetic Coagulopathies	0 (0%)	7 (0%)	-0.1
DMARDs			
cDMARDs, during baseline			
n, total	115 (61%)	1062 (63%)	0.0
Mean (SD)	0.9 (1)	0.8 (1)	0.2
Median	1.0	1.0	
Min, Max	0.0, 4.0	0.0, 4.0	0.0, 4.0
>1 cDMARD concomitantly	20 (11%)	93 (6%)	0.2
Hydroxychloroquine	47 (25%)	331 (20%)	0.1

Characteristic[a,b]	Baricitinib[c] (N=188)	TNFi (N=1686)	Std. Diff.
Leflunomide	33 (18%)	191 (11%)	0.2
Methotrexate	61 (32%)	648 (38%)	-0.1
Minocycline	0 (0%)	0 (0%)	0.0
Sulfasalazine	12 (6%)	100 (6%)	0.0
bDMARDs, during baseline			
n, total	114 (61%)	1686 (100%)	-1.1
Mean (SD)	0.7 (1)	1.0 (0)	-0.8
Median	1.0	1.0	
Min, Max	0.0, 2.0	1.0, 2.0	0.0, 2.0
cDMARDs, concomitant	20 (11%)	501 (30%)	-0.5
abatacept	21 (11%)	24 (1%)	0.4
adalimumab[d]	27 (14%)	970 (58%)	-1.0
anakinra	2 (1%)	0 (0%)	0.1
certolizumab pegol[d]	10 (5%)	142 (8%)	-0.1
etanercept[d]	12 (6%)	290 (17%)	-0.3
golimumab[d]	6 (3%)	144 (9%)	-0.2
infliximab[d]	6 (3%)	145 (9%)	-0.2
rituximab	6 (3%)	2 (0%)	0.2
sarilumab	19 (10%)	3 (0%)	0.5
tocilizumab	19 (10%)	13 (1%)	0.4
Other Prescription Medications			
Antibiotics	11 (6%)	53 (3%)	0.1
Antidiabetic agents	18 (10%)	237 (14%)	-0.1
Insulins	3 (2%)	71 (4%)	-0.2
Non-insulins	18 (10%)	215 (13%)	-0.1
Aspirin	1 (1%)	4 (0%)	0.0
Cardiovascular			
Anticoagulant	2 (1%)	35 (2%)	-0.1
Antihypertensives	105 (56%)	898 (53%)	0.1
Antiplatelet	4 (2%)	57 (3%)	-0.1
Nitrates	4 (2%)	40 (2%)	0.0
Hormonal			
HRT	12 (6%)	110 (7%)	0.0
Oral Contraceptives	5 (3%)	52 (3%)	0.0
SERMs	1 (1%)	12 (1%)	0.0
Lipid-lowering agents			
Bile acid binding	4 (2%)	17 (1%)	0.1
Cholesterol absorption inhibitor	4 (2%)	39 (2%)	0.0
Fibrates	5 (3%)	49 (3%)	0.0

Characteristic[a,b]	Baricitinib[c] (N=188)	TNFi (N=1686)	Std. Diff.
Niacin	0 (0%)	3 (0%)	-0.1
Omega-3 fatty acids	0 (0%)	4 (0%)	-0.1
Statins	58 (31%)	499 (30%)	0.0
Rheumatoid arthritis-related			
Cox-2 Inhibitor	21 (11%)	181 (11%)	0.0
Glucocorticosteroid	152 (81%)	1180 (70%)	0.3
Vaccinations	62 (33%)	454 (27%)	0.1

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; cDMARD = conventional disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff. = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics except for the use of bDMARD and cDMARD are measured during the 6 months prior to initiation of study medication until and including the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d TNF inhibitors. Unless otherwise noted, characteristics in this table and similar tables are measured during baseline, including on the index day.

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Table 9_MDR. Clinical Characteristics Incident Serious Infection Cohorts, Matched [MDR]

Characteristic[a,b]	Baricitinib (N=115)	TNFi (N=115)	Std. Diff.
Clinical Conditions during baseline			
Cancer	13 (11%)	6 (5%)	0.2
NMSC	5 (4%)	3 (3%)	0.1
Chronic lung disease	27 (23%)	27 (23%)	0.0
Cardiovascular conditions	13 (11%)	18 (16%)	-0.1
Atrial arrhythmia/fibrillation	5 (4%)	10 (9%)	-0.2
Cardiovascular revascularization	0 (0%)	0 (0%)	0.0
Congestive Heart Failure, hospitalized	1 (1%)	3 (3%)	-0.1
Coronary artery disease	9 (8%)	10 (9%)	0.0
Ischemic heart disease	9 (8%)	11 (10%)	-0.1
Unstable angina	1 (1%)	0 (0%)	0.1
Ventricular arrhythmia	2 (2%)	5 (4%)	-0.2
Diabetes Mellitus	17 (15%)	16 (14%)	0.0
Type I	3 (3%)	0 (0%)	0.2
Type II	17 (15%)	16 (14%)	0.0
Dyslipidaemia	50 (43%)	43 (37%)	0.1
Hypertension	62 (54%)	55 (48%)	0.1
Immune disorders	17 (15%)	8 (7%)	0.3
AIDS/HIV	0 (0%)	0 (0%)	0.0
Antiphospholipid syndrome	0 (0%)	0 (0%)	0.0
SLE	4 (3%)	1 (1%)	0.2
Primary Sjögren Syndrome	16 (14%)	7 (6%)	0.3
Liver Disorder	2 (2%)	4 (3%)	-0.1
Obesity	23 (20%)	21 (18%)	0.0
Pregnancy	0 (0%)	0 (0%)	0.0
RA Severity (CIRAS Index), mean (SD)	4.0 (1)	4.2 (2)	-0.1
Smoking	16 (14%)	16 (14%)	0.0
Surgery, trauma & hospitalization, recent	5 (4%)	6 (5%)	0.0
TIA	1 (1%)	1 (1%)	0.0
Genetic Coagulopathies	0 (0%)	0 (0%)	0.0
DMARDs			
csDMARDs, during baseline			
n, total	68 (59%)	76 (66%)	-0.1
Mean (SD)	0.9 (1)	0.9 (1)	0.1
Median	1.0	1.0	
Min, Max	0.0, 3.0	0.0, 3.0	
>1 csDMARD concomitantly	12 (10%)	6 (5%)	0.2
Hydroxychloroquine	26 (23%)	23 (20%)	0.1

Characteristic[a,b]	Baricitinib (N=115)	TNFi (N=115)	Std. Diff.
Leflunomide	20 (17%)	17 (15%)	0.1
Methotrexate	35 (30%)	45 (39%)	-0.2
Minocycline	0 (0%)	0 (0%)	0.0
Sulfasalazine	7 (6%)	9 (8%)	-0.1
bDMARDs, during baseline			
n, total	115 (100%)	115 (100%)	0.0
Mean (SD)	1.1 (0)	1.0 (0)	0.5
Median	1.0	1.0	
Min, Max	1, 2	1, 2	
csDMARDs, concomitant	22 (19%)	38 (33%)	-0.3
abatacept	21 (18%)	0 (0%)	0.7
adalimumab[c]	26 (23%)	69 (60%)	-0.8
anakinra	1 (1%)	0 (0%)	0.1
certolizumab pegol[c]	10 (9%)	13 (11%)	-0.1
etanercept[c]	13 (11%)	18 (16%)	-0.1
golimumab[c]	6 (5%)	8 (7%)	-0.1
infliximab[c]	7 (6%)	7 (6%)	0.0
rituximab	6 (5%)	0 (0%)	0.3
sarilumab	20 (17%)	1 (1%)	0.6
tocilizumab	19 (17%)	0 (0%)	0.6
Other Prescription Medications			
Antibiotics	6 (5%)	6 (5%)	0.0
Antidiabetic agents	10 (9%)	15 (13%)	-0.1
Insulins	2 (2%)	4 (3%)	-0.1
Non-insulins	10 (9%)	15 (13%)	-0.1
Aspirin	0 (0%)	0 (0%)	0.0
Cardiovascular			
Anticoagulant	5 (4%)	9 (8%)	-0.1
Antihypertensives	67 (58%)	68 (59%)	0.0
Antiplatelet	3 (3%)	4 (3%)	-0.1
Nitrates	2 (2%)	1 (1%)	0.1
Hormonal			
HRT	8 (7%)	8 (7%)	0.0
Oral Contraceptives	3 (3%)	3 (3%)	0.0
SERMs	1 (1%)	0 (0%)	0.1
Lipid-lowering agents			
Bile acid binding	2 (2%)	1 (1%)	0.1
Cholesterol absorption inhibitor	3 (3%)	2 (2%)	0.1
Fibrates	5 (4%)	3 (3%)	0.1

Characteristic[a,b]	Baricitinib (N=115)	TNFi (N=115)	Std. Diff.
Niacin	0 (0%)	0 (0%)	0.0
Omega-3 fatty acids	0 (0%)	0 (0%)	0.0
Statins	34 (30%)	36 (31%)	0.0
Rheumatoid arthritis-related			
Cox-2 Inhibitor	10 (9%)	7 (6%)	0.1
Glucocorticosteroid	93 (81%)	94 (82%)	0.0
Vaccinations	42 (37%)	35 (30%)	0.1

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; csDMARD = conventional synthetic disease-modifying antirheumatic drugs; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff. = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics except for use of bDMARD and concomitant csDMARD are measured during the 6 months prior to initiation of study medication until and including the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c TNF inhibitors

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Table 11_MDR. Baseline Healthcare Resource Utilization, Unmatched [MDR]

Type of Resource Use	Baricitinib (N=188)	TNFi (N=1686)	Std. Diff.
Physician Office Visits			
n, patients	184	1647	0.0
n, events	2924	24733	
Mean (SD)	15.6 (11)	14.7 (13)	0.1
Median	13.0	11.0	
Min, Max	0.0, 56.0	0.0, 121.0	
Rheumatologist Visits			
n, patients	136	1172	0.1
n, events	381	3827	
Mean (SD)	2.0 (2)	2.3 (3)	-0.1
Median	2.0	2.0	
Min, Max	0.0, 10.0	0.0, 34.0	
Other Outpatient Visits			
n, patients	113	1035	0.0

Type of Resource Use	Baricitinib (N=188)	TNFi (N=1686)	Std. Diff.
n, events	429	3399	
Mean (SD)	2.3 (3)	2.0 (3)	0.1
Median	1.0	1.0	
Min, Max	0.0, 13.0	0.0, 24.0	
Inpatient Visits			
n, patients	16	142	0.0
n, events	18	161	
Mean (SD)	0.1 (0)	0.1 (0)	0.0
Median	0.0	0.0	
Min, Max	0.0, 2.0	0.0, 3.0	
ED Visits			
n, patients	54	420	0.1
n, events	75	704	
Mean (SD)	0.4 (1)	0.4 (1)	0.0
Median	0.0	0.0	
Min, Max	0.0, 3.0	0.0, 12.0	

Abbreviations: ED = emergency department; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits. Other outpatient visits do not include physician office visits or rheumatologist visits.

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Table 14_MDR. Baseline Healthcare Resource Utilization Incident Serious Infection Cohorts, Matched [MDR]

Type of Resource Use	Baricitinib (N=115)	TNFi (N=115)	Std. Diff.
Physician Office Visits			
n, patients	115	115	0.0
n, events	1848	1954	
Mean (SD)	16.1 (11)	17.0 (12)	-0.1
Median	14.0	15.0	
Min, Max	1.0, 56.0	1.0, 61.0	
Rheumatologist Visits			
n, patients	88	93	-0.1
n, events	262	337	
Mean (SD)	2.3 (2)	2.9 (3)	-0.3
Median	2.0	2.0	

Type of Resource Use	Baricitinib (N=115)	TNFi (N=115)	Std. Diff.
Min, Max	0.0, 10.0	0.0, 17.0	
Other Outpatient Visits			
n, patients	75	75	0.0
n, events	283	299	
Mean (SD)	2.5 (3)	2.6 (4)	0.0
Median	1.0	1.0	
Min, Max	0.0, 12.0	0.0, 20.0	
Inpatient Visits			
n, patients	7	9	-0.1
n, events	7	10	
Mean (SD)	0.1 (0)	0.1 (0)	-0.1
Median	0.0	0.0	
Min, Max	0.0, 1.0	0.0, 2.0	
ED Visits			
n, patients	35	32	0.1
n, events	46	56	
Mean (SD)	0.4 (1)	0.5 (1)	-0.1
Median	0.0	0.0	
Min, Max	0.0, 3.0	0.0, 7.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits. Other outpatient visits do not include physician office visits or rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\military health_MDR\Lilly Baricitinib Results_Serious Infection_Military Health_v1.0.docx -page 5

Table 16_MDR. Baseline Prevalence of Outcomes [MDR]

Outcome in Each Matched Cohort[a,b]	Unmatched		
	Baricitinib (N=301)	TNFi (N=1812)	Std. Diff.
VTE			
Main case definition	1 (0%)	9 (0%)	0.0
Alternate case definition I	1 (0%)	9 (0%)	0.0
Alternative case definition II	2 (1%)	29 (2%)	-0.1
MACE	2 (1%)	4 (0%)	0.1
Serious Infection	5 (2%)	17 (1%)	0.1
Hospitalized Tuberculosis	0 (0%)	0 (0%)	0.0

Abbreviations: MACE = major adverse cardiovascular event, defined as hospital primary discharge diagnosis code of acute MI or hospital primary discharge diagnosis code of ischemic or hemorrhagic stroke; N = number of patients in specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism, defined based on the case definitions.

a Baseline prevalence was calculated for each distinct matched cohort for VTE, MACE, serious infection, and hospitalized tuberculosis.

b Patients with the prevalent outcomes enumerated in this table are those excluded from the main analyses of each outcome.

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Table 17_MDR. Duration of Follow-up Period (Days), Unmatched [MDR]

	Baricitinib (N=188)	TNFi (N=1686)	Std. Diff
N	188	1686	
Mean (SD)	185.0 (150)	207.7 (166)	-0.1
Median	143.0	158.0	
Min, Max	2.0, 759.0	1.0, 822.0	

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = standardised difference; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\military health_MDR\Lilly Baricitinib Results_Unmatched_Military Health_v1.0.docx -page 4

Table 18_MDR. Duration of Follow-up Period (Days) Primary VTE Cohorts, Matched [MDR]

	Baricitinib (N=114)	TNFi (N=114)	Std. Diff
N	114	114	
Mean (SD)	194.6 (157)	224.5 (192)	-0.2
Median	150	159	
Min, Max	3.0, 759.0	8.0, 790.0	
Reasons for censoring			
Incident event	1 (1%)	1 (1%)	
Medication discontinued	91 (80%)	73 (64%)	
Initiated b/tsDMARD	0 (0%)	0 (0%)	
End of patient record	0 (0%)	0 (0%)	
Death (where available)	1 (1%)	1 (1%)	
End of study period (31 August 2020)	21 (18%)	39 (34%)	

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; Std Diff = standardised difference; VTE = venous thromboembolism.
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Table 39_MDR. Pattern of VTE and Related Diagnostic Codes in Patients with RA [MDR]

Code	Total Patients (N=228)
ICD-10 (PE)	
I26.0	0 (0%)
I26.02	0 (0%)
I26.09	0 (0%)
I26.9	0 (0%)
I26.92	0 (0%)
I26.99	4 (2%)
ICD-10 (DVT lower extremities)	
I82.401	3 (1%)
I82.402	0 (0%)
I82.403	0 (0%)
I82.409	2 (1%)
I82.411	1 (0%)
I82.412	1 (0%)
I82.413	0 (0%)
I82.419	0 (0%)
I82.421	0 (0%)
I82.422	0 (0%)
I82.423	0 (0%)
I82.429	0 (0%)
I82.4y1	0 (0%)
I82.4y2	0 (0%)
I82.4y3	0 (0%)
I82.4y9	0 (0%)
I82.491	0 (0%)
I82.492	0 (0%)
I82.493	0 (0%)
I82.499	0 (0%)
I82.431	1 (0%)
I82.432	0 (0%)
I82.433	0 (0%)
I82.439	0 (0%)
I82.441	0 (0%)

Code	Total Patients (N=228)
I82.442	0 (0%)
I82.443	0 (0%)
I82.449	0 (0%)
I82.4z1	0 (0%)
I82.4z2	0 (0%)
I82.4z3	0 (0%)
I82.4z9	0 (0%)
ICD-10 (DVT upper extremities)	
I82.621	0 (0%)
I82.622	0 (0%)
I82.623	0 (0%)
I82.629	0 (0%)
I82.601	0 (0%)
I82.602	0 (0%)
I82.603	0 (0%)
I82.609	0 (0%)
I82.a11	0 (0%)
I82.a12	0 (0%)
I82.a13	0 (0%)
I82.a19	0 (0%)
I82.c11	0 (0%)
I82.c12	0 (0%)
I82.c13	0 (0%)
I82.c19	0 (0%)
I82.210	0 (0%)
I82.290	0 (0%)
ICD-10 (Phlebitis and thrombophlebitis of lower extremity)	
I80.10	0 (0%)
I80.11	0 (0%)
I80.12	0 (0%)
I80.13	0 (0%)
I80.201	0 (0%)
I80.202	0 (0%)
I80.203	0 (0%)
I80.209	0 (0%)
I80.291	0 (0%)
I80.292	0 (0%)
I80.293	0 (0%)
I80.299	0 (0%)

Code	Total Patients (N=228)
I80.3	0 (0%)
I80.211	0 (0%)
I80.212	0 (0%)
I80.213	0 (0%)
I80.219	0 (0%)
I80.221	0 (0%)
I80.222	0 (0%)
I80.223	0 (0%)
I80.229	0 (0%)
I80.231	0 (0%)
I80.232	0 (0%)
I80.233	0 (0%)
I80.239	0 (0%)
ICD-10 (Other venous thrombosis)	
I80.8	0 (0%)
I80.9	0 (0%)
I81	0 (0%)
I82.0	0 (0%)
I82.1	0 (0%)
I82.220	0 (0%)
I82.3	0 (0%)
I82.890	1 (0%)
I82.90	1 (0%)
I82.b11	0 (0%)
I82.b12	0 (0%)
I82.b13	0 (0%)
I82.b19	0 (0%)

Abbreviations: ICD-10 = International Classification of Disease, 10th Revision; N = number of patients in the specified category; PE = pulmonary embolism; DVT = deep vein thrombosis; RA = rheumatoid arthritis; VTE = venous thromboembolism.

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Table 40_MDR. Clinical Characteristics of RA Patients with VTE, Primary Definition [MDR]

Characterstic[a,b]	Baricitinib (N=1)	TNFi (N=1)	Total (N=2)
Age (mean) [SD]	82.0 (NA)	58.0 (NA)	70.0 (17)
Sex			
Female	1 (100%)	1 (100%)	2 (100%)

Characterstic[a,b]	Baricitinib (N=1)	TNFi (N=1)	Total (N=2)
Male	0 (0%)	0 (0%)	0 (0%)
Clinical Conditions during baseline			
Cancer	1 (100%)	0 (0%)	1 (50%)
NMSC	0 (0%)	0 (0%)	0 (0%)
Chronic Lung disease	0 (0%)	0 (0%)	0 (0%)
Cardiovascular conditions	1 (100%)	1 (100%)	2 (100%)
Atrial arrhythmia/ fibrillation	0 (0%)	0 (0%)	0 (0%)
Cardiovascular revascularization	0 (0%)	0 (0%)	0 (0%)
Congestive Heart Failure, hospitalized	0 (0%)	1 (100%)	1 (50%)
Coronary artery disease	0 (0%)	1 (100%)	1 (50%)
Ischemic heart disease	0 (0%)	1 (100%)	1 (50%)
Unstable angina	0 (0%)	0 (0%)	0 (0%)
Ventricular arrhythmia	1 (100%)	0 (0%)	1 (50%)
Diabetes Mellitus	0 (0%)	1 (100%)	1 (50%)
Type I	0 (0%)	0 (0%)	0 (0%)
Type II	0 (0%)	1 (100%)	1 (50%)
Dyslipidaemia	1 (100%)	1 (100%)	2 (100%)
Hypertension	1 (100%)	1 (100%)	2 (100%)
Immune disorders	0 (0%)	0 (0%)	0 (0%)
AIDS/HIV	0 (0%)	0 (0%)	0 (0%)
Antiphospholipid syndrome	0 (0%)	0 (0%)	0 (0%)
SLE	0 (0%)	0 (0%)	0 (0%)
Primary Sjögren Syndrome	0 (0%)	0 (0%)	0 (0%)
Liver Disorder	0 (0%)	0 (0%)	0 (0%)
Obesity	0 (0%)	1 (100%)	1 (50%)
Pregnancy	0 (0%)	0 (0%)	0 (0%)
RA Severity (CIRAS), mean (SD)	3.1 (NA)	4.6 (NA)	3.9 (1)
Smoking	1 (100%)	1 (100%)	2 (100%)
Surgery, trauma, & hospitalization, recent	0 (0%)	1 (100%)	1 (50%)
Genetic Coagulopathies	0 (0%)	0 (0%)	0 (0%)
TIA	0 (0%)	0 (0%)	0 (0%)
Other Prescription Medication			
Antibiotics	0 (0%)	0 (0%)	0 (0%)
Antidiabetic agents	0 (0%)	0 (0%)	0 (0%)
Insulins	0 (0%)	0 (0%)	0 (0%)
Non-insulins	0 (0%)	0 (0%)	0 (0%)
Aspirin	0 (0%)	0 (0%)	0 (0%)
Cardiovascular			
Antihypertensives	1 (100%)	1 (100%)	2 (100%)
Nitrates	0 (0%)	0 (0%)	0 (0%)
Anticoagulant	0 (0%)	0 (0%)	0 (0%)

Characterstic[a,b]	Baricitinib (N=1)	TNFi (N=1)	Total (N=2)
Antiplatelet	0 (0%)	0 (0%)	0 (0%)
Hormonal			
Oral contraceptives	0 (0%)	0 (0%)	0 (0%)
HRT	0 (0%)	0 (0%)	0 (0%)
SERM	0 (0%)	0 (0%)	0 (0%)
Lipid-lowering agents			
Bile acid binding	0 (0%)	0 (0%)	0 (0%)
Cholesterol absorption inhibitor	0 (0%)	0 (0%)	0 (0%)
Fibrates	0 (0%)	0 (0%)	0 (0%)
Niacin	0 (0%)	0 (0%)	0 (0%)
Omega-3 fatty acids	0 (0%)	0 (0%)	0 (0%)
Statins	1 (100%)	1 (100%)	2 (100%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0%)	0 (0%)	0 (0%)
Glucocorticosteroid	1 (100%)	1 (100%)	2 (100%)
Vaccinations	1 (100%)	0 (0%)	1 (50%)
Post-index Occurrence[c]			
Cancer	0 (0%)	1 (100%)	1 (50%)
Hospitalization	1 (100%)	1 (100%)	2 (100%)
Surgery and Trauma	0 (0%)	0 (0%)	0 (0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics except for use of bDMARD and concomitant csDMARD are measured during the 6 months prior to initiation of study medication until and including the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Except for cancer diagnosed within 90 days of VTE diagnosis, events in this category must have occurred in the 4 weeks immediately prior to VTE (Kline et al. 2017).

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Table 41_MDR. Pattern of RA Medication Use in Patients with VTE, Primary Definition [MDR]

Characteristic[a]	Unmatched		Matched		
	Baricitinib	TNFi	Baricitinib	TNFi	Total
	(N=2)	(N=3)	(N=1)	(N=1)	(N=2)
Baseline Medication					
csDMARDs, during baseline					
n, total	2 (100%)	3 (100%)	1 (100%)	1 (100%)	2 (100%)
Mean (SD)	2.0 (1)	1.0 (0)	3.0 (NA)	1.0 (NA)	2.0 (1)
Median	2.0	1.0	3.0	1.0	2.0
Min, Max	1.0, 3.0	1.0, 1.0	3.0, 3.0	1.0, 1.0	1.0, 3.0
>1 csDMARD concomitantly	1 (50%)	0 (0%)	1 (100%)	0 (0%)	1 (50%)
Hydroxychloroquine	2 (100%)	1 (33%)	1 (100%)	0 (0%)	1 (50%)
Leflunomide	1 (50%)	1 (33%)	1 (100%)	0 (0%)	1 (50%)
Methotrexate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Minocycline	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Sulfasalazine	0 (0%)	1 (33%)	0 (0%)	1 (100%)	1 (50%)
bDMARDs, during baseline					
n, total	1 (50%)	3 (100%)	1 (100%)	1 (100%)	2 (100%)
Mean (SD)	0.5 (1)	1.0 (0)	1.0 (NA)	1.0 (NA)	1.0 (0)
Median	0.5	1.0	1.0	1.0	1.0
Min, Max	0.0, 1.0	1.0, 1.0	1.0, 1.0	1.0, 1.0	1.0, 1.0
csDMARDs, concomitantly	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Abatacept	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Adalimumab[b]	1 (50%)	2 (67%)	1 (100%)	1 (100%)	2 (100%)
Anakinra	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Certolizumab pegol[b]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Etanercept[b]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Golimumab[b]	0 (0%)	1 (33%)	0 (0%)	0 (0%)	0 (0%)
Infliximab[b]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Rituximab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Tocilizumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Post-index Medication[c]					
Methotrexate,concomitant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Other Concomitant csDMARD	1 (50%)	1 (33%)	1 (100%)	0 (0%)	1 (50%)
Dose change, baricitinib	NA	NA	NA	NA	NA

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; csDMARD = conventional synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics except for use of bDMARD and concomitant csDMARD are measured during the 6 months prior to initiation of study medication until and including the index date.

b TNF inhibitors.

c Only baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked 'NA' as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\military health_MDR\Lilly Baricitinib Results_VTE_Military Health_v1.0.docx -page 19

Table 42_MDR. Time to First VTE Event (Days), Primary Definition [MDR]

Time	Unmatched		Matched		
	Baricitinib	TNFi	Baricitinib	TNFi	Total
	(N=188)	(N=1686)	(N=114)	(N=114)	(N=228)
n	2	3	1	1	2
Mean (SD)	371.5 (158)	282.3 (397)	483.0 (NA)	88.0 (NA)	285.5 (279)
Median	371.5	88.0	483.0	88.0	285.5
Min, Max	(260.0, 483.0)	(20.0, 739.0)	(483.0, 483.0)	(88.0, 88.0)	(88.0, 483.0)

Abbreviations: Max = maximum; Min = minimum; N = number of patients in specified category; NA = not applicable; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism, defined as hospitalization for the composite endpoint of incident VTE, either pulmonary embolism or deep vein thrombosis, based on the primary discharge diagnosis code.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\military health_MDR\Lilly Baricitinib Results_VTE_Military Health_v1.0.docx -page 20

Table 52_MDR. Pattern of RA Medication Use in Patients with MACE [MDR]

Characteristic[a]	Unmatched		Matched		
	Baricitinib	TNFi	Baricitinib[b]	TNFi	Total
	(N=0)	(N=4)	(N=0)	(N=0)	(N=0)
Baseline Medication					
csDMARDs, during baseline					
n, total	0	3	0	0	0
Mean (SD)	0 (0)	0.8 (1)	0 (0)	0 (0)	0 (0)
Median	0.0	1.0	0.0	0.0	0.0
Min, Max	0, 0	0.0, 1.0	0, 0	0, 0	0, 0
>1 csDMARD concomitantly	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Hydroxychloroquine	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Leflunomide	0 (0%)	1 (25%)	0 (0%)	0 (0%)	0 (0%)
Methotrexate	0 (0%)	2 (50%)	0 (0%)	0 (0%)	0 (0%)
Minocycline	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Sulfasalazine	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
bDMARDs, during baseline					

n, total	0	4	0	0	0
Mean (SD)	0 (0)	1 (0)	0 (0)	0 (0)	0 (0)
Median	0.0	1.0	0.0	0.0	0.0
Min, Max	0, 0	1.0, 1.0	0, 0	0, 0	0, 0
csDMARDs, concomitantly	0 (0%)	2 (50%)	0 (0%)	0 (0%)	0 (0%)
Abatacept	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Adalimumab[b]	0 (0%)	2 (50%)	0 (0%)	0 (0%)	0 (0%)
Anakinra	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Certolizumab pegol[b]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Etanercept[b]	0 (0%)	1 (25%)	0 (0%)	0 (0%)	0 (0%)
Golimumab[b]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Infliximab[b]	0 (0%)	1 (25%)	0 (0%)	0 (0%)	0 (0%)
Rituximab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Sarilumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Tocilizumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Post-index Medication					
Concomitant Methotrexate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Other Concomitant csDMARD	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Dose change[c], baricitinib	NA	NA	NA	NA	NA

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; csDMARD = conventional synthetic disease-modifying antirheumatic drug; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor

a All conditions and characteristics except for use of bDMARD and concomitant csDMARD are measured during the 6 months prior to initiation of study medication until and including the index date.

b TNF inhibitors.

c Only baricitinib 2-mg dose is available in the US, so the baricitinib dose change should be marked 'NA' in US data

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\military health_MDR\Lilly Baricitinib Results_MACE_Military Health_v1.0.docx -page 10

Table 55_MDR. Comparative Risk of Incident MACE [MDR]

	TNFi	Baricitinib		p-value
		HR	95% CI	
Base Model	Ref	NA	NA	NA

Abbreviations: CI = confidence interval; HR = hazard ratio; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; NA = not applicable; Ref = Referent group; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\military health_MDR\Lilly Baricitinib Results_Top-Line_Military Health_v2.0.docx -page 16

Table 56_MDR. Clinical Characteristics of RA Patients with Incident Serious Infections [MDR]

Characteristics[a,b]	Baricitinib (N=0)	TNFi (N=2)	Total (N=2)
Age (mean) [SD]	0 (0)	66.0 (14)	66.0 (14)
Sex			
Female	0 (0%)	2 (100%)	2 (100%)
Male	0 (0%)	0 (0%)	0 (0%)
Clinical Conditions during baseline			
Cancer	0 (0%)	0 (0%)	0 (0%)
NMSC	0 (0%)	0 (0%)	0 (0%)
Chronic Lung disease	0 (0%)	1 (50%)	1 (50%)
Cardiovascular conditions	0 (0%)	0 (0%)	0 (0%)
Atrial arrhythmia/ fibrillation	0 (0%)	0 (0%)	0 (0%)
Cardiovascular revascularization	0 (0%)	0 (0%)	0 (0%)
Congestive Heart Failure, hospitalized	0 (0%)	0 (0%)	0 (0%)
Coronary artery disease	0 (0%)	0 (0%)	0 (0%)
Ischemic heart disease	0 (0%)	0 (0%)	0 (0%)
Unstable angina	0 (0%)	0 (0%)	0 (0%)
Ventricular arrhythmia	0 (0%)	0 (0%)	0 (0%)
Diabetes Mellitus	0 (0%)	0 (0%)	0 (0%)
Type I	0 (0%)	0 (0%)	0 (0%)
Type II	0 (0%)	0 (0%)	0 (0%)
Dyslipidaemia	0 (0%)	0 (0%)	0 (0%)
Hypertension	0 (0%)	2 (100%)	2 (100%)
Immune disorders	0 (0%)	0 (0%)	0 (0%)
AIDS/HIV	0 (0%)	0 (0%)	0 (0%)
Antiphospholipid syndrome	0 (0%)	0 (0%)	0 (0%)
SLE	0 (0%)	0 (0%)	0 (0%)
Primary Sjögren Syndrome	0 (0%)	0 (0%)	0 (0%)
Liver Disorder	0 (0%)	0 (0%)	0 (0%)
Obesity	0 (0%)	1 (50%)	1 (50%)
Pregnancy	0 (0%)	0 (0%)	0 (0%)
RA Severity (CIRAS), mean (SD)	0 (0)	2.7 (1)	2.7 (1)
Smoking	0 (0%)	0 (0%)	0 (0%)
Surgery, trauma, & hospitalization, recent	0 (0%)	0 (0%)	0 (0%)
TIA	0 (0%)	0 (0%)	0 (0%)
Genetic Coagulopathies	0 (0%)	0 (0%)	0 (0%)
Other Prescription Medications			
Antibiotics	0 (0%)	0 (0%)	0 (0%)
Antidiabetic agents	0 (0%)	0 (0%)	0 (0%)
Insulins	0 (0%)	0 (0%)	0 (0%)

Characteristics[a,b]	Baricitinib (N=0)	TNFi (N=2)	Total (N=2)
Non-insulins	0 (0%)	0 (0%)	0 (0%)
Aspirin	0 (0%)	0 (0%)	0 (0%)
Cardiovascular			
Anticoagulant	0 (0%)	0 (0%)	0 (0%)
Antihypertensives	0 (0%)	2 (100%)	2 (100%)
Antiplatelet	0 (0%)	0 (0%)	0 (0%)
Nitrates	0 (0%)	0 (0%)	0 (0%)
Hormonal			
HRT	0 (0%)	1 (50%)	1 (50%)
Oral Contraceptives	0 (0%)	0 (0%)	0 (0%)
SERMs	0 (0%)	0 (0%)	0 (0%)
Lipid-lowering agents			
Bile acid binding	0 (0%)	0 (0%)	0 (0%)
Cholesterol absorption inhibitor	0 (0%)	0 (0%)	0 (0%)
Fibrates	0 (0%)	0 (0%)	0 (0%)
Niacin	0 (0%)	0 (0%)	0 (0%)
Omega-3 fatty acids	0 (0%)	0 (0%)	0 (0%)
Statins	0 (0%)	0 (0%)	0 (0%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0%)	0 (0%)	0 (0%)
Glucocorticosteroid	0 (0%)	1 (50%)	1 (50%)
Vaccinations	0 (0%)	1 (50%)	1 (50%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics except for use of bDMARD and concomitant csDMARD are measured during the 6 months prior to initiation of study medication until and including the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19). for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

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Table 58_MDR. Time to First Serious Infection Event (Days) [MDR]

Time	Unmatched		Matched		
	Baricitinib (N=191)	TNFi (N=1743)	Baricitinib (N=115)	TNFi (N=115)	Total (N=230)
n	0	16	0	2	2

Mean (SD)	0.0 (0)	145.9 (126)	0.0 (0)	127.0 (7)	127.0 (7)
Median	0.0	127.0	0.0	127.0	127.0
Min, Max	0.0, 0.0	(25.0, 489.0)	0.0, 0.0	(122.0, 132.0)	(122.0, 132.0)

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\military health_MDR\Lilly Baricitinib Results_Serious Infection_Military Health_v1.0.docx -page 12

Table 60_MDR. Serious Infection Events Per Patient During All Available Follow-up [MDR]

Number of Infections per Person	Unmatched		Matched		
	Baricitinib (N=191)	TNFi (N=1743)	Baricitinib (N=115)	TNFi (N=115)	Total (N=230)
0	191 (100%)	1727 (99%)	115 (100%)	113 (98%)	228 (99%)
1	0 (0%)	15 (1%)	0 (0%)	1 (1%)	1 (0%)
2	0 (0%)	1 (0%)	0 (0%)	1 (1%)	1 (0%)
3	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
4	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
6	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
>6	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Abbreviations: N = number of patients in the specified category; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\military health_MDR\Lilly Baricitinib Results_Serious Infection_Military Health_v1.0.docx -page 13

Table 61_MDR. Comparative Risk of First Serious Infection Event [MDR]

	TNFi	Baricitinib		p-value
		HR	95% CI	
Base Model	Ref	0.00	NA	1.00

Abbreviations: CI = confidence interval; HR = hazard ratio; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; NA = not applicable; Ref = Referent group; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\military health_MDR\Lilly Baricitinib Results_Top-Line_Military Health_v2.0.docx -page 18

Table 64_MDR. Incidence Rate of Hospitalized TB Event [MDR]

	Unmatched		Matched		
	Baricitinib (N=195)	TNFi (N=1758)	Baricitinib (N=118)	TNFi (N=118)	Total (N=236)
Overall					
Person-Years	98	1005	62	69	131
TB Events	0.0	0.0	0.0	0.0	0
TB Events/100 PY	0.0	0.0	0.0	0.0	0.0

95% CI	NA	NA	NA	NA	NA

Abbreviations: CI = confidence interval; N = number of patients in the specified category; NA = not applicable; PY = person-years; TB = tuberculosis; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\military health_MDR\Lilly Baricitinib Results_TB_Military Health_v1.0.docx -page 9

Annex 8. Optum – Additional Results

This annex includes information about results for the following analyses:

I. Additional analysis

These additional results were not presented in the body of the report. These results, like those included in the report body, are based on 1:1 baricitinib:TNFi propensity score matching. Specifically, this section in the annex includes:

- Descriptive tables for unmatched eligible patients.
- Descriptive tables for matched patient cohorts for the serious infection analyses

II. Variable Ratio Matching

These results were not presented in the body of this report. They are based on matching baricitinib:TNFi using Variable Ratio matching, i.e., as many matched 1:3 as possible, then the maximum number matched 1:2, then the remaining patients matched 1:1.

I. Additional analysis

Table 1_Optum. Baseline Demographics, Unmatched [Optum]

	Baricitinib			TNFi (N=1,441)	Std. Diff. (Any vs TNFi)
	Any (N=348)	4-mg (N=0)	2-mg (N=348)		
Age [yrs]					
N	348	-	348	1,441	
Mean (SD)	59.19 (11.86)	-	59.19 (11.86)	54.63 (13.96)	0.35
Median	60.00 [52.00, 67.00]	-	60.00 [52.00, 67.00]	56.00 [45.00, 65.00]	
Min, Max	19.0, 89.0	-	19.0, 89.0	18.0, 89.0	
≥ 65 years	122 (35.1%)	-	122 (35.1%)	375 (26.0%)	0.20
Sex					
Male	45 (12.9%)	-	45 (12.9%)	313 (21.7%)	0.23
Female	303 (87.1%)	-	303 (87.1%)	1,128 (78.3%)	0.23

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.1. Baseline Demographics, Unmatched [Optum CDM RA].docx

Table 4_Optum. Baseline Demographics Incident Serious Infections, Matched [Optum]

	Baricitinib			TNFi (N=300)	Std. Diff. (Any vs TNFi)	Total (N=600)
	Any (N=300)	4-mg (N=0)	2-mg (N=300)			
Age [yrs]						
N	300	-	300	300		600
Mean (SD)	59.02 (12.42)	-	59.02 (12.42)	60.29 (11.80)	0.10	59.66 (12.12)
Median	60.00 [50.25, 68.00]	-	60.00 [50.25, 68.00]	61.00 [53.00, 69.00]		61.00 [52.00, 68.75]
Min, Max	19.0, 89.0	-	19.0, 89.0	27.0, 87.0		19.0, 89.0
≥ 65 years	107 (35.7%)	-	107 (35.7%)	119 (39.7%)	0.08	226 (37.7%)
Sex						
Male	44 (14.7%)	-	44 (14.7%)	38 (12.7%)	0.06	82 (13.7%)
Female	256 (85.3%)	-	256 (85.3%)	262 (87.3%)	0.06	518 (86.3%)

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.4. - Baseline Demographics Incident Serious Infections, Matched [Optum CDM RA].docx

Table 6_Optum. Clinical History at Baseline, Unmatched Cohorts [Optum]

Characteristic[a,b]	Baricitinib[c] (N=348)	TNFi (N=1,441)	Std. Diff.
Clinical Conditions during baseline			
Cancer	43 (12.4%)	123 (8.5%)	0.13
NMSC	[redacted] (CCI	14 (1.0%)	0.11
Chronic lung disease	66 (19.0%)	233 (16.2%)	0.07
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	13 (3.7%)	37 (2.6%)	0.07
Cardiovascular revascularization	0 (0.0%)	[redacted] (CCI	0.08
Congestive heart failure, hospitalized	[redacted] (CCI	11 (0.8%)	0.01
Coronary artery disease	30 (8.6%)	98 (6.8%)	0.07
Ischemic heart disease	30 (8.6%)	98 (6.8%)	0.07
Unstable angina	[redacted] (CCI	[redacted] (CCI	0.05
Ventricular arrhythmia	15 (4.3%)	45 (3.1%)	0.06
Diabetes Mellitus	77 (22.1%)	270 (18.7%)	0.08
Type I	[redacted] (CCI	17 (1.2%)	0.03
Type II	76 (21.8%)	267 (18.5%)	0.08
Dyslipidaemia	118 (33.9%)	472 (32.8%)	0.02
Hypertension	163 (46.8%)	612 (42.5%)	0.09
Immune disorders	44 (12.6%)	103 (7.1%)	0.19
AIDS/HIV	[redacted] (CCI	[redacted] (0.3%)	0.01
Antiphospholipid syndrome	[redacted] (CCI	[redacted] (0.1%)	0.05
SLE	21 (6.0%)	34 (2.4%)	0.18
Primary Sjögren syndrome	23 (6.6%)	72 (5.0%)	0.07
Liver disorder	[redacted] (CCI	26 (1.8%)	0.04
Obesity	84 (24.1%)	357 (24.8%)	0.02
Pregnancy	0 (0.0%)	[redacted] (CCI	0.11
RA severity (CIRAS Index), mean (SD)	4.13 (1.25)	4.57 (1.33)	0.35
Smoking	52 (14.9%)	213 (14.8%)	0.01
Surgery, trauma & hospitalization, recent	18 (5.2%)	93 (6.5%)	0.06
TIA	[redacted] (CCI	[redacted] (CCI	0.00
DMARDs			
cDMARDs, during baseline			
n, total	209 (60.1%)	789 (54.8%)	0.11
Mean (SD)	0.88 (0.83)	0.72 (0.72)	0.21
Median	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-
Min, Max	0.0, 4.0	0.0, 3.0	-
>1 cDMARD concomitantly	68 (19.5%)	190 (13.2%)	0.17
Hydroxychloroquine	77 (22.1%)	212 (14.7%)	0.19
Leflunomide	67 (19.3%)	168 (11.7%)	0.21
Methotrexate	98 (28.2%)	460 (31.9%)	0.08
Minocycline	[redacted] (CCI	[redacted] (CCI	0.08
Sulfasalazine	26 (7.5%)	96 (6.7%)	0.03
bDMARDs, during baseline[a]			
n, total	154 (44.3%)	1,352 (93.8%)	1.27

Characteristic[a,b]	Baricitinib[c] (N=348)	TNFi (N=1,441)	Std. Diff.
Mean (SD)	0.66 (0.72)	1.15 (0.38)	0.84
Median	1.00 [0.00, 1.00]	1.00 [1.00, 1.00]	-
Min, Max	0.0, 4.0	1.0, 3.0	-
cDMARDs, concomitant	80 (23.0%)	663 (46.0%)	0.50
abatacept	32 (9.2%)	40 (2.8%)	0.27
adalimumab[d]	28 (8.0%)	500 (34.7%)	0.69
anakinra	0 (0.0%)	0 (0.0%)	-
certolizumab pegol[d]	18 (5.2%)	149 (10.3%)	0.19
etanercept[d]	19 (5.5%)	225 (15.6%)	0.34
golimumab[d]	14 (4.0%)	208 (14.4%)	0.37
infliximab[d]	(CCI	279 (19.4%)	0.60
rituximab	(CCI	(CCI	0.08
sarilumab	17 (4.9%)	(CCI	0.26
tocilizumab	30 (8.6%)	20 (1.4%)	0.34
Other Prescription Medications			
Antibiotics	164 (47.1%)	688 (47.7%)	0.01
Antidiabetic agents	62 (17.8%)	200 (13.9%)	0.11
Insulins	18 (5.2%)	57 (4.0%)	0.06
Non-insulins	58 (16.7%)	181 (12.6%)	0.12
Aspirin	0 (0.0%)	16 (1.1%)	0.15
Cardiovascular			
Anticoagulant	12 (3.4%)	43 (3.0%)	0.03
Antihypertensives	202 (58.0%)	687 (47.7%)	0.21
Antiplatelet	(CCI	48 (3.3%)	0.04
Nitrates	(CCI	28 (1.9%)	0.04
Hormonal			
HRT	29 (8.3%)	91 (6.3%)	0.08
Oral Contraceptives	(CCI	58 (4.0%)	0.12
SERMs	(CCI	(CCI	0.08
Lipid-lowering agents			
Bile acid binding	(CCI	14 (1.0%)	0.09
Cholesterol absorption inhibitor	(CCI	29 (2.0%)	0.02
Fibrates	(CCI	21 (1.5%)	0.00
Niacin	0 (0.0%)	(CCI	0.05
Omega-3 fatty acids	(CCI	14 (1.0%)	0.02
Statins	90 (25.9%)	353 (24.5%)	0.03
Rheumatoid arthritis-related			
Cox-2 Inhibitor	34 (9.8%)	95 (6.6%)	0.12
Glucocorticosteroid	213 (61.2%)	848 (58.8%)	0.05
Vaccinations	124 (35.6%)	441 (30.6%)	0.11

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = conventional disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum, Min = minimum; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics, except for bDMARDs, are measured during the 6 months prior to initiation of study medication including the date at which the qualifying exposure of baricitinib or TNFi occurs (index date). bDMARDs are measured from the 6 months prior to the initiation of study medication until the day prior to baricitinib or the index TNFi exposure, excluding the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d TNF inhibitors.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.6. - Clinical History at Baseline, Unmatched Cohorts [Optum CDM RA]_.docx

Table 9_Optum. Clinical Characteristics Incident Serious Infection Cohorts, Matched [Optum]

Characteristic[a,b]	Baricitinib[c] (N=300)	TNFi (N=300)	Std. Diff.
Clinical Conditions during baseline			
Cancer	35 (11.7%)	31 (10.3%)	0.04
NMSC	[redacted]	[redacted]	0.19
Chronic lung disease	57 (19.0%)	50 (16.7%)	0.06
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	20 (6.7%)	15 (5.0%)	0.07
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	-
Congestive heart failure, hospitalized	[redacted]	[redacted]	0.04
Coronary artery disease	26 (8.7%)	27 (9.0%)	0.01
Ischemic heart disease	26 (8.7%)	27 (9.0%)	0.01
Unstable angina	[redacted]	[redacted]	0.04
Ventricular arrhythmia	15 (5.0%)	[redacted]	0.10
Diabetes Mellitus	63 (21.0%)	66 (22.0%)	0.02
Type I	[redacted]	[redacted]	0.12
Type II	62 (20.7%)	65 (21.7%)	0.02
Dyslipidaemia	104 (34.7%)	111 (37.0%)	0.05
Hypertension	142 (47.3%)	139 (46.3%)	0.02
Immune disorders	29 (9.7%)	26 (8.7%)	0.04
AIDS/HIV	0 (0.0%)	0 (0.0%)	-
Antiphospholipid syndrome	[redacted]	[redacted]	0.00
SLE	14 (4.7%)	[redacted]	0.15
Primary Sjögren syndrome	15 (5.0%)	20 (6.7%)	0.07
Liver disorder	[redacted]	[redacted]	0.02
Obesity	69 (23.0%)	71 (23.7%)	0.02
Pregnancy	0 (0.0%)	0 (0.0%)	-
RA severity (CIRAS Index), mean (SD)	4.19 (1.27)	4.15 (1.26)	0.03
Smoking	41 (13.7%)	40 (13.3%)	0.01
Surgery, trauma & hospitalization, recent	12 (4.0%)	16 (5.3%)	0.06
TIA	[redacted]	[redacted]	0.08
DMARDs			
cDMARDs, during baseline			
n, total	192 (64.0%)	143 (47.7%)	0.33
Mean (SD)	0.94 (0.85)	0.65 (0.73)	0.36
Median	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-
Min, Max	0.0, 4.0	0.0, 3.0	-
>1 cDMARD concomitantly	65 (21.7%)	39 (13.0%)	0.23
Hydroxychloroquine	66 (22.0%)	45 (15.0%)	0.18
Leflunomide	64 (21.3%)	27 (9.0%)	0.35
Methotrexate	94 (31.3%)	80 (26.7%)	0.10
Minocycline	3 (1.0%)	0 (0.0%)	0.14
Sulfasalazine	25 (8.3%)	19 (6.3%)	0.08
bDMARDs, during baseline[a]			

Characteristic[a,b]	Baricitinib[c] (N=300)	TNFi (N=300)	Std. Diff.
n, total	110 (36.7%)	281 (93.7%)	1.49
Mean (SD)	0.47 (0.57)	1.46 (0.56)	1.73
Median	0.00 [0.00, 1.00]	1.00 [1.00, 2.00]	-
Min, Max	0.0, 2.0	1.0, 3.0	-
cDMARDs, concomitant	61 (20.3%)	121 (40.3%)	0.45
abatacept	22 (7.3%)	27 (9.0%)	0.06
adalimumab[d]	21 (7.0%)	104 (34.7%)	0.73
anakinra	CCI	0 (0.0%)	0.08
certolizumab pegol[d]	13 (4.3%)	32 (10.7%)	0.24
etanercept[d]	CCI	54 (18.0%)	0.49
golimumab[d]	CCI	49 (16.3%)	0.46
infliximab[d]	CCI	49 (16.3%)	0.53
rituximab	CCI	CCI	0.04
sarilumab	CCI	CCI	0.12
tocilizumab	20 (6.7%)	CCI	0.15
Other Prescription Medications			
Antibiotics	136 (45.3%)	137 (45.7%)	0.01
Antidiabetic agents	52 (17.3%)	50 (16.7%)	0.02
Insulins	14 (4.7%)	13 (4.3%)	0.02
Non-insulins	48 (16.0%)	46 (15.3%)	0.02
Aspirin	0 (0.0%)	CCI	0.08
Cardiovascular			
Anticoagulant	27 (9.0%)	19 (6.3%)	0.10
Antihypertensives	173 (57.7%)	161 (53.7%)	0.08
Antiplatelet	CCI	CCI	0.00
Nitrates	CCI	CCI	0.00
Hormonal			
HRT	20 (6.7%)	23 (7.7%)	0.04
Oral Contraceptives	CCI	CCI	0.06
SERMs	CCI	0 (0.0%)	0.14
Lipid-lowering agents			
Bile acid binding	CCI	CCI	0.07
Cholesterol absorption inhibitor	CCI	CCI	0.10
Fibrates	CCI	CCI	0.03
Niacin	0 (0.0%)	0 (0.0%)	-
Omega-3 fatty acids	CCI	CCI	0.07
Statins	77 (25.7%)	99 (33.0%)	0.16
Rheumatoid arthritis-related			
Cox-2 Inhibitor	29 (9.7%)	20 (6.7%)	0.11
Glucocorticosteroid	181 (60.3%)	172 (57.3%)	0.06
Vaccinations	102 (34.0%)	90 (30.0%)	0.09

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = conventional disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum, Min = minimum; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics, except for bDMARDs, are measured during the 6 months prior to initiation of study medication including the date at which the qualifying exposure of baricitinib or TNFi occurs (index date). bDMARDs are measured from the 6 months prior to the initiation of study medication until the day prior to baricitinib or the index TNFi exposure, excluding the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d TNF inhibitors.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.9. - Clinical Characteristics Incident Serious Infection Cohorts, Matched [Optum CDM RA].docx

Table 11A_Optum. Baseline Healthcare Resource Utilization, Unmatched [Optum]

Type of Resource Use	Baricitinib (N=348)	TNFi (N=1,441)	Std. Diff.
Physician Office Visits			
n, patients	328 (94.3%)	1,376 (95.5%)	0.06
n, events	5822	27033	
Mean (SD)	16.73 (18.22)	18.76 (20.20)	0.11
Median	11.00 [5.00, 22.00]	13.00 [6.00, 25.00]	
Min, Max	0.0, 135.0	0.0, 211.0	
Rheumatologist Visits			
n, patients	243 (69.8%)	1,137 (78.9%)	0.21
n, events	1771	12090	
Mean (SD)	5.09 (7.19)	8.39 (10.73)	0.36
Median	2.00 [0.00, 7.00]	4.00 [1.00, 13.00]	
Min, Max	0.0, 47.0	0.0, 99.0	
Other Outpatient Visits			
n, patients	329 (94.5%)	1,388 (96.3%)	0.09
n, events	10339	44340	
Mean (SD)	29.71 (30.55)	30.77 (36.27)	0.03
Median	20.00 [10.25, 37.00]	20.00 [10.00, 39.00]	
Min, Max	0.0, 186.0	0.0, 547.0	
Inpatient Visits			
n, patients	29 (8.3%)	144 (10.0%)	0.06
n, events	891	4222	
Mean (SD)	2.56 (11.51)	2.93 (14.51)	0.03
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 102.0	0.0, 306.0	
ED Visits			
n, patients	65 (18.7%)	263 (18.3%)	0.01
n, events	310	1023	
Mean (SD)	0.89 (2.96)	0.71 (2.12)	0.07
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 28.0	0.0, 23.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.11A. Baseline Healthcare Resource Utilization, Unmatched [Optum].docx

Table 11B_Optum. Baseline Healthcare Resource Utilization, Unmatched [Optum], count at most one visit per day[1]

Type of Resource Use	Baricitinib (N=348)	TNFi (N=1,441)	Std. Diff.
Physician Office Visits[1]			
n, patients	328 (94.3%)	1,376 (95.5%)	0.06
n, events	2,638	11,600	
Mean (SD)	7.58 (7.05)	8.05 (7.22)	0.07
Median	6.00 [3.00, 10.00]	6.00 [3.00, 11.00]	
Min, Max	0.0, 45.0	0.0, 66.0	
Rheumatologist Visits[1]			
n, patients	243 (69.8%)	1,137 (78.9%)	0.21
n, events	696	3,905	
Mean (SD)	2.00 (1.95)	2.71 (2.48)	0.32
Median	2.00 [0.00, 3.00]	2.00 [1.00, 4.00]	
Min, Max	0.0, 9.0	0.0, 25.0	
Other Outpatient Visits[1]			
n, patients	329 (94.5%)	1,388 (96.3%)	0.09
n, events	2,286	9,136	
Mean (SD)	6.57 (7.58)	6.34 (7.69)	0.03
Median	5.00 [2.00, 8.00]	4.00 [2.00, 8.00]	
Min, Max	0.0, 80.0	0.0, 106.0	
Inpatient Visits[1]			
n, patients	29 (8.3%)	144 (10.0%)	0.06
n, events	167	749	
Mean (SD)	0.48 (2.57)	0.52 (2.62)	0.01
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 32.0	0.0, 48.0	
ED Visits[1]			
n, patients	65 (18.7%)	263 (18.3%)	0.01
n, events	157	605	
Mean (SD)	0.45 (1.86)	0.42 (1.36)	0.02
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 27.0	0.0, 20.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

[1] In this table, results describe utilization of healthcare where a maximum of one event was allowed per day. In the PS matching analyses, multiple claims on the same day were allowed to capture additional information on the amount of services received in a given visit. These results are presented in table 6.11A.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.11B (count at most one visit per day). Baseline Healthcare Resource Utilization, Unmatched [Optum].docx

Table 12A_Optum. Baseline Healthcare Resource Utilization Primary VTE Cohorts, Matched [Optum]

Type of Resource Use	Baricitinib (N=284)	TNFi (N=284)	Std. Diff.
Physician Office Visits			
n, patients	266 (93.7%)	272 (95.8%)	0.10
n, events	4680	5263	
Mean (SD)	16.48 (17.90)	18.53 (18.83)	0.11
Median	11.00 [5.00, 22.00]	13.00 [6.00, 24.75]	
Min, Max	0.0, 108.0	0.0, 150.0	
Rheumatologist Visits			
n, patients	198 (69.7%)	208 (73.2%)	0.08
n, events	1531	1676	
Mean (SD)	5.39 (7.60)	5.90 (7.89)	0.07
Median	2.00 [0.00, 8.00]	3.00 [0.00, 9.00]	
Min, Max	0.0, 47.0	0.0, 40.0	
Other Outpatient Visits			
n, patients	267 (94.0%)	277 (97.5%)	0.18
n, events	8656	8426	
Mean (SD)	30.48 (32.48)	29.67 (28.72)	0.03
Median	19.50 [10.00, 37.00]	22.00 [11.00, 40.00]	
Min, Max	0.0, 186.0	0.0, 233.0	
Inpatient Visits			
n, patients	23 (8.1%)	24 (8.5%)	0.01
n, events	744	642	
Mean (SD)	2.62 (12.08)	2.26 (8.87)	0.03
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 102.0	0.0, 63.0	
ED Visits			
n, patients	53 (18.7%)	70 (24.6%)	0.15
n, events	258	304	
Mean (SD)	0.91 (3.15)	1.07 (2.56)	0.06
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 28.0	0.0, 20.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.12A. Baseline Healthcare Resource Utilization, Primary VTE Cohorts, Matched [Optum].docx

Table 13A_Optum. Baseline Healthcare Resource Utilization MACE Cohorts, Matched [Optum]

Type of Resource Use	Baricitinib (N=287)	TNFi (N=287)	Std. Diff.
Physician Office Visits			
n, patients	270 (94.1%)	272 (94.8%)	0.03
n, events	4730	4796	
Mean (SD)	16.48 (17.52)	16.71 (16.42)	0.01
Median	11.00 [5.00, 22.00]	13.00 [6.00, 23.00]	
Min, Max	0.0, 108.0	0.0, 116.0	
Rheumatologist Visits			
n, patients	201 (70.0%)	205 (71.4%)	0.03
n, events	1504	1690	
Mean (SD)	5.24 (7.38)	5.89 (7.88)	0.09
Median	2.00 [0.00, 8.00]	2.00 [0.00, 9.00]	
Min, Max	0.0, 47.0	0.0, 40.0	
Other Outpatient Visits			
n, patients	271 (94.4%)	277 (96.5%)	0.10
n, events	8449	8501	
Mean (SD)	29.44 (30.59)	29.62 (28.98)	0.01
Median	19.00 [10.00, 37.00]	23.00 [11.00, 38.00]	
Min, Max	0.0, 186.0	0.0, 233.0	
Inpatient Visits			
n, patients	22 (7.7%)	20 (7.0%)	0.03
n, events	703	732	
Mean (SD)	2.45 (11.46)	2.55 (13.54)	0.01
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 102.0	0.0, 151.0	
ED Visits			
n, patients	50 (17.4%)	62 (21.6%)	0.11
n, events	255	270	
Mean (SD)	0.89 (3.14)	0.94 (2.50)	0.02
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 28.0	0.0, 20.0	

Abbreviations: ED = emergency department; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.13A. Baseline Healthcare Resource Utilization MACE Cohorts, Matched [Optum].docx

Table 14A_Optum. Baseline Healthcare Resource Utilization Serious Infection Cohorts, Matched [Optum]

Type of Resource Use	Baricitinib (N=300)	TNFi (N=300)	Std. Diff.
Physician Office Visits			
n, patients	281 (93.7%)	287 (95.7%)	0.09
n, events	5115	5133	
Mean (SD)	17.05 (19.02)	17.11 (14.81)	0.00
Median	11.00 [5.00, 22.00]	13.00 [7.00, 23.00]	
Min, Max	0.0, 136.0	0.0, 113.0	
Rheumatologist Visits			
n, patients	214 (71.3%)	225 (75.0%)	0.08
n, events	1623	1722	
Mean (SD)	5.41 (7.80)	5.74 (7.91)	0.04
Median	2.00 [0.00, 7.00]	2.00 [0.25, 8.00]	
Min, Max	0.0, 47.0	0.0, 48.0	
Other Outpatient Visits			
n, patients	283 (94.3%)	292 (97.3%)	0.15
n, events	8718	8370	
Mean (SD)	29.06 (30.03)	27.90 (23.52)	0.04
Median	20.00 [10.00, 37.00]	20.50 [12.00, 38.00]	
Min, Max	0.0, 186.0	0.0, 131.0	
Inpatient Visits			
n, patients	22 (7.3%)	19 (6.3%)	0.04
n, events	507	522	
Mean (SD)	1.69 (7.98)	1.74 (8.49)	0.01
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 66.0	0.0, 75.0	
ED Visits			
n, patients	57 (19.0%)	62 (20.7%)	0.04
n, events	249	264	
Mean (SD)	0.83 (2.77)	0.88 (2.38)	0.02
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 28.0	0.0, 20.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.14A. Baseline Healthcare Resource Utilization Incident Serious Infection Cohorts, Matched [Optum].docx

Table 14B_Optum. Baseline Healthcare Resource Utilization Serious Infection Cohorts, Matched [Optum], count at most one visit per day[1]

Type of Resource Use	Baricitinib (N=300)	TNFi (N=300)	Std. Diff.
Physician Office Visits[1]			
n, patients	281 (93.7%)	287 (95.7%)	0.09
n, events	2313	2289	
Mean (SD)	7.71 (7.71)	7.63 (5.66)	0.01
Median	6.00 [3.00, 10.00]	7.00 [4.00, 10.00]	
Min, Max	0.0, 63.0	0.0, 42.0	
Rheumatologist Visits[1]			
n, patients	214 (71.3%)	225 (75.0%)	0.08
n, events	600	702	
Mean (SD)	2.00 (1.95)	2.34 (2.50)	0.15
Median	2.00 [0.00, 3.00]	2.00 [0.25, 3.00]	
Min, Max	0.0, 9.0	0.0, 25.0	
Other Outpatient Visits[1]			
n, patients	283 (94.3%)	292 (97.3%)	0.15
n, events	1848	1881	
Mean (SD)	6.16 (6.28)	6.27 (5.60)	0.02
Median	5.00 [2.00, 8.00]	5.00 [3.00, 8.00]	
Min, Max	0.0, 57.0	0.0, 39.0	
Inpatient Visits[1]			
n, patients	22 (7.3%)	19 (6.3%)	0.04
n, events	99	90	
Mean (SD)	0.33 (2.09)	0.30 (1.67)	0.02
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 32.0	0.0, 21.0	
ED Visits[1]			
n, patients	57 (19.0%)	62 (20.7%)	0.04
n, events	129	156	
Mean (SD)	0.43 (1.85)	0.52 (1.69)	0.05
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 27.0	0.0, 20.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

[1] In this table, results describe utilization of healthcare where a maximum of one event was allowed per day. In the PS matching analyses, multiple claims on the same day were allowed to capture additional information on the amount of services received in a given visit. These results are presented in table 6.14A.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.14B (count at most one visit per day). Baseline Healthcare Resource Utilization Serious Infection Cohorts, Matched [Optum].docx

Table 16_Optum. Baseline Prevalence of Outcomes [Optum]

Outcome in Each Matched Cohort[a,c,d]	Unmatched			Matched			
	Baricitinib[b]	TNFi	Std. Diff	Baricitinib[b]	TNFi	Std. Diff	Total
VTE	N=351	N=1,444	-	N=282	N=282	-	N=564
Main case definition in baseline	[redacted]	[redacted]	0.09	[redacted]	[redacted]	0.05	[redacted]
Alternate case definition I in baseline	[redacted]	[redacted]	0.09	[redacted]	[redacted]	0.05	[redacted]
Alternative case definition II in baseline	[redacted]	[redacted]	0.09	[redacted]	[redacted]	0.11	[redacted]
MACE	N=351	N=1,444	-	N=290	N=290	-	N=580
MACE in baseline	0 (0.0%)	[redacted]	0.08	0 (0.0%)	[redacted]	0.12	[redacted]
Serious Infection	N=370	N=1,498	-	N=303	N=303	-	N=606
Serious Infection in baseline	[redacted]	21 (1.4%)	0.00	[redacted]	0 (0.0%)	0.16	[redacted]
Hospitalized Tuberculosis	N=370	N=1,498	-	N=303	N=303	-	N=606
Hospitalized Tuberculosis in baseline	0 (0.0%)	[redacted]	0.04	0 (0.0%)	0 (0.0%)	-	0 (0.0%)

Abbreviations: MACE = major adverse cardiovascular event, defined as hospital primary discharge diagnosis code of acute MI or hospital primary discharge diagnosis code of ischemic or hemorrhagic stroke; N = number of patients in specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism, defined based on the case definitions.

a Baseline prevalence was calculated for each distinct matched cohort for VTE, MACE, serious infection and hospitalized tuberculosis.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c Patients with the prevalent outcomes enumerated in this table are those excluded from the main analyses of each outcome, except for VTE alternative case definitions I and II. Only the VTE main case definition was used as an exclusion criterion in the main analyses.

d In the VTE and MACE analyses, cohorts additionally excluded the use of anticoagulants at the time of cohort entry (see protocol Section 8.7.7), resulting in a different N compared to the Serious Infection and Hospitalized Tuberculosis cohorts.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.16. Baseline Prevalence of Outcomes [Optum]_.docx

Table 17_Optum. Duration of Follow-up Period (Days), Unmatched [Optum]

	Baricitinib[a] (N=348)	TNFi (N=1,441)	Std. Diff.
N	348	1,441	
Mean (SD)	159.01 (139.03)	200.75 (184.91)	0.26
Median	111.00 [59.00, 212.00]	134.00 [68.00, 268.00]	
Min, Max	2.0, 707.0	0.0, 943.0	

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be reported for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.17. Duration of Follow-up Period (Days), Unmatched [Optum CDM RA].docx

Table 18_Optum. Duration of Follow-up Period (Days) Primary VTE Cohorts, Matched [Optum]

	Baricitinib[a,b] (N=284)	TNFi (N=284)	Std. Diff.
N	284	284	0
Mean (SD)	151.68 (139.04)	209.56 (174.33)	0.37
Median	96.00 [59.00, 197.50]	153.00 [82.25, 289.25]	
Min, Max	2.0, 707.0	0.0, 909.0	
Reasons for censoring [c]			
Incident event	[redacted]	0	-
Medication discontinued	149 (52.5%)	134 (47.2%)	-
Initiated b/tsDMARD	13 (4.6%)	16 (5.6%)	-
End of patient record	101 (35.6%)	107 (37.7%)	-
Death (where available)	0 (0.0%)	1 (0.4%)	-
End of study period (12/31/2020)	72 (25.4%)	78 (27.5%)	-

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be reported for each dose where numbers of patients are sufficient to warrant separate reporting.

b There were 0 patients with a baricitinib dose of 4 mg. Hence, 100% of the patients presented in this column have a baricitinib dose of 2 mg.

c A single patient can be censored on the same day for multiple reasons, e.g., medication discontinued could also be the same day as initiated b/tsDMARD. Further, additional censoring criteria (e.g., switching medication) were specified in the SAP. For these reasons, the total number of reasons for censoring may be less than or greater than the total number of patients.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.18. Duration of Follow-up Period (Days) Primary VTE Cohorts, Matched [Optum].docx

Table 21_Optum. Duration of Follow-up Period (Days) MACE Cohorts, Matched [Optum]

	Baricitinib[a,b] (N=287)	TNFi (N=287)	Std. Diff.
N	287	287	
Mean (SD)	154.54 (136.71)	205.48 (186.19)	0.31
Median	102.00 [59.00, 204.00]	137.00 [65.00, 287.00]	
Min, Max	2.0, 707.0	0.0, 943.0	
Reasons for censoring			
Incident event	[redacted]	[redacted]	-
Medication discontinued	147 (51.2%)	133 (46.3%)	-
Initiated b/tsDMARD	15 (5.2%)	12 (4.2%)	-
End of patient record	100 (34.8%)	119 (41.5%)	-
Death (where available)	0 (0.0%)	0 (0.0%)	-
End of study period (12/31/2020)	71 (24.7%)	87 (30.3%)	-

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = standardised difference; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be reported for each dose where numbers of patients are sufficient to warrant separate reporting.

b There were 0 patients with a baricitinib dose of 4 mg. Hence, 100% of the patients presented in this column have a baricitinib dose of 2 mg.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.21. Duration of Follow-up Period (Days) MACE Cohorts, Matched [Optum].docx

Table 22_Optum. Duration of Follow-up Period (Days) Incident Serious Infection Cohorts, Matched [Optum]

	Baricitinib[a,b] (N=300)	TNFi (N=300)	Std. Diff.
N	300	300	
Mean (SD)	152.42 (132.82)	212.11 (185.35)	0.37
Median	108.00 [59.00, 204.00]	146.00 [72.00, 302.75]	
Min, Max	2.0, 670.0	0.0, 943.0	
Reasons for censoring			
Incident event	[redacted]	[redacted]	-
Medication discontinued	149 (49.7%)	137 (45.7%)	-
Initiated b/tsDMARD	13 (4.3%)	15 (5.0%)	-
End of patient record	108 (36.0%)	113 (37.7%)	-
Death (where available)	0 (0.0%)	0 (0.0%)	-
End of study period (07/05/2021)	78 (26.0%)	85 (28.3%)	-

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b There were 0 patients with a baricitinib dose of 4 mg. Hence, 100% of the patients presented in this column have a baricitinib dose of 2 mg.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.22. Duration of Follow-up Period (Days) Incident Serious Infection Cohorts, Matched [Optum CDM RA].docx

Table 39_Optum. Pattern of VTE and Related Diagnostic Codes in Patients with RA [Optum]

Code	Total Patients (N=11)
Pulmonary Embolism	
I26.0 - Pulmonary embolism with acute cor pulmonale	0 (0.0%)
I26.02 - Saddle embolus of pulmonary artery with acute cor pulmonale	0 (0.0%)
I26.09 - Other pulmonary embolism with acute cor pulmonale	[redacted] (CCI
I26.9 - Pulmonary embolism without acute cor pulmonale	0 (0.0%)
I26.92 - Saddle embolus of pulmonary artery without acute cor pulmonale	0 (0.0%)
I26.99 - Other pulmonary embolism without acute cor pulmonale	[redacted] (CCI
Deep Vein Thrombosis, lower	
I80.10 - Phlebitis and thrombophlebitis of unspecified femoral vein	0 (0.0%)
I80.11 - Phlebitis and thrombophlebitis of right femoral vein	0 (0.0%)
I80.13 - Phlebitis and thrombophlebitis of femoral vein, bilateral	0 (0.0%)
I80.211 - Phlebitis and thrombophlebitis of right iliac vein	0 (0.0%)
I80.221 - Phlebitis and thrombophlebitis of right popliteal vein	0 (0.0%)
I80.223 - Phlebitis and thrombophlebitis of popliteal vein, bilateral	0 (0.0%)
I80.232 - Phlebitis and thrombophlebitis of left tibial vein	0 (0.0%)
I80.233 - Phlebitis and thrombophlebitis of tibial vein, bilateral	0 (0.0%)
I80.292 - Phlebitis and thrombophlebitis of other deep vessels of left lower extremity	0 (0.0%)
I80.293 - Phlebitis and thrombophlebitis of other deep vessels of lower extremity, bilateral	0 (0.0%)
I80.3 - Phlebitis and thrombophlebitis of lower extremities, unspecified	0 (0.0%)
I82.419 - Acute embolism and thrombosis of unspecified femoral vein	0 (0.0%)
I82.423 - Acute embolism and thrombosis of iliac vein, bilateral	0 (0.0%)
I82.431 - Acute embolism and thrombosis of right popliteal vein	0 (0.0%)
I82.432 - Acute embolism and thrombosis of left popliteal vein	[redacted] (CCI
I82.433 - Acute embolism and thrombosis of popliteal vein, bilateral	0 (0.0%)
I82.441 - Acute embolism and thrombosis of right tibial vein	0 (0.0%)
I82.442 - Acute embolism and thrombosis of left tibial vein	[redacted] (CCI
I82.443 - Acute embolism and thrombosis of tibial vein, bilateral	0 (0.0%)
I82.449 - Acute embolism and thrombosis of unspecified tibial vein	0 (0.0%)

Code	Total Patients (N=11)
I82.491 - Acute embolism and thrombosis of other specified deep vein of right lower extremity	0 (0.0%)
I82.4Y1 - Acute embolism and thrombosis of unspecified deep veins of right proximal lower extremity	0 (0.0%)
I82.4Y3 - Acute embolism and thrombosis of unspecified deep veins of proximal lower extremity, bilateral	0 (0.0%)
I82.4Y9 - Acute embolism and thrombosis of unspecified deep veins of unspecified proximal lower extremity	0 (0.0%)
I82.4Z1 - Acute embolism and thrombosis of unspecified deep veins of right distal lower extremity	0 (0.0%)
I82.4Z2 - Acute embolism and thrombosis of unspecified deep veins of left distal lower extremity	0 (0.0%)
I82.4Z3 - Acute embolism and thrombosis of unspecified deep veins of distal lower extremity, bilateral	0 (0.0%)
I80.12 - Phlebitis and thrombophlebitis of left femoral vein	0 (0.0%)
I80.201 - Phlebitis and thrombophlebitis of unspecified deep vessels of right lower extremity	0 (0.0%)
I80.202 - Phlebitis and thrombophlebitis of unspecified deep vessels of left lower extremity	0 (0.0%)
I80.203 - Phlebitis and thrombophlebitis of unspecified deep vessels of lower extremities, bilateral	0 (0.0%)
I80.209 - Phlebitis and thrombophlebitis of unspecified deep vessels of unspecified lower extremity	0 (0.0%)
I80.212 - Phlebitis and thrombophlebitis of left iliac vein	0 (0.0%)
I80.213 - Phlebitis and thrombophlebitis of iliac vein, bilateral	0 (0.0%)
I80.219 - Phlebitis and thrombophlebitis of unspecified iliac vein	0 (0.0%)
I80.222 - Phlebitis and thrombophlebitis of left popliteal vein	0 (0.0%)
I80.229 - Phlebitis and thrombophlebitis of unspecified popliteal vein	0 (0.0%)
I80.231 - Phlebitis and thrombophlebitis of right tibial vein	0 (0.0%)
I80.291 - Phlebitis and thrombophlebitis of other deep vessels of right lower extremity	0 (0.0%)
I80.299 - Phlebitis and thrombophlebitis of other deep vessels of unspecified lower extremity	0 (0.0%)
I82.401 - Acute embolism and thrombosis of unspecified deep veins of right lower extremity	[redacted] (CCI)
I82.402 - Acute embolism and thrombosis of unspecified deep veins of left lower extremity	[redacted] (CCI)

Code	Total Patients (N=11)
I82.403 - Acute embolism and thrombosis of unspecified deep veins of lower extremity, bilateral	0 (0.0%)
I82.409 - Acute embolism and thrombosis of unspecified deep veins of unspecified lower extremity	0 (0.0%)
I82.411 - Acute embolism and thrombosis of right femoral vein	[redacted] (CCI
I82.412 - Acute embolism and thrombosis of left femoral vein	[redacted] (CCI
I82.413 - Acute embolism and thrombosis of femoral vein, bilateral	0 (0.0%)
I82.421 - Acute embolism and thrombosis of right iliac vein	0 (0.0%)
I82.422 - Acute embolism and thrombosis of left iliac vein	[redacted] (CCI
I82.429 - Acute embolism and thrombosis of unspecified iliac vein	0 (0.0%)
I82.439 - Acute embolism and thrombosis of unspecified popliteal vein	0 (0.0%)
I82.492 - Acute embolism and thrombosis of other specified deep vein of left lower extremity	0 (0.0%)
I82.493 - Acute embolism and thrombosis of other specified deep vein of lower extremity, bilateral	0 (0.0%)
I82.499 - Acute embolism and thrombosis of other specified deep vein of unspecified lower extremity	0 (0.0%)
I82.4Y2 - Acute embolism and thrombosis of unspecified deep veins of left proximal lower extremity	0 (0.0%)
Deep Vein Thrombosis, upper	
I82.210 - Acute embolism and thrombosis of superior vena cava	0 (0.0%)
I82.601 - Acute embolism and thrombosis of unspecified veins of right upper extremity	0 (0.0%)
I82.621 - Acute embolism and thrombosis of deep veins of right upper extremity	0 (0.0%)
I82.622 - Acute embolism and thrombosis of deep veins of left upper extremity	0 (0.0%)
I82.623 - Acute embolism and thrombosis of deep veins of upper extremity, bilateral	0 (0.0%)
I82.A12 - Acute embolism and thrombosis of left axillary vein	0 (0.0%)
I82.C11 - Acute embolism and thrombosis of right internal jugular vein	0 (0.0%)
I82.C13 - Acute embolism and thrombosis of internal jugular vein, bilateral	0 (0.0%)
I82.C19 - Acute embolism and thrombosis of unspecified internal jugular vein	0 (0.0%)
I82.602 - Acute embolism and thrombosis of unspecified veins of left upper extremity	0 (0.0%)
I82.603 - Acute embolism and thrombosis of unspecified veins of upper extremity, bilateral	0 (0.0%)

Code	Total Patients (N=11)
I82.609 - Acute embolism and thrombosis of unspecified veins of unspecified upper extremity	0 (0.0%)
I82.629 - Acute embolism and thrombosis of deep veins of unspecified upper extremity	0 (0.0%)
I82.A11 - Acute embolism and thrombosis of right axillary vein	0 (0.0%)
I82.A13 - Acute embolism and thrombosis of axillary vein, bilateral	0 (0.0%)
I82.A19 - Acute embolism and thrombosis of unspecified axillary vein	0 (0.0%)
I82.C12 - Acute embolism and thrombosis of left internal jugular vein	0 (0.0%)
Other Venous Thrombosis	
I81 - Portal vein thrombosis	0 (0.0%)
I82.0 - Budd-Chiari syndrome	0 (0.0%)
I82.1 - Thrombophlebitis migrans	0 (0.0%)
I82.3 - Embolism and thrombosis of renal vein	0 (0.0%)
I82.90 - Acute embolism and thrombosis of unspecified vein	0 (0.0%)
I82.B13 - Acute embolism and thrombosis of subclavian vein, bilateral	0 (0.0%)
I80.8 - Phlebitis and thrombophlebitis of other sites	[redacted] (CCI)
I80.9 - Phlebitis and thrombophlebitis of unspecified site	0 (0.0%)
I82.220 - Acute embolism and thrombosis of inferior vena cava	0 (0.0%)
I82.890 - Acute embolism and thrombosis of other specified veins	0 (0.0%)
I82.B11 - Acute embolism and thrombosis of right subclavian vein	0 (0.0%)
I82.B12 - Acute embolism and thrombosis of left subclavian vein	0 (0.0%)

Abbreviations: ICD-10 = International Classification of Disease, 10th Revision; N = number of patients in the specified category; RA = rheumatoid arthritis; VTE = venous thromboembolis

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.39. Pattern of VTE and Related Diagnostic Codes in Patients with RA [Optum CDM RA].docx

Table 40_Optum. Clinical Characteristics of RA Patients with VTE, Primary Definition [Optum]

Characteristic [a, b]	Baricitinib [c] (N=CCI)	TNFi (N=0)	Total (N=CCI)
Age (mean) [SD]	62.00 (8.49)	- (-)	62.00 (8.49)
Sex			
Female	CCI (CCI)	0 (0.0%)	CCI (CCI)
Male	0 (0.0%)	0 (0.0%)	0 (0.0%)
Clinical Conditions during baseline			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic Lung disease Disease	CCI (CCI)	0 (0.0%)	CCI (CCI)
Cardiovascular conditions			
Atrial arrhythmia/ fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	CCI (CCI)	0 (0.0%)	CCI (CCI)
Ischemic heart disease	CCI (CCI)	0 (0.0%)	CCI (CCI)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dyslipidaemia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertension	CCI (CCI)	0 (0.0%)	CCI (CCI)
Immune disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Primary Sjögren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	1 (50.0%)	0 (0.0%)	1 (50.0%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	3.58 (1.03)	- (-)	3.58 (1.03)
Smoking	CCI (CCI)	0 (0.0%)	CCI
Surgery, trauma, & hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medication			
Antibiotics	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antidiabetic agents	0 (0.0%)	0 (0.0%)	0 (0.0%)
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)

Characteristic [a, b]	Baricitinib [c] (N=2)	TNFi (N=0)	Total (N=2)
Non-insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			
Antihypertensives	[redacted]	0 (0.0%)	[redacted]
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anticoagulant	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiplatelet	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			
Oral contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERM	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucocorticosteroid	[redacted]	0 (0.0%)	[redacted]
Vaccinations	[redacted]	0 (0.0%)	[redacted]
Post-index Occurrence[d]			
Cancer	[redacted]	0 (0.0%)	[redacted]
Hospitalization	[redacted]	0 (0.0%)	[redacted]
Surgery	0 (0.0%)	0 (0.0%)	0 (0.0%)
Trauma	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modifier; SLE = systemic lupus erythematosus; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = Venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d Except for cancer diagnosed within 90 days of VTE diagnosis, events in this category must have occurred in the 4 weeks immediately prior to VTE (Kline et al. 2017).

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.40. - Clinical Characteristics of RA Patients with VTE, Primary Definition [Optum CDM RA].docx

Table 41_Optum. Pattern of RA Medication Use in Patients with VTE, Primary Definition [Optum]

Characteristic [a]	Unmatched		Matched		
	Baricitinib[b] (N=CCI	TNFi (N=CCI	Baricitinib[b] (N=CCI	TNFi (N=0)	Total (N=CCI
Baseline Medication					
cDMARDs, during baseline					
n, total	CCI	CCI	CCI	0 (0.0%)	CCI
Mean (SD)	2.00 (1.41)	0.67 (0.71)	2.00 (1.41)	- (-)	2.00 (1.41)
Median	2.00 [1.00, 3.00]	1.00 [0.00, 1.00]	2.00 [1.00, 3.00]	- [-, -]	2.00 [1.00, 3.00]
Min, Max	1.0, 3.0	0.0, 2.0	1.0, 3.0	-, -	1.0, 3.0
>1 cDMARD concomitantly	CCI	CCI	CCI	0 (0.0%)	CCI
Hydroxychloroquine	CCI	CCI	CCI	0 (0.0%)	CCI
Leflunomide	CCI	CCI	CCI	0 (0.0%)	CCI
Methotrexate	CCI	CCI	CCI	0 (0.0%)	CCI
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
bDMARDs, during baseline					
n, total	0 (0.0%)	8 (88.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	0.00 (0.00)	1.00 (0.00)	0.00 (0.00)	- (-)	0.00 (0.00)
Median	0.00 [0.00, 0.00]	1.00 [1.00, 1.00]	0.00 [0.00, 0.00]	- [-, -]	0.00 [0.00, 0.00]
Min, Max	0.0, 0.0	0.0, 1.0	0.0, 0.0	-, -	0.0, 0.0
cDMARDs, concomitant	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abatacept	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adalimumab [c]	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Etanercept [c]	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Golimumab [c]	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infliximab [c]	0 (0.0%)	CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Medication [d]					
Methotrexate, concomitant	CCI	CCI	CCI	0 (0.0%)	CCI
Other Concomitant cDMARD	CCI	CCI	CCI	0 (0.0%)	CCI
Dose change, baricitinib	NA[d]	0 (0.0%)	NA[d]	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c TNF inhibitors.

d Only baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked 'NA' as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.41. - Pattern of RA Medication Use in Patients with VTE, Primary Definition [Optum].docx

Table 42_Optum. Time to First Event Outcome (days) - VTE, Primary Definition [Optum]

Time	Unmatched		Matched		
	Baricitinib[a,b] (N=348)	TNFi (N=1,441)	Baricitinib[a,b] (N=284)	TNFi (N=284)	Total (N=568)
n	348	1,441	284	284	568
Mean (SD)	198.00 (141.42)	154.89 (208.43)	198.00 (141.42)	- (-)	198.00 (141.42)
Median	198.00 [98.00, 298.00]	62.00 [37.50, 260.50]	198.00 [98.00, 298.00]	- [-, -]	198.00 [98.00, 298.00]
Min, Max	98.0, 298.0	14.0, 606.0	98.0, 298.0	-,-	98.0, 298.0

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; VTE = venous thromboembolism.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Only baricitinib 2-mg dose is available in the US

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.42. Time to First Event Outcome (days) - VTE, Primary Definition [Optum].docx

Table 48_Optum. Comparative Risk of Incident VTE, Primary Definition [Optum]

	TNFi	Baricitinib		p-value
		HR	95%CI	
Base Model[1,2]	Ref	>999.999	<0.001, >999.999	0.85

Abbreviations: cDMARD = conventional disease-modifying antirheumatic drug; CI = confidence interval; HR = Cox proportional hazard ratio; Ref = referent group; TNFi = tumour necrosis factor inhibitor ; VTE = venous thromboembolism.

1 Base model - propensity score-matched model with confounders, outcome and baricitinib exposure.

2 Zero events in the TNFi referent group preclude the interpretability of the HR.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.48. Comparative Risk of Incident VTE, Primary Definition [Optum CDM RA], updated base model = PS matched.docx

Table 51_Optum. Clinical Characteristics of RA Patients with MACE [Optum]

Characteristic[a,b]	Baricitinib[c] (N=CCI)	TNFi (N=CCI)	Total (N=CCI)
Age (mean) [SD]	64.00 (22.63)	65.00 (0.00)	64.33 (16.01)
Sex			
Female	CCI (CCI)	CCI (CCI)	CCI (CCI)
Male	CCI (CCI)	0 (0.0%)	CCI (CCI)
Clinical Conditions during baseline			
Cancer	CCI (CCI)	0 (0.0%)	CCI (CCI)
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic lung disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	CCI (CCI)	0 (0.0%)	CCI (CCI)
Ischemic heart disease	CCI (CCI)	0 (0.0%)	CCI (CCI)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	CCI (CCI)	0 (0.0%)	CCI (CCI)
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	CCI (CCI)	0 (0.0%)	CCI (CCI)
Dyslipidaemia	CCI (CCI)	0 (0.0%)	CCI (CCI)
Hypertension	CCI (CCI)	0 (0.0%)	CCI (CCI)
Immune disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Primary Sjögren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	4.88 (0.27)	3.71 (0.00)	4.49 (0.70)
Smoking	0 (0.0%)	CCI (CCI)	CCI (CCI)
Surgery, Trauma, & Hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medications			
Antibiotics	CCI (CCI)	0 (0.0%)	CCI (CCI)
Antidiabetic agents	CCI (CCI)	0 (0.0%)	CCI (CCI)
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-insulins	CCI (CCI)	0 (0.0%)	CCI (CCI)
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			
Anticoagulant	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antihypertensives	CCI (CCI)	0 (0.0%)	CCI (CCI)
Antiplatelet	0 (0.0%)	0 (0.0%)	0 (0.0%)

Characteristic[a,b]	Baricitinib[c] (N=CCI	TNFi (N=CCI	Total (N=CCI
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			
Oral contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERM	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	CCI (CCI	CCI (CCI	CCI (CCI
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucocorticosteroid	CCI (CCI	CCI (CCI	CCI (CCI
Vaccinations	CCI (CCI	0 (0.0%)	CCI (CCI
Post-index Occurrence[d]			
Methotrexate, concomitant	0 (0.0%)	CCI (CCI	CCI (CCI

Abbreviations: AIDS = acquired immunodeficiency syndrome; CIRAS = claims-based index for RA severity; HIV = ; HRT = hormone replacement therapy; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; SD = standard deviation; SLE = systemic lupus erythematosus; RA = rheumatoid arthritis; SERM = selective estrogen receptor modifier; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d Events in this category must have occurred in the 7 days immediately prior to MACE.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.51. - Clinical Characteristics of RA Patients with MACE [Optum CDM RA]_.docx

Table 52_Optum. Pattern of RA Medication Use in Patients with MACE [Optum]

Characteristic [a]	Unmatched		Matched		
	Baricitinib[b] (N=CCI	TNFi (N=CCI	Baricitinib[b] (N=CCI	TNFi (N=CCI	Total (N=CCI
Baseline Medication					
cDMARDs, during baseline					
n, total	CCI (CCI	CCI (CCI	CCI (CCI	CCI (CCI	CCI (CCI
Mean (SD)	1.00 (1.41)	1.50 (0.71)	1.00 (1.41)	1.00 (0.00)	1.00 (1.00)
Median [IQR]	1.00 [0.00, 2.00]	1.50 [1.00, 2.00]	1.00 [0.00, 2.00]	1.00 [1.00, 1.00]	1.00 [0.00, 2.00]
Min, Max	0.0, 2.0	1.0, 2.0	0.0, 0.2	1.0, 1.0	0.0, 2.0
>1 cDMARD concomitantly	CCI (CCI	CCI (CCI	CCI (CCI	0 (0.0%)	CCI (CCI
Hydroxychloroquine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Leflunomide	CCI (CCI	0 (0.0%)	CCI (CCI	0 (0.0%)	CCI (CCI
Methotrexate	CCI (CCI	CCI (CCI	CCI (CCI	CCI (CCI	CCI (CCI
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	CCI (CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
bDMARDs, during baseline					
n, total	CCI (CCI	CCI (CCI	CCI (CCI	CCI (CCI	CCI (CCI
Mean (SD)	0.50 (0.71)	1.00 (0.00)	0.50 (0.71)	1.00 (0.00)	0.67 (0.58)
Median	0.50 [0.00, 1.00]	1.00 [1.00, 1.00]	0.50 [0.00, 1.00]	1.00 [1.00, 1.00]	1.00 [0.00, 1.00]
Min, Max	0.0, 1.0	0.0, 1.0	0.0, 1.0	1.0, 10	0.0, 1.0
cDMARDs, concomitant	0 (0.0%)	CCI (CCI	0 (0.0%)	CCI (CCI	CCI (CCI
Abatacept	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adalimumab[c]	0 (0.0%)	CCI (CCI	0 (0.0%)	CCI (CCI	CCI (CCI
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Etanercept[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Golimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infliximab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	CCI (CCI	0 (0.0%)	CCI (CCI	0 (0.0%)	CCI (CCI
Post-index Medication[d]					
Methotrexate, concomitant	0 (0.0%)	CCI (CCI	0 (0.0%)	CCI (CCI	CCI (CCI
Other Concomitant cDMARD	0 (0.0%)	CCI (CCI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dose change, baricitinib	NA[d]	0 (0.0%)	NA[d]	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; IQR = interquartile range; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c TNF inhibitors.

d Only baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked 'NA' as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.52. - Pattern of RA Medication Use in Patients with MACE [Optum].docx

Table 53_Optum. Time to First MACE (Days) [Optum]

	Unmatched		Matched		
	Baricitiniba,b (N=351)	**TNFi (N=1,440)**	**Baricitiniba,b (N=287)**	**TNFi (N=287)**	**Total (N=574)**
n	351	1,440	287	287	574
Mean (SD)	153.50 (181.73)	175.00 (93.34)	153.50 (181.73)	109.00 (0.00)	138.67 (131.04)
Median	153.50 [25.00, 282.00]	175.00 [109.00, 241.00]	153.50 [25.00, 282.00]	109.00 [109.00, 109.00]	109.00 [25.00, 282.00]
Min, Max	25.0, 282.0	109.0, 241.0	25.0, 282.0	109.0, 109.0	25.0, 282.0

Abbreviations: MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis code of acute myocardial infarction or ischemic or haemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Only baricitinib 2-mg dose is available in the US.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.53. - Time to First MACE (Days) [Optum].docx

Table 56_Optum. Clinical Characteristics of RA Patients with Incident Serious Infections [Optum]

Characteristics[a,b]	**Baricitinib[c] (N=CCI**	**TNFi (N=CCI**	**Total (N=CCI**
Age (mean) [SD]	55.00 (15.72)	69.00 (5.06)	64.33 (11.26)
Sex			
Female	CCI (CCI	CCI (CCI	CCI (CCI
Male	0 (0.0%)	CCI (CCI	CCI (CCI
Clinical Conditions during baseline			
Cancer	0 (0.0%)	CCI (CCI	CCI (CCI

Characteristics[a,b]	Baricitinib[c] (N=CCI	TNFi (N=CCI	Total (N=CCI
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic Lung disease	CCI	CCI	CCI
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	0 (0.0%)	CCI	CCI
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive Heart Failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	CCI	CCI
Ischemic heart disease	0 (0.0%)	CCI	CCI
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	CCI	CCI
Diabetes Mellitus	CCI	CCI	CCI
Type I	CCI	CCI	CCI
Type II	CCI	CCI	CCI
Dyslipidaemia	0 (0.0%)	CCI	CCI
Hypertension	CCI	CCI	CCI
Immune disorders	CCI	CCI	CCI
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Primary Sjögren Syndrome	CCI	CCI	CCI
Liver Disorder	0 (0.0%)	CCI	CCI
Obesity	CCI	CCI	CCI
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	4.20 (1.52)	3.13 (0.61)	3.49 (1.05)
Smoking	CCI	CCI	CCI
Surgery, Trauma, & Hospitalization, recent	CCI	CCI	CCI
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medications			
Antibiotics	CCI	CCI	CCI
Antidiabetic agents	CCI	CCI	CCI
Insulins	CCI	CCI	CCI
Non-insulins	0 (0.0%)	CCI	CCI
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			
Anticoagulant	CCI	CCI	CCI
Antihypertensives	CCI	CCI	CCI
Antiplatelet	0 (0.0%)	CCI	CCI
Nitrates	CCI	0 (0.0%)	CCI
Hormonal			
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oral Contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)

Characteristics[a,b]	Baricitinib[c] (N=CCI	TNFi (N=CCI	Total (N=CCI
SERMs	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol absorption inhibitor	0 (0.0%)	CCI	CCI
Fibrates	0 (0.0%)	CCI	CCI
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	0 (0.0%)	CCI	CCI
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	CCI	CCI
Glucocorticosteroid	CCI	CCI	CCI
Vaccinations	CCI	CCI	CCI

Abbreviations: AIDS = acquired immunodeficiency syndrome; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; N = number of patients in the analysis in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERM = selective estrogen receptor modifier; SLE = systemic lupus erythematosus; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.56. Clinical Characteristics of RA Patients with Incident Serious Infections [Optum CDM RA].docx

Table 57_Optum. Pattern of RA Medication Use in Patients with Serious Infection Event [Optum]

Characteristic[a]	Unmatched		Matched		
	Baricitinib[b] (N=4)	TNFi (N=28)	Baricitinib[b] (N=2)	TNFi (N=7)	Total (N=9)
Baseline Medication DMARDS					
cDMARDs, during baseline					
n, total	4 (100.0%)	23 (82.1%)	2 (100.0%)	6 (85.7%)	8 (88.9%)
Mean (SD)	1.25 (0.50)	1.00 (0.72)	1.50 (0.71)	1.14 (0.69)	1.22 (0.67)
Median	1.00 [1.00, 1.75]	1.00 [1.00, 1.00]	1.50 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]
Min, Max	1.0, 2.0	0.0, 3.0	1.0, 2.0	0.0, 2.0	0.0, 2.0
>1 cDMARD concomitantly	1 (25.0%)	5 (17.9%)	1 (50.0%)	2 (28.6%)	3 (33.3%)
Hydroxychloroquine	2 (50.0%)	5 (17.9%)	2 (100.0%)	1 (14.3%)	3 (33.3%)
Leflunomide	1 (25.0%)	6 (21.4%)	1 (50.0%)	1 (14.3%)	2 (22.2%)
Methotrexate	2 (50.0%)	15 (53.6%)	0 (0.0%)	4 (57.1%)	4 (44.4%)
Minocycline	0 (0.0%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
bDMARDs, during baseline					
n, total	2 (50.0%)	28 (100.0%)	0 (0.0%)	7 (100.0%)	7 (77.8%)
Mean (SD)	1.00 (0.82)	1.25 (0.59)	0.50 (0.71)	1.57 (0.79)	1.33 (0.87)
Median	1.00 [0.25, 1.75]	1.00 [1.00, 1.00]	0.50 [0.00, 1.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]
Min, Max	0.0, 2.0	1.0, 3.0	0.0, 1.0	1.0, 3.0	0.0, 3.0
cDMARDs, concomitant	2 (50.0%)	22 (78.6%)	0 (0.0%)	6 (85.7%)	6 (66.7%)
Abatacept	0 (0.0%)	1 (3.6%)	0 (0.0%)	1 (14.3%)	1 (11.1%)
Adalimumab[c]	0 (0.0%)	16 (57.1%)	0 (0.0%)	3 (42.9%)	3 (33.3%)
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	8 (28.6%)	0 (0.0%)	3 (42.9%)	3 (33.3%)
Etanercept[c]	1 (25.0%)	11 (39.3%)	0 (0.0%)	2 (28.6%)	2 (22.2%)
Golimumab[c]	0 (0.0%)	5 (17.9%)	0 (0.0%)	1 (14.3%)	1 (11.1%)
Infliximab[c]	0 (0.0%)	13 (46.4%)	0 (0.0%)	4 (57.1%)	4 (44.4%)
Rituximab	0 (0.0%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	1 (25.0%)	1 (3.6%)	0 (0.0%)	1 (14.3%)	1 (11.1%)
Post-index Medication					
Methotrexate, concomitant	2 (50.0%)	10 (35.7%)	0 (0.0%)	5 (71.4%)	5 (55.6%)
Other Concomitant cDMARD	2 (50.0%)	13 (46.4%)	2 (100.0%)	4 (57.1%)	6 (66.7%)
Dose change, baricitinib	NA	0 (0.0%)	NA	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c TNF inhibitors.

d Only baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked 'NA' as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.57. Pattern of RA Medication Use in Patients with Serious Infection Event [Optum].docx

Table 58_Optum. Time to First Serious Infection (Days) [Optum]

	Unmatched		Matched		
	Baricitinib[a,b] (N=366)	**TNFi (N=1,478)**	**Baricitinib[a,b] (N=300)**	**TNFi (N=300)**	**Total (N=600)**
n	366	1,478	300	300	600
Mean (SD)	80.25 (62.07)	197.89 (187.48)	79.67 (76.00)	204.67 (119.83)	163.00 (119.69)
Median [IQR]	80.50 [22.75, 137.50]	133.00 [72.25, 288.00]	79.00 [4.00, 156.00]	215.50 [75.25, 319.50]	156.00 [68.50, 282.50]
Min, Max	4.0, 156.0	8.0, 853.0	4.0, 156.0	58.0, 348.0	4.0, 348.0

Abbreviations: IQR = intequartile range; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis code of acute myocardial infarction or ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Only baricitinib 2-mg dose is available in the US

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.58. Time to First Seroius Infection (Days) [Optum].docx

Table 60_Optum. Serious Infection Events Per Patient During All Available Follow-up [Optum]

Number of Infections per Person	Unmatched		Matched		
	Baricitinib (N=366)	TNFi (N=1,478)	Baricitinib (N=302)	TNFi (N=302)	Total (N=604)
0	352 (96.2%)	1,416 (95.8%)	292 (96.7%)	292 (96.7%)	584 (96.7%)
1	0 (0.0%)	1 (0.1%)	0 (0.0%)	1 (0.3%)	1 (0.2%)
2	1 (0.3%)	3 (0.2%)	1 (0.3%)	1 (0.3%)	2 (0.3%)
3	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
4	0 (0.0%)	2 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
5	0 (0.0%)	3 (0.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
6	0 (0.0%)	4 (0.3%)	0 (0.0%)	1 (0.3%)	1 (0.2%)
>6	12 (3.3%)	45 (3.0%)	9 (3.0%)	5 (1.7%)	14 (2.3%)
N/A[a]	0 (0.0%)	4 (0.3%)	0 (0.0%)	2 (0.7%)	2 (0.3%)

Abbreviations: N = number of patients in the specified category; N/A = not available; TNFi = tumour necrosis factor inhibitor.

a Patients who start their follow-up on the same day as the last day of available data are censored and have less than 1 day of follow-up. These patients are excluded from any of the Serious Infections count categories.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.60. Serious Infection Events Per Patient During All Available Follow-up [Optum CDM RA].docx

Table 64_Optum. Incidence Rate of Hospitalized TB Event [Optum]

	Unmatched		Matched		
	Baricitinib (N=370)	**TNFi (N=1,497)**	**Baricitinib (N=302)**	**TNFi (N=302)**	**Total (N=604)**
Overall					
Person-Years	164.94	823.89	126.29	177.71	303.99
TB Events	0.0	0.0	0.0	0.0	0.0
TB Events/100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 2.24	0.00, 0.45	0.00, 2.92	0.00, 2.08	0.00, 1.21

Abbreviations: CI = confidence interval; N = number of patients in the specified category; PY = person-years; TB = tuberculosis; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.64. Incidence Rate of Hospitalized TB Event [Optum].docx

II. Variable Ratio Matching

All prior tables presented were based on propensity score matched baricitinib:TNFi cohorts using a 1:1 matching strategy. In this section, the tables include results that are based on a variable ratio matching (VRM) approach as described in Section 9.9.6.1 of the final study report.

The main analysis was modified to use 1:1 matching, as this allows the results in the meta-analysis to be directly proportional to the amount of baricitinib exposure in each data source. For transparency, comparative results generated using VRM prior to the adoption of the 1:1 matching are included here.

Table 45_Optum_VRM. Incidence Rate of Event - VTE, Primary Definition [Optum]

	Unmatched		Matched		
	Baricitinib[a] (N=348)	**TNFi (N=1,441)**	**Baricitinib[a] (N=262)**	**TNFi (N=659)**	**Total (N=921)**
Overall					
Person-Years	CCI	CCI	CCI	CCI	CCI
VTE Events	CCI	CCI	CCI	CCI	CCI
VTE Events/100 PY	1.32	1.14	0.93	0.26	0.41
95% CI	0.16, 4.77	0.52, 2.16	0.02, 5.21	0.01, 1.46	0.05, 1.48
Concomitant MTX Use[b]					
Total, n	60 (17.2%)	289 (20.1%)	47 (17.9%)	139 (21.1%)	186 (20.2%)
Person-Years	CCI	CCI	CCI	CCI	CCI
VTE Events	CCI	CCI	CCI	CCI	CCI
VTE Events/100 PY	2.80	0.91	3.77	0.92	1.48
95% CI	0.07, 15.61	0.11, 3.29	0.10, 21.00	0.02, 5.12	0.18, 5.34
No Concomitant MTX Use[b]					
Total, n	288 (82.8%)	1,152 (79.9%)	215 (82.1%)	520 (78.9%)	735 (79.8%)
Person-Years	CCI	CCI	CCI	CCI	CCI
VTE Events	CCI	CCI	0	0	0
VTE Events/100 PY	0.86	1.22	0.00	0.00	0.00
95% CI	0.02, 4.81	0.49, 2.52	0.00, 4.58	0.00, 1.36	0.00, 1.05

Abbreviations: CI = confidence intervals; MTX = methotrexate; N = number of patients in the specified category; PY = person-year; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available.

b Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period

c N (%) of subgroups may not always sum precisely to total group N (%) due to rounding

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.45. Incidence Rate of Event - VTE, Primary Definition [Optum CDM RA]_vrm.docx

Table 48_Optum_VRM. Comparative Risk of Incident VTE, Primary Definition [Optum]

	TNFi	Baricitinib		p-value
		HR	95%CI	
Base Model	Ref	1.14	0.24, 5.33	0.87
Adjusted – Model [1][1]	Ref	6.89	0.39, 120.42	0.19

Abbreviations: CI = confidence interval; HR = Cox proportional hazard ratio; Ref = referent group; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

1 Model [1] = propensity score-matched model with outcome and baricitinib exposure, adjusted for any variables that remain unbalanced after PS matching.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.48. Comparative Risk of Incident VTE, Primary Definition [Optum CDM RA]_vrm.docx

Table 54_Optum_VRM. Incidence Rate of Event - MACE [Optum]

Model	Unmatched		Matched		
	Baricitinib[a] (N=351)	TNFi (N=1,440)	Baricitinib[a] (N=258)	TNFi (N=634)	Total (N=892)
Overall					
Person-Years	CCI	CCI	CCI	CCI	CCI
MACE	CCI	CCI	CCI	0	CCI
MACE/100 PY	1.30	0.25	1.93	0.00	0.43
95% CI	0.16, 4.71	0.03, 0.91	0.23, 6.98	0.00, 1.01	0.05, 1.54
MI					
MI	0	CCI	0	0	0
Person-Years	153.38	CCI	103.65	365.30	468.96
IR per100 PY	0.00	0.13	0.00	0.00	0.00
95% CI	0.00, 2.41	0.00, 0.70	0.00, 3.56	0.00, 1.01	0.00, 0.79
Stroke, any					
Stroke	CCI	CCI	CCI	0	CCI
Person-Years	CCI	CCI	CCI	365.30	CCI
IR per 100 PY	1.30	0.13	1.93	0.00	0.43
95% CI	0.16, 4.71	0.00, 0.70	0.23, 6.98	0.00, 1.01	0.05, 1.54
Concomitant MTX Use[b]					
MACE	0	CCI	0	0	0
Person-Years	37.09	CCI	28.15	100.41	128.55
IR per 100 PY	0.00	0.91	0.00	0.00	0.00
95% CI	0.00, 9.95	0.11, 3.28	0.00, 13.11	0.00, 3.67	0.00, 2.87
No Concomitant MTX Use[b]					
MACE	CCI	0	CCI	0	CCI
Person-Years	CCI	575.11	CCI	264.89	CCI

Model	Unmatched		Matched		
	Baricitinib[a] (N=351)	TNFi (N=1,440)	Baricitinib[a] (N=258)	TNFi (N=634)	Total (N=892)
IR per 100 PY	1.72	0.00	2.65	0.00	0.59
95% CI	0.21, 6.22	0.00, 0.64	0.32, 9.58	0.00, 1.39	0.07, 2.12

Abbreviations: CI = confidence interval; IR = incidence rate; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; MI = myocardial infarction; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

c N in subgroups may not always sum precisely to total group N due to rounding

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.54. Incidence Rate of Event - MACE [Optum CDM RA]_vrm.docx

Table 59_Optum_VRM. Incidence Rate of Event - First Serious Infection [Optum]

	Unmatched		Matched		
	Baricitinib (N=366)	TNFi (N=1,478)	Baricitinib (N=274)	TNFi (N=674)	Total (N=948)
SI Events	CCI	28	CCI	15	CCI
Person-years	CCI	806.12	CCI	363.14	CCI
IR per 100 PY	2.44	3.47	0.85	4.13	3.33
95% CI	0.67, 6.26	2.19, 4.76	0.02, 4.76	2.04, 6.22	1.70, 4.97

Abbreviations: CI = confidence interval; IR = incidence rate; N = number of patients in the specified category; PY = person-years; SI = serious infection; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\optum_OPTUM\2. Table 6.59. Incidence Rate of Event - First Serious Infection [Optum CDM RA]_vrm.docx

Annex 9. PharMetrics Plus – Additional Results

This annex includes information about results for the following analyses:

I. Additional analysis

These additional results were not presented in the body of the report. These results, like those included in the report body, are based on 1:1 baricitinib:TNFi propensity score matching. Specifically, this section of the annex includes:

- Descriptive tables for unmatched eligible patients.
- Descriptive tables for matched patient cohorts for the serious infection analyses.

I. Additional analysis

Table 1_PP. Baseline Demographics, Unmatched [PP]

	Baricitinib			TNFi	Std. Diff.
	Any	4-mg	2-mg	(N=6576)	(Any vs TNFi)
	(N=473)	(n=0)	(n=473)		
Age [yrs]					
N	473	0	473	6576	0.3
Mean (SD)	54.0 (10)	NA	54.0 (10)	50.8 (11)	
Median	56.0	NA	56.0	53.0	
Min, Max	21.0, 84.0	NA	21.0, 84.0	18.0, 85.0	
≥ 65 years	51 (11%)	0 (0%)	51 (11%)	433 (7%)	
Sex					
Male	86 (18%)	0 (0%)	86 (18%)	1504 (23%)	-0.1
Female	387 (82%)	0 (0%)	387 (82%)	5072 (77%)	

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

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Table 4_PP. Baseline Demographics Incident Serious Infections, Matched [PP]

	Baricitinib			TNFi	Std. Diff.	Total
	Any	4-mg	2-mg	(N=265)	(Any vs TNFi)	(N=530)
	(N=265)	(n=0)	(n=265)			
Age [yrs]						
N	265	0	265	265	-0.1	530
Mean (SD)	53.6 (11)	NA	53.6 (11)	54.3 (11)		54.0 (11)
Median	56.0	NA	56.0	56.0		56.0
Min, Max	21.0, 84.0	NA	21.0, 84.0	20.0, 85.0		20.0, 85.0

≥ 65 years	29 (11%)	0 (0%)	29 (11%)	31 (12%)		60 (11%)
Sex						
Male	45 (17%)	0 (0%)	45 (17%)	49 (18%)	0.0	94 (18%)
Female	220 (83%)	0 (0%)	220 (83%)	216 (82%)		436 (82%)

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus; SD = standard deviation.

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Table 6_PP. Clinical History at Baseline, Unmatched Cohorts [PP]

Characteristic[a,b]	Baricitinib[c] (N=473)	TNFi (N=6576)	Std. Diff.
Clinical Conditions during baseline			
Cancer	16 (3%)	321 (5%)	-0.1
NMSC	7 (1%)	63 (1%)	0.0
Chronic lung disease	59 (12%)	714 (11%)	0.1
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	8 (2%)	75 (1%)	0.0
Cardiovascular revascularization	0 (0%)	11 (0%)	-0.1
Congestive Heart Failure, hospitalized	3 (1%)	8 (0%)	0.1
Coronary artery disease	20 (4%)	238 (4%)	0.0
Ischemic heart disease	21 (4%)	266 (4%)	0.0
Unstable angina	0 (0%)	21 (0%)	-0.1
Ventricular arrhythmia	5 (1%)	115 (2%)	-0.1
Diabetes Mellitus	65 (14%)	800 (12%)	0.0
Type I	5 (1%)	86 (1%)	0.0
Type II	63 (13%)	769 (12%)	0.0
Dyslipidaemia	146 (31%)	1579 (24%)	0.2
Hypertension	153 (32%)	2101 (32%)	0.0
Immune disorders	64 (14%)	592 (9%)	0.1
AIDS/HIV	1 (0%)	13 (0%)	0.0
Antiphospholipid syndrome	1 (0%)	8 (0%)	0.0
SLE	22 (5%)	135 (2%)	0.1
Primary Sjögren Syndrome	42 (9%)	468 (7%)	0.1
Liver Disorder	4 (1%)	70 (1%)	0.0
Obesity	83 (18%)	1344 (20%)	-0.1
Pregnancy	0 (0%)	8 (0%)	0.0
RA Severity (CIRAS Index), mean (SD)	4.4 (1)	4.7 (1)	-0.3
Smoking	39 (8%)	717 (11%)	-0.1
Surgery, trauma & hospitalization, recent	10 (2%)	164 (2%)	0.0
TIA	1 (0%)	26 (0%)	0.0
Genetic Coagulopathies	1 (0%)	15 (0%)	0.0
DMARDs			
cDMARDs, during baseline			
n, total	274 (58%)	4207 (64%)	-0.1
Mean (SD)	0.8 (1)	0.8 (1)	-0.1
Median	1.0	1.0	
Min, Max	0.0, 3.0	0.0, 5.0	
>1 cDMARD concomitantly	45 (10%)	521 (8%)	0.1

Characteristic[a,b]	Baricitinib[c] (N=473)	TNFi (N=6576)	Std. Diff.
Hydroxychloroquine	93 (20%)	1239 (19%)	0.0
Leflunomide	78 (16%)	731 (11%)	0.2
Methotrexate	138 (29%)	2697 (41%)	-0.3
Minocycline	0 (0%)	0 (0%)	0.0
Sulfasalazine	31 (7%)	537 (8%)	-0.1
bDMARDs, during baseline			
n, total	261 (55%)	6576 (100%)	-1.3
Mean (SD)	0.6 (1)	1.0 (0)	-0.9
Median	1.0	1.0	
Min, Max	0.0, 3.0	1.0, 3.0	
cDMARDs, concomitant	69 (15%)	2229 (34%)	-0.5
abatacept	53 (11%)	67 (1%)	0.4
adalimumab[d]	39 (8%)	2760 (42%)	-0.8
anakinra	2 (0%)	1 (0%)	0.1
certolizumab pegol[d]	32 (7%)	340 (5%)	0.1
etanercept[d]	36 (8%)	2560 (39%)	-0.8
golimumab[d]	16 (3%)	423 (6%)	-0.1
infliximab[d]	13 (3%)	513 (8%)	-0.2
rituximab	19 (4%)	8 (0%)	0.3
sarilumab	33 (7%)	19 (0%)	0.4
tocilizumab	48 (10%)	40 (1%)	0.4
Other Prescription Medications			
Antibiotics	29 (6%)	402 (6%)	0.0
Antidiabetic agents	61 (13%)	813 (12%)	0.0
Insulins	20 (4%)	245 (4%)	0.0
Non-insulins	57 (12%)	727 (11%)	0.0
Aspirin	1 (0%)	14 (0%)	0.0
Cardiovascular			
Anticoagulant	7 (1%)	130 (2%)	0.0
Antihypertensives	216 (46%)	2773 (42%)	0.1
Antiplatelet	5 (1%)	94 (1%)	0.0
Nitrates	4 (1%)	61 (1%)	0.0
Hormonal			
HRT	37 (8%)	379 (6%)	0.1
Oral Contraceptives	32 (7%)	377 (6%)	0.0
SERMs	3 (1%)	23 (0%)	0.0
Lipid-lowering agents			
Bile acid binding	6 (1%)	92 (1%)	0.0
Cholesterol absorption inhibitor	3 (1%)	78 (1%)	-0.1

Characteristic[a,b]	Baricitinib[c] (N=473)	TNFi (N=6576)	Std. Diff.
Fibrates	8 (2%)	113 (2%)	0.0
Niacin	0 (0%)	4 (0%)	0.0
Omega-3 fatty acids	0 (0%)	9 (0%)	-0.1
Statins	128 (27%)	1285 (20%)	0.2
Rheumatoid arthritis-related			
Cox-2 Inhibitor	49 (10%)	523 (8%)	0.1
Glucocorticosteroid	351 (74%)	4834 (74%)	0.0
Vaccinations	168 (36%)	1935 (29%)	0.1

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = conventional disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; Concom. cDMARDs = concomitant cDMARDs; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff. = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics except for the use of bDMARD and cDMARD are measured during the 6 months prior to initiation of study medication until and including the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d TNF inhibitors. Unless otherwise noted, characteristics in Table table and similar tables are measured during baseline, including on the index day.

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Table 9_PP. Clinical Characteristics Incident Serious Infection Cohorts, Matched [PP]

Characteristic[a,b]	Baricitinib (N=265)	TNFi (N=265)	Std. Diff.
Clinical Conditions during baseline			
Cancer	11 (4%)	19 (7%)	-0.1
NMSC	7 (3%)	4 (2%)	0.1
Chronic lung disease	30 (11%)	21 (8%)	0.1
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	4 (2%)	4 (2%)	0.0
Cardiovascular revascularization	0 (0%)	0 (0%)	0.0
Congestive Heart Failure, hospitalized	1 (0%)	0 (0%)	0.1
Coronary artery disease	7 (3%)	5 (2%)	0.1
Ischemic heart disease	8 (3%)	6 (2%)	0.0

Characteristic[a,b]	Baricitinib (N=265)	TNFi (N=265)	Std. Diff.
Unstable angina	0 (0%)	0 (0%)	0.0
Ventricular arrhythmia	2 (1%)	3 (1%)	0.0
Diabetes Mellitus	35 (13%)	24 (9%)	0.1
Type I	4 (2%)	2 (1%)	0.1
Type II	34 (13%)	22 (8%)	0.1
Dyslipidaemia	74 (28%)	53 (20%)	0.2
Hypertension	95 (36%)	93 (35%)	0.0
Immune disorders	30 (11%)	24 (9%)	0.1
AIDS/HIV	0 (0%)	1 (0%)	-0.1
Antiphospholipid syndrome	1 (0%)	1 (0%)	0.0
SLE	10 (4%)	7 (3%)	0.1
Primary Sjögren Syndrome	20 (8%)	18 (7%)	0.0
Liver Disorder	1 (0%)	0 (0%)	0.1
Obesity	55 (21%)	44 (17%)	0.1
Pregnancy	0 (0%)	2 (1%)	-0.1
RA Severity (CIRAS Index), mean (SD)	4.4 (1)	4.5 (1)	0.0
Smoking	20 (8%)	20 (8%)	0.0
Surgery, trauma & hospitalization, recent	3 (1%)	4 (2%)	0.0
TIA	0 (0%)	0 (0%)	0.0
Genetic Coagulopathies	0 (0%)	1 (0%)	-0.1
DMARDs			
csDMARDs, during baseline			
n, total	167 (63%)	186 (70%)	-0.2
Mean (SD)	0.8 (1)	1.0 (1)	-0.2
Median	1.0	1.0	
Min, Max	0.0, 3.0	0.0, 3.0	
>1 csDMARD concomitantly	25 (9%)	33 (12%)	-0.1
Hydroxychloroquine	56 (21%)	57 (22%)	0.0
Leflunomide	43 (16%)	33 (12%)	0.1
Methotrexate	91 (34%)	131 (49%)	-0.3
Minocycline	0 (0%)	0 (0%)	0.0
Sulfasalazine	19 (7%)	26 (10%)	-0.1
bDMARDs, during baseline			
n, total	265 (100%)	265 (100%)	0.0
Mean (SD)	1.1 (0)	1.0 (0)	0.4
Median	1.0	1.0	
Min, Max	1.0, 3.0	1.0, 2.0	
csDMARDs, concomitant	71 (27%)	100 (38%)	-0.2
abatacept	53 (20%)	1 (0%)	0.7

Characteristic[a,b]	Baricitinib (N=265)	TNFi (N=265)	Std. Diff.
adalimumab[c]	41 (15%)	112 (42%)	-0.6
anakinra	2 (1%)	0 (0%)	0.1
certolizumab pegol[c]	32 (12%)	15 (6%)	0.2
etanercept[c]	38 (14%)	103 (39%)	-0.6
golimumab[c]	17 (6%)	12 (5%)	0.1
infliximab[c]	12 (5%)	23 (9%)	-0.2
rituximab	19 (7%)	0 (0%)	0.4
sarilumab	33 (12%)	1 (0%)	0.5
tocilizumab	49 (18%)	0 (0%)	0.7
Other Prescription Medications			
Antibiotics	16 (6%)	13 (5%)	0.1
Antidiabetic agents	30 (11%)	23 (9%)	0.1
Insulins	7 (3%)	6 (2%)	0.0
Non-insulins	28 (11%)	21 (8%)	0.1
Aspirin	0 (0%)	2 (1%)	-0.1
Cardiovascular			
Anticoagulant	11 (4%)	9 (3%)	0.0
Antihypertensives	123 (46%)	125 (47%)	0.0
Antiplatelet	2 (1%)	3 (1%)	0.0
Nitrates	2 (1%)	1 (0%)	0.1
Hormonal			
HRT	24 (9%)	13 (5%)	0.2
Oral Contraceptives	20 (8%)	12 (5%)	0.1
SERMs	2 (1%)	1 (0%)	0.1
Lipid-lowering agents			
Bile acid binding	2 (1%)	2 (1%)	0.0
Cholesterol absorption inhibitor	0 (0%)	3 (1%)	-0.2
Fibrates	2 (1%)	3 (1%)	0.0
Niacin	0 (0%)	0 (0%)	0.0
Omega-3 fatty acids	0 (0%)	1 (0%)	-0.1
Statins	66 (25%)	55 (21%)	0.1
Rheumatoid arthritis-related			
Cox-2 Inhibitor	26 (10%)	13 (5%)	0.2
Glucocorticosteroid	215 (81%)	214 (81%)	0.0
Vaccinations	103 (39%)	89 (34%)	0.1

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; csDMARD = conventional synthetic disease-modifying antirheumatic drugs; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff. = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics except for use of bDMARD and concomitant csDMARD are measured during the 6 months prior to initiation of study medication until and including the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c TNF inhibitors.

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Table 11_PP. Baseline Healthcare Resource Utilization, Unmatched [PP]

Type of Resource Use	Baricitinib (N=473)	TNFi (N=6576)	Std. Diff.
Physician Office Visits			
n, patients	449	6190	0.0
n, events	3604	48639	
Mean (SD)	7.6 (10)	7.4 (8)	0.0
Median	5.0	5.0	
Min, Max	0.0, 117.0	0.0, 118.0	
Rheumatologist Visits			
n, patients	330	4264	0.1
n, events	739	9653	
Mean (SD)	1.6 (1)	1.5 (1)	0.1
Median	2.0	1.0	
Min, Max	0.0, 8.0	0.0, 18.0	
Other Outpatient Visits			
n, patients	462	6513	-0.1
n, events	4673	66269	
Mean (SD)	9.9 (8)	10.1 (8)	0.0
Median	8.0	8.0	
Min, Max	0.0, 81.0	0.0, 210.0	
Inpatient Visits			
n, patients	21	270	0.0
n, events	28	320	
Mean (SD)	0.1 (0)	0.0 (0)	0.0

Type of Resource Use	Baricitinib (N=473)	TNFi (N=6576)	Std. Diff.
Median	0.0	0.0	
Min, Max	0.0, 3.0	0.0, 4.0	
ED Visits			
n, patients	67	1038	0.0
n, events	110	1632	
Mean (SD)	0.2 (1)	0.2 (1)	0.0
Median	0.0	0.0	
Min, Max	0.0, 7.0	0.0, 16.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits. Other outpatient visits do not include physician office visits or rheumatologist visits.

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Table 14_PP. Baseline Healthcare Resource Utilization Incident Serious Infection Cohorts, Matched [PP]

Type of Resource Use	Baricitinib (N=265)	TNFi (N=265)	Std. Diff.
Physician Office Visits			
n, patients	254	254	0.0
n, events	2029	1729	
Mean (SD)	7.7 (9)	6.5 (7)	0.1
Median	5.0	4.0	
Min, Max	0.0, 72.0	0.0, 48.0	
Rheumatologist Visits			
n, patients	188	182	0.0
n, events	437	431	
Mean (SD)	1.6 (1)	1.6 (2)	0.0
Median	2.0	2.0	
Min, Max	0.0, 8.0	0.0, 13.0	
Other Outpatient Visits			
n, patients	264	265	-0.1
n, events	2685	2734	
Mean (SD)	10.1 (7)	10.3 (7)	0.0
Median	8.0	8.0	
Min, Max	0.0, 36.0	1.0, 43.0	
Inpatient Visits			
n, patients	8	7	0.0

Type of Resource Use	Baricitinib (N=265)	TNFi (N=265)	Std. Diff.
n, events	9	8	
Mean (SD)	0.0 (0)	0.0 (0)	0.0
Median	0.0	0.0	
Min, Max	0.0, 2.0	0.0, 2.0	
ED Visits			
n, patients	36	30	0.1
n, events	64	45	
Mean (SD)	0.2 (1)	0.2 (1)	0.1
Median	0.0	0.0	
Min, Max	0.0, 7.0	0.0, 9.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits. Other outpatient visits do not include physician office visits or rheumatologist visits.

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Table 16_PP. Baseline Prevalence of Outcomes [PP]

Outcome in Each Matched Cohort[a,b]	Unmatched		
	Baricitinib (N=700)	TNFi (N=6896)	Std. Diff.
VTE			
Main case definition	2 (0%)	28 (0%)	0.0
Alternate case definition I	2 (0%)	28 (0%)	0.0
Alternative case definition II	3 (0%)	53 (1%)	0.0
MACE	1 (0%)	5 (0%)	0.0
Serious Infection	7 (1%)	33 (0%)	0.1
Hospitalized Tuberculosis	0 (0%)	0 (0%)	0.0

Abbreviations: MACE = major adverse cardiovascular event, defined as hospital primary discharge diagnosis code of acute MI or hospital primary discharge diagnosis code of ischemic or hemorrhagic stroke; N = number of patients in specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism, defined based on the case definitions.

a Baseline prevalence was calculated for each distinct matched cohort for VTE, MACE, serious infection, and hospitalized tuberculosis.

b Patients with the prevalent outcomes enumerated in this table are those excluded from the main analyses of each outcome

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Table 17_PP. Duration of Follow-up Period (Days), Unmatched [PP]

	Baricitinib (N=473)	TNFi (N=6576)	Std. Diff
N	473	6576	
Mean (SD)	191.7 (166)	213.8 (184)	-0.1
Median	131.0	151.0	
Min, Max	1.0, 814.0	1.0, 945.0	

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

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Table 18_PP. Duration of Follow-up Period (Days) Primary VTE Cohorts, Matched [PP]

	Baricitinib (N=261)	TNFi (N=261)	Std. Diff
N	261	261	
Mean (SD)	197.5 (168)	223.0 (204)	-0.1
Median	141	146.4	
Min, Max	1.0, 814.0	2.0, 934.0	
Reasons for censoring			
Incident event	0 (0%)	0 (0%)	
Medication discontinued **or switching**	192 (74%)	157 (60%)	
Initiated b/tsDMARD	0 (0%)	0 (0%)	
End of patient record	45 (17%)	72 (28%)	
Death (where available)	0 (0%)	0 (0%)	
End of study period (31 December 2020)	24 (9%)	33 (13%)	

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; Std Diff = standardised difference; VTE = venous thromboembolism.

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Table 22_PP. Duration of Follow-up Period (Days) Incident Serious Infection Cohorts, Matched [PP]

	Baricitinib (N=265)	TNFi (N=265)	Std. Diff
N	265	265	
Mean (SD)	195.6 (168)	221.6 (188)	-0.1
Median	139	151	
Min, Max	1.0, 814.0	1.0, 927.0	

Reasons for censoring			
Incident event	3 (1%)	3 (1%)	
Medication discontinued **or switching**	192 (72%)	148 (56%)	
Initiated b/tsDMARD	0 (0%)	0 (0%)	
End of patient record	47 (18%)	82 (31%)	
Death (where available)	0 (0%)	0 (0%)	
End of study period (31 December 2020)	24 (9%)	32 (12%)	

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

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Table 39_PP. Pattern of VTE and Related Diagnostic Codes in Patients with RA [PP]

Code	**Total Patients (N=522)**
ICD-10 (PE)	
I26.0	0 (0%)
I26.02	0 (0%)
I26.09	0 (0%)
I26.9	0 (0%)
I26.92	0 (0%)
I26.99	2 (0%)
ICD-10 (DVT lower extremities)	
I82.401	1 (0%)
I82.402	1 (0%)
I82.403	0 (0%)
I82.409	1 (0%)
I82.411	1 (0%)
I82.412	0 (0%)
I82.413	1 (0%)
I82.419	0 (0%)
I82.421	0 (0%)
I82.422	0 (0%)
I82.423	0 (0%)
I82.429	0 (0%)
I82.4y1	0 (0%)
I82.4y2	0 (0%)
I82.4y3	0 (0%)
I82.4y9	0 (0%)

Code	Total Patients (N=522)
I82.491	0 (0%)
I82.492	0 (0%)
I82.493	0 (0%)
I82.499	0 (0%)
I82.431	0 (0%)
I82.432	2 (0%)
I82.433	0 (0%)
I82.439	0 (0%)
I82.441	0 (0%)
I82.442	0 (0%)
I82.443	0 (0%)
I82.449	0 (0%)
I82.4z1	0 (0%)
I82.4z2	0 (0%)
I82.4z3	0 (0%)
I82.4z9	0 (0%)
ICD-10 (DVT upper extremities)	
I82.621	0 (0%)
I82.622	0 (0%)
I82.623	0 (0%)
I82.629	0 (0%)
I82.601	0 (0%)
I82.602	0 (0%)
I82.603	0 (0%)
I82.609	0 (0%)
I82.a11	0 (0%)
I82.a12	0 (0%)
I82.a13	0 (0%)
I82.a19	0 (0%)
I82.c11	0 (0%)
I82.c12	0 (0%)
I82.c13	0 (0%)
I82.c19	0 (0%)
I82.210	0 (0%)
I82.290	0 (0%)
ICD-10 (Phlebitis and thrombophlebitis of lower extremity)	
I80.10	0 (0%)
I80.11	0 (0%)
I80.12	0 (0%)

Code	Total Patients (N=522)
I80.13	0 (0%)
I80.201	0 (0%)
I80.202	0 (0%)
I80.203	0 (0%)
I80.209	0 (0%)
I80.291	0 (0%)
I80.292	0 (0%)
I80.293	0 (0%)
I80.299	0 (0%)
I80.3	1 (0%)
I80.211	0 (0%)
I80.212	0 (0%)
I80.213	0 (0%)
I80.219	0 (0%)
I80.221	0 (0%)
I80.222	0 (0%)
I80.223	0 (0%)
I80.229	0 (0%)
I80.231	0 (0%)
I80.232	0 (0%)
I80.233	0 (0%)
I80.239	0 (0%)
ICD-10 (Other venous thrombosis)	
I80.8	0 (0%)
I80.9	0 (0%)
I81	0 (0%)
I82.0	0 (0%)
I82.1	0 (0%)
I82.220	1 (0%)
I82.3	0 (0%)
I82.890	0 (0%)
I82.90	1 (0%)
I82.b11	0 (0%)
I82.b12	0 (0%)
I82.b13	0 (0%)
I82.b19	0 (0%)

Abbreviations: ICD-10 = International Classification of Disease, 10th Revision; N = number of patients in specified category; RA = rheumatoid arthritis; PE = pulmonary embolism; DVT = deep vein thrombosis; VTE = venous thromboembolism.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\pharmetrics plus_PP\ Lilly Baricitinib Results_VTE_PharMetrics Plus_v1.0.docx -pages 13-15

Table 40_PP. Clinical Characteristics of RA Patients with VTE, Primary Definition [PP]

Characterstic[a,b]	Baricitinib[c] (N=0)	TNFi (N=0)	Total (N=0)
Age (mean) [SD]	0 (0)	0 (0)	0 (0)
Sex			
Female	0 (0%)	0 (0%)	0 (0%)
Male	0 (0%)	0 (0%)	0 (0%)
Clinical Conditions during baseline			
Cancer	0 (0%)	0 (0%)	0 (0%)
NMSC	0 (0%)	0 (0%)	0 (0%)
Chronic Lung disease	0 (0%)	0 (0%)	0 (0%)
Cardiovascular conditions	0 (0%)	0 (0%)	0 (0%)
Atrial arrhythmia/ fibrillation	0 (0%)	0 (0%)	0 (0%)
Cardiovascular revascularization	0 (0%)	0 (0%)	0 (0%)
Congestive Heart Failure, hospitalized	0 (0%)	0 (0%)	0 (0%)
Coronary artery disease	0 (0%)	0 (0%)	0 (0%)
Ischemic heart disease	0 (0%)	0 (0%)	0 (0%)
Unstable angina	0 (0%)	0 (0%)	0 (0%)
Ventricular arrhythmia	0 (0%)	0 (0%)	0 (0%)
Diabetes Mellitus	0 (0%)	0 (0%)	0 (0%)
Type I	0 (0%)	0 (0%)	0 (0%)
Type II	0 (0%)	0 (0%)	0 (0%)
Dyslipidaemia	0 (0%)	0 (0%)	0 (0%)
Hypertension	0 (0%)	0 (0%)	0 (0%)
Immune disorders	0 (0%)	0 (0%)	0 (0%)
AIDS/HIV	0 (0%)	0 (0%)	0 (0%)
Antiphospholipid syndrome	0 (0%)	0 (0%)	0 (0%)
SLE	0 (0%)	0 (0%)	0 (0%)
Primary Sjögren Syndrome	0 (0%)	0 (0%)	0 (0%)
Liver Disorder	0 (0%)	0 (0%)	0 (0%)
Obesity	0 (0%)	0 (0%)	0 (0%)
Pregnancy	0 (0%)	0 (0%)	0 (0%)
RA Severity (CIRAS), mean (SD)	0 (0)	0 (0)	0 (0)
Smoking	0 (0%)	0 (0%)	(0%)
Surgery, trauma, & hospitalization, recent	0 (0%)	0 (0%)	(0%)
Genetic Coagulopathies	0 (0%)	0 (0%)	(0%)

Characterstic[a,b]	Baricitinib[c] (N=0)	TNFi (N=0)	Total (N=0)
TIA	0 (0%)	0 (0%)	(0%)
Other Prescription Medication			
Antibiotics	0 (0%)	0 (0%)	0 (0%)
Antidiabetic agents	0 (0%)	0 (0%)	0 (0%)
Insulins	0 (0%)	0 (0%)	0 (0%)
Non-insulins	0 (0%)	0 (0%)	0 (0%)
Aspirin	0 (0%)	0 (0%)	0 (0%)
Cardiovascular			
Antihypertensives	0 (0%)	0 (0%)	0 (0%)
Nitrates	0 (0%)	0 (0%)	0 (0%)
Anticoagulant	0 (0%)	0 (0%)	0 (0%)
Antiplatelet	0 (0%)	0 (0%)	0 (0%)
Hormonal			
Oral contraceptives	0 (0%)	0 (0%)	0 (0%)
HRT	0 (0%)	0 (0%)	0 (0%)
SERM	0 (0%)	0 (0%)	0 (0%)
Lipid-lowering agents			
Bile acid binding	0 (0%)	0 (0%)	0 (0%)
Cholesterol absorption inhibitor	0 (0%)	0 (0%)	0 (0%)
Fibrates	0 (0%)	0 (0%)	0 (0%)
Niacin	0 (0%)	0 (0%)	0 (0%)
Omega-3 fatty acids	0 (0%)	0 (0%)	0 (0%)
Statins	0 (0%)	0 (0%)	0 (0%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0%)	0 (0%)	0 (0%)
Glucocorticosteroid	0 (0%)	0 (0%)	0 (0%)
Vaccinations	0 (0%)	0 (0%)	0 (0%)
Post-index Occurrence[c]			
Cancer	0 (0%)	0 (0%)	0 (0%)
Hospitalization	0 (0%)	0 (0%)	0 (0%)
Surgery and Trauma	0 (0%)	0 (0%)	0 (0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] All conditions and characteristics except for use of bDMARD and concomitant csDMARD are measured during the 6 months prior to initiation of study medication until and including the index date.

[b] Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

[c] Except for cancer diagnosed within 90 days of VTE diagnosis, events in this category must have occurred in the 4 weeks immediately prior to VTE (Kline et al. 2017).

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\pharmetrics plus_PP\Lilly Baricitinib Results_VTE_PharMetrics Plus_v1.0.docx -pages 16-17

Table 41_PP. Pattern of RA Medication Use in Patients with VTE, Primary Definition [PP]

Characteristic[a]	Unmatched		Matched		
	Baricitinib (N=0)	TNFi (N=15)	Baricitinib (N=0)	TNFi (N=0)	Total (N=0)
Baseline Medication					
csDMARDs, during baseline					
n, total	0 (0%)	9 (60%)	0 (0%)	0 (0%)	0 (0%)
Mean (SD)	0 (0)	0.7 (1)	0 (0)	0 (0)	0 (0)
Median	0.0	1.0			
Min, Max	0, 0	0.0, 2.0	0, 0	0, 0	0, 0
>1 csDMARD concomitantly	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Hydroxychloroquine	0 (0%)	3 (20%)	0 (0%)	0 (0%)	0 (0%)
Leflunomide	0 (0%)	3 (20%)	0 (0%)	0 (0%)	0 (0%)
Methotrexate	0 (0%)	4 (27%)	0 (0%)	0 (0%)	0 (0%)
Minocycline	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Sulfasalazine	0 (0%)	1 (7%)	0 (0%)	0 (0%)	0 (0%)
bDMARDs, during baseline					
n, total	0 (0%)	15 (100%)	0 (0%)	0 (0%)	0 (0%)
Mean (SD)	0 (0)	2.0 (0)	0 (0)	0 (0)	0 (0)
Median	0.0	2.0	0.0	0.0	0.0
Min, Max	0, 0	2.0, 2.0	0, 0	0, 0	0, 0
csDMARDs, concomitantly	0 (0%)	4 (27%)	0 (0%)	0 (0%)	0 (0%)
Abatacept	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Adalimumab[b]	0 (0%)	9 (60%)	0 (0%)	0 (0%)	0 (0%)
Anakinra	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Certolizumab pegol[b]	0 (0%)	2 (13%)	0 (0%)	0 (0%)	0 (0%)

Characteristic[a]	Unmatched		Matched		
	Baricitinib (N=0)	TNFi (N=15)	Baricitinib (N=0)	TNFi (N=0)	Total (N=0)
Etanercept[b]	0 (0%)	7 (47%)	0 (0%)	0 (0%)	0 (0%)
Golimumab[b]	0 (0%)	7 (47%)	0 (0%)	0 (0%)	0 (0%)
Infliximab[b]	0 (0%)	5 (33%)	0 (0%)	0 (0%)	0 (0%)
Rituximab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Tocilizumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Post-index Medication[c]					
Methotrexate,concomitant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Other Concomitant csDMARD	0 (0%)	1 (7%)	0 (0%)	0 (0%)	0 (0%)
Dose change, baricitinib	NA	NA	NA	NA	NA

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; csDMARD = conventional synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics except for use of bDMARD and concomitant csDMARD are measured during the 6 months prior to initiation of study medication until and including the index date.

b TNF inhibitors.

c Only baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked 'NA' as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\pharmetrics plus_PP\Lilly Baricitinib Results_VTE_PharMetrics Plus_v1.0.docx -page 18

Table 42_PP. Time to First VTE Event (Days), Primary Definition [PP]

Time	Unmatched		Matched		
	Baricitinib (N=473)	TNFi (N=6576)	Baricitinib (N=261)	TNFi (N=261)	Total (N=522)
n	0	15	0	0	0
Mean (SD)	0.0 (0)	204.7 (282)	0.0 (0)	0.0 (0)	0.0 (0)
Median	0.0	96.0	0.0	0.0	0.0
Min, Max	0.0, 0.0	26.0, 910.0	0.0, 0.0	0.0, 0.0	0.0, 0.0

Abbreviations: N = number of patients in specified category; NA = not applicable; Max = maximum; Min = minimum; TNFi = tumour necrosis factor inhibitor; SD = standard deviation; VTE = venous thromboembolism, defined as hospitalization for the composite endpoint of incident VTE, either pulmonary embolism or deep vein thrombosis, based on the primary discharge diagnosis code.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\pharmetrics plus_PP\Lilly Baricitinib Results_VTE_PharMetrics Plus_v1.0.docx -page 19

Table 48_PP Comparative Risk of Incident VTE, Primary Definition [PP]

	TNFi	Baricitinib		P-value
		HR	95% CI	
Base Model	Ref	NA	NA	NA

Abbreviations: CI = confidence interval; HR = hazard ratio; NA = not applicable; Ref = referent group; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\pharmetrics plus_PP\Lilly Baricitinib Results_Top-Line_Pharmetrics Plus_v3.0.docx - page(s) 14

Table 51_PP. Clinical Characteristics of RA Patients with MACE [PP]

Characterstic[a,b]	Baricitinib (N=1)	TNFi (N=0)	Total (N=1)
Age (mean) [SD]	64 (0)	0 (0)	64 (0)
Sex			
Female	1 (100%)	0 (0%)	1 (100%)
Male	0 (0%)	0 (0%)	0 (0%)
Clinical Conditions during baseline			
Cancer	0 (0%)	0 (0%)	0 (0%)
NMSC	0 (0%)	0 (0%)	0 (0%)
Chronic Lung disease	0 (0%)	0 (0%)	0 (0%)
Cardiovascular conditions	0 (0%)	0 (0%)	0 (0%)
Atrial arrhythmia/fibrillation	0 (0%)	0 (0%)	0 (0%)
Cardiovascular revascularization	0 (0%)	0 (0%)	0 (0%)
Congestive Heart Failure, hospitalized	0 (0%)	0 (0%)	0 (0%)
Coronary artery disease	0 (0%)	0 (0%)	0 (0%)
Ischemic heart disease	0 (0%)	0 (0%)	0 (0%)
Unstable angina	0 (0%)	0 (0%)	0 (0%)
Ventricular arrhythmia	0 (0%)	0 (0%)	0 (0%)
Diabetes Mellitus	0 (0%)	0 (0%)	0 (0%)
Type I	0 (0%)	0 (0%)	0 (0%)
Type II	0 (0%)	0 (0%)	0 (0%)
Dyslipidaemia	0 (0%)	0 (0%)	0 (0%)
Hypertension	0 (0%)	0 (0%)	0 (0%)
Immune disorders	0 (0%)	0 (0%)	0 (0%)
AIDS/HIV	0 (0%)	0 (0%)	0 (0%)
Antiphospholipid syndrome	0 (0%)	0 (0%)	0 (0%)
SLE	0 (0%)	0 (0%)	0 (0%)
Primary Sjögren Syndrome	0 (0%)	0 (0%)	0 (0%)
Liver Disorder	0 (0%)	0 (0%)	0 (0%)
Obesity	1 (100%)	0 (0%)	1 (100%)
Pregnancy	0 (0%)	0 (0%)	0 (0%)
RA Severity (CIRAS), mean (SD)	3.6 (0)	0 (0)	3.6 (0)

Characterstic[a,b]	Baricitinib (N=1)	TNFi (N=0)	Total (N=1)
Smoking	0 (0%)	0 (0%)	0 (0%)
Surgery, trauma, & hospitalization, recent	0 (0%)	0 (0%)	0 (0%)
TIA	0 (0%)	0 (0%)	0 (0%)
Genetic Coagulopathies	0 (0%)	0 (0%)	0 (0%)
Other Prescription Medications			
Antibiotics	0 (0%)	0 (0%)	0 (0%)
Antidiabetic agents	0 (0%)	0 (0%)	0 (0%)
Insulins	0 (0%)	0 (0%)	0 (0%)
Non-insulins	0 (0%)	0 (0%)	0 (0%)
Aspirin	0 (0%)	0 (0%)	0 (0%)
Cardiovascular			
Anticoagulant	0 (0%)	0 (0%)	0 (0%)
Antihypertensives	1 (100%)	0 (0%)	1 (100%)
Antiplatelet	0 (0%)	0 (0%)	0 (0%)
Nitrates	0 (0%)	0 (0%)	0 (0%)
Hormonal			
Oral contraceptives	0 (0%)	0 (0%)	0 (0%)
HRT	0 (0%)	0 (0%)	0 (0%)
SERM	0 (0%)	0 (0%)	0 (0%)
Lipid-lowering agents			
Bile acid binding	0 (0%)	0 (0%)	0 (0%)
Cholesterol absorption inhibitor	0 (0%)	0 (0%)	0 (0%)
Fibrates	0 (0%)	0 (0%)	0 (0%)
Niacin	0 (0%)	0 (0%)	0 (0%)
Omega-3 fatty acids	0 (0%)	0 (0%)	0 (0%)
Statins	0 (0%)	0 (0%)	0 (0%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0%)	0 (0%)	0 (0%)
Glucocorticosteroid	1 (100%)	0 (0%)	1 (100%)
Vaccinations	0 (0%)	0 (0%)	0 (0%)
Postindex Occurrence[c]			
Methotrexate, concomitant	0 (0%)	0 (0%)	0 (0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; CIRAS = claims-based index for RA severity; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; SD = standard deviation; RA = rheumatoid arthritis; SERM = selective estrogen receptor modifier; SLE = systemic lupus erythematosus; TIA= transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] All conditions and characteristics except for use of bDMARD and concomitant csDMARD are measured during the 6 months prior to initiation of study medication until and including the index date.

[b] Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

[c] Events in this category must have occurred in the 7 days immediately prior to MACE.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\pharmetrics plus_PP\Lilly Baricitinib Results_MACE_PharMetrics Plus_v1.0.docx -pages 9-10

Table 52_PP. Pattern of RA Medication Use in Patients with MACE [PP]

Characteristic[a]	Unmatched		Matched		
	Baricitinib (N=4)	**TNFi (N=8)**	**Baricitinib (N=1)**	**TNFi (N=0)**	**Total (N=1)**
Baseline Medication					
csDMARDs, during baseline					
n, total	3	6	1	0	1
Mean (SD)	0.8 (1)	0.9 (1)	1 (0)	0 (0)	1 (0)
Median	1.0	1.0	1.0	0.0	1.0
Min, Max	0.0, 1.0	0.0, 2.0	1.0, 1.0	0.0, 0.0	1.0, 1.0
>1 csDMARD concomitantly	0 (0%)	1 (13%)	0 (0%)	0 (0%)	0 (0%)
Hydroxychloroquine	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Leflunomide	0 (0%)	1 (13%)	0 (0%)	0 (0%)	0 (0%)
Methotrexate	2 (50%)	5 (63%)	1 (100%)	0 (0%)	1 (100%)
Minocycline	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Sulfasalazine	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
bDMARDs, during baseline					
n, total	1	8	1	0	1
Mean (SD)	0.5 (1)	2 (0)	2 (0)	0 (0)	2 (0)
Median	0.0	2.0	2.0	0.0	2.0
Min, Max	0.0, 2.0	2.0, 2.0	2.0, 2.0	0.0, 0.0	2.0, 2.0
csDMARDs, concomitantly	0 (0%)	4 (50%)	0 (0%)	0 (0%)	0 (0%)
Abatacept	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Adalimumab[b]	1 (25%)	6 (75%)	1 (100%)	0 (0%)	1 (100%)
Anakinra	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Characteristic[a]	Unmatched		Matched		
	Baricitinib (N=4)	TNFi (N=8)	Baricitinib (N=1)	TNFi (N=0)	Total (N=1)
Certolizumab pegol[b]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Etanercept[b]	1 (25%)	6 (75%)	1 (100%)	0 (0%)	1 (100%)
Golimumab[b]	0 (0%)	2 (25%)	0 (0%)	0 (0%)	0 (0%)
Infliximab[b]	0 (0%)	2 (25%)	0 (0%)	0 (0%)	0 (0%)
Rituximab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Sarilumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Tocilizumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Post-index Medication					
Concomitant Methotrexate	0 (0%)	1 (13%)	0 (0%)	0 (0%)	0 (0%)
Other Concomitant csDMARD	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Dose change[c], baricitinib	NA	NA	NA	NA	NA

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; csDMARD = conventional synthetic disease-modifying antirheumatic drug; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a All conditions and characteristics except for use of bDMARD and concomitant csDMARD are measured during the 6 months prior to initiation of study medication until and including the index date.

b TNF inhibitors.

c Only baricitinib 2-mg dose is available in the US, so the baricitinib dose change should be marked 'NA' in US data

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\pharmetrics plus_PP\Lilly Baricitinib Results_MACE_PharMetrics Plus_v1.0.docx -pages 11-12

Table 53_PP. Time to First MACE (Days) [PP]

	Unmatched		Matched		
	Baricitinib (N=473)	TNFi (N=6579)	Baricitinib (N=262)	TNFi (N=262)	Total (N=524)
n	4	8	1	0	1
Mean (SD)	67.3 (51)	205.3 (140)	78.0 (NA)	0 (0)	78.0 (NA)
Median	67.5	189.0	78.0	0.0	78.0
Min, Max	6.0, 128.0	16.0, 448.0	78.0, 78.0	0.0, 0.0	78.0, 78.0

Abbreviations: MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis code of acute myocardial infarction or ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\pharmetrics plus_PP\Lilly Baricitinib Results_MACE_PharMetrics Plus_v1.0.docx -page 13

Table 55_PP. Comparative Risk of Incident MACE [PP]

	TNFi	Baricitinib		p-value
		HR	95% CI	
Base Model	Ref	31261169.00	NA	1.0

Abbreviations: CI = confidence interval; HR = hazard ratio; NA = not applicable; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Ref = Referent group; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\pharmetrics plus_PP\Lilly Baricitinib Results_Top-Line_Pharmetrics Plus_v3.0.docx - page(s) 16

Table 56_PP. Clinical Characteristics of RA Patients with Incident Serious Infections [PP]

Characteristics[a,b]	Baricitinib (N=3)	TNFi (N=3)	Total (N=6)
Age (mean) [SD]	52.7 (13)	66.7 (3)	59.7 (11)
Sex			
Female	2 (67%)	2 (67%)	4 (67%)
Male	1 (33%)	1 (33%)	2 (33%)
Clinical Conditions during baseline	0 (0%)	0 (0%)	0 (0%)
Cancer	0 (0%)	0 (0%)	0 (0%)
NMSC	0 (0%)	0 (0%)	0 (0%)
Chronic Lung disease	0 (0%)	1 (33%)	1 (17%)
Cardiovascular conditions	0 (0%)	1 (33%)	1 (17%)
Atrial arrhythmia/ fibrillation	0 (0%)	1 (33%)	1 (17%)
Cardiovascular revascularization	0 (0%)	0 (0%)	0 (0%)
Congestive Heart Failure, hospitalized	0 (0%)	0 (0%)	0 (0%)
Coronary artery disease	0 (0%)	0 (0%)	0 (0%)
Ischemic heart disease	0 (0%)	0 (0%)	0 (0%)
Unstable angina	0 (0%)	0 (0%)	0 (0%)
Ventricular arrhythmia	0 (0%)	0 (0%)	0 (0%)
Diabetes Mellitus	1 (33%)	0 (0%)	1 (17%)
Type I	0 (0%)	0 (0%)	0 (0%)
Type II	1 (33%)	0 (0%)	1 (17%)
Dyslipidaemia	1 (33%)	1 (33%)	2 (33%)
Hypertension	1 (33%)	1 (33%)	2 (33%)
Immune disorders	0 (0%)	1 (33%)	1 (17%)
AIDS/HIV	0 (0%)	0 (0%)	0 (0%)
Antiphospholipid syndrome	0 (0%)	0 (0%)	0 (0%)
SLE	0 (0%)	1 (33%)	1 (17%)
Primary Sjögren Syndrome	0 (0%)	0 (0%)	0 (0%)
Liver Disorder	0 (0%)	0 (0%)	0 (0%)
Obesity	1 (33%)	1 (33%)	2 (33%)
Pregnancy	0 (0%)	0 (0%)	0 (0%)
RA Severity (CIRAS), mean (SD)	5.9 (2)	3.5 (0)	4.7 (2)
Smoking	1 (33%)	0 (0%)	1 (17%)
Surgery, Trauma, & Hospitalization, recent	0 (0%)	0 (0%)	0 (0%)
TIA	0 (0%)	0 (0%)	0 (0%)
Genetic Coagulopathies	0 (0%)	0 (0%)	0 (0%)
Other Prescription Medications			
Antibiotics	1 (33%)	0 (0%)	1 (17%)
Antidiabetic agents	0 (0%)	1 (33%)	1 (17%)
Insulins	0 (0%)	0 (0%)	0 (0%)

Characteristics[a,b]	Baricitinib (N=3)	TNFi (N=3)	Total (N=6)
Non-insulins	0 (0%)	1 (33%)	1 (17%)
Aspirin	0 (0%)	0 (0%)	0 (0%)
Cardiovascular			
Anticoagulant	0 (0%)	0 (0%)	0 (0%)
Antihypertensives	0 (0%)	1 (33%)	1 (17%)
Antiplatelet	0 (0%)	0 (0%)	0 (0%)
Nitrates	0 (0%)	0 (0%)	0 (0%)
Hormonal			
HRT	0 (0%)	1 (33%)	1 (17%)
Oral Contraceptives	0 (0%)	0 (0%)	0 (0%)
SERMs	0 (0%)	0 (0%)	0 (0%)
Lipid-lowering agents	0 (0%)	0 (0%)	0 (0%)
Bile acid binding	0 (0%)	0 (0%)	0 (0%)
Cholesterol absorption inhibitor	0 (0%)	0 (0%)	0 (0%)
Fibrates	0 (0%)	0 (0%)	0 (0%)
Niacin	0 (0%)	0 (0%)	0 (0%)
Omega-3 fatty acids	0 (0%)	0 (0%)	0 (0%)
Statins	0 (0%)	2 (67%)	2 (33%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0%)	0 (0%)	0 (0%)
Glucocorticosteroid	2 (67%)	1 (33%)	3 (50%)
Vaccinations	0 (0%)	0 (0%)	0 (0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics except for use of bDMARD and concomitant csDMARD are measured during the 6 months prior to initiation of study medication until and including the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\pharmetrics plus_PP Lilly Baricitinib Results_Serious Infection_PharMetrics Plus_v1.0.docx -pages 9-10

Table 57_PP. Pattern of RA Medication Use in Patients with Serious Infection Event [PP]

Characteristic[a]	Unmatched		Matched		
	Baricitinib (N=6)	TNFi (N=54)	Baricitinib (N=3)	TNFi (N=3)	Total (N=6)
Baseline Medication					
DMARDS					
csDMARDs, during baseline					
n, total	3	41	2	2	4
Mean (SD)	0.8 (1)	1 (1)	1.3 (2)	0.7 (1)	1 (1)
Median	0.5	1.0	1.0	1.0	1.0
Min, Max	0.0, 3.0	0.0, 3.0	0.0, 3.0	0.0, 1.0	0.0, 3.0
>1 csDMARD, concomitantly	0 (0%)	4 (7%)	0 (0%)	0 (0%)	0 (0%)
Hydroxychloroquine	2 (33%)	4 (7%)	1 (33%)	0 (0%)	1 (17%)
Leflunomide	0 (0%)	10 (19%)	0 (0%)	0 (0%)	0 (0%)
Methotrexate	2 (33%)	31 (57%)	2 (67%)	2 (67%)	4 (67%)
Minocycline	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Sulfasalazine	1 (17%)	5 (9%)	1 (33%)	0 (0%)	1 (17%)
bDMARDs, during baseline					
n, total	3	54	3	3	6
Mean (SD)	0.5 (1)	2 (0)	1 (0)	2 (0)	1.5 (1)
Median	0.5	2.0	1.0	2.0	1.5
Min, Max	0.0, 1.0	2.0, 3.0	1.0, 1.0	2.0, 2.0	1.0, 2.0
Concomitant csDMARDs	1 (17%)	28 (52%)	1 (33%)	2 (67%)	3 (50%)
Abatacept	1 (17%)	1 (2%)	1 (33%)	0 (0%)	1 (17%)
Adalimumab[b]	0 (0%)	39 (72%)	0 (0%)	2 (67%)	2 (33%)
Anakinra	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Certolizumab pegol[b]	1 (17%)	7 (13%)	1 (33%)	0 (0%)	1 (17%)
Etanercept[b]	0 (0%)	34 (63%)	0 (0%)	2 (67%)	2 (33%)
Golimumab[b]	1 (17%)	14 (26%)	1 (33%)	1 (33%)	2 (33%)
Infliximab[b]	0 (0%)	14 (26%)	0 (0%)	1 (33%)	1 (17%)
Rituximab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Sarilumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Tocilizumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Post-index Medication					
Methotrexate, concomitant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Other Concomitant csDMARD	0 (0%)	4 (7%)	0 (0%)	0 (0%)	0 (0%)
Dose change[c], baricitinib	NA	NA	NA	NA	NA

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; csDMARD = conventional synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

[a] All conditions and characteristics except for use of bDMARD and concomitant csDMARD are measured during the 6 months prior to initiation of study medication until and including the index date.

[b] TNF inhibitors.

[c] Only baricitinib 2-mg dose is available in the US, so the baricitinib dose change should be marked 'NA' in US data.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\pharmetrics plus_PP\Lilly Baricitinib Results_Serious Infection_PharMetrics Plus_v1.0.docx -pages 11-12

Table 58_PP. Time to First Serious Infection Event (Days) [PP]

	Unmatched		Matched		
	Baricitinib (N=478)	**TNFi (N=6688)**	**Baricitinib (N=265)**	**TNFi (N=265)**	**Total (N=530)**
n	6	54	3	3	6
Mean (SD)	151.3 (157)	159.9 (141)	226.7 (200)	140.7 (52)	183.7 (139)
Median	102.0	118.5	188.0	132.0	160.0
Min, Max	35.0, 443.0	19.0, 728.0	49.0, 443.0	94.0, 196.0	49.0, 443.0

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\pharmetrics plus_PP\Lilly Baricitinib Results_Serious Infection_PharMetrics Plus_v1.0.docx -page 13

Table 60_PP. Serious Infection Events Per Patient During All Available Follow-up [PP]

Number of Infections per Person	Unmatched		Matched		
	Baricitinib (N=478)	**TNFi (N=6688)**	**Baricitinib (N=265)**	**TNFi (N=265)**	**Total (N=530)**
0	472 (99%)	6634 (99%)	262 (99%)	262 (99%)	524 (99%)
1	5 (1%)	52 (1%)	3 (1%)	3 (1%)	6 (1%)
2	1 (0%)	1 (0%)	0 (0%)	0 (0%)	0 (0%)
3	0 (0%)	1 (0%)	0 (0%)	0 (0%)	0 (0%)
4	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
6	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
>6	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Abbreviations: N = number of patients in the specified category; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\pharmetrics plus_PP\Lilly Baricitinib Results_Serious Infection_PharMetrics Plus_v1.0.docx -page 14

Table 64_PP. Incidence Rate of Hospitalized TB Event [PP]

	Unmatched		Matched		
	Baricitinib (N=483)	TNFi (N=6719)	Baricitinib (N=268)	TNFi (N=268)	Total (N=536)
Overall					
Person-Years	252	3943	144	173	316
TB Events	0.0	0.0	0.0	0.0	0.0
TB Events/100 PY	0.0	0.0	0.0	0.0	0.0
95% CI	NA	NA	NA	NA	NA

Abbreviations: CI = confidence interval; N = number of patients in the specified category; NA = not applicable; PY = person-years; TB = tuberculosis; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\pharmetrics plus_PP\Lilly Baricitinib Results_TB_PharMetrics Plus_v1.0.docx -page 9

Annex 10. HealthVerity PS20 – Additional Results

This annex includes information about results for the following analyses:

I. Additional analysis

These additional results were not presented in the body of the report. These results, like those included in the report body, are based on 1:1 baricitinib:TNFi propensity score matching. Specifically, this section of the annex includes:

- Descriptive tables for unmatched eligible patients.
- Descriptive tables for matched patient cohorts for the serious infection analyses

II. Variable Ratio Matching

These results were not presented in the body of this report. They are based on matching baricitinib:TNFi using Variable Ratio matching, i.e., as many matched 1:3 as possible, then the maximum number matched 1:2, then the remaining patients matched 1:1.

I. Additional analysis

Table 1_PS20. Baseline Demographics, Unmatched [HealthVerity, PS20]

	Baricitinib			TNFi (N=3,953)	Std. Diff. (Any vs TNFi)
	Any (N=933)	4-mg (N=0)	2-mg (N=933)		
Age [yrs]					
N	933	-	933	3,953	
Mean (SD)	55.13 (11.07)	-	55.13 (11.07)	50.51 (12.35)	0.39
Median	57.00 [48.00, 62.00]	-	57.00 [48.00, 62.00]	52.00 [42.00, 60.00]	
Min, Max	21.0, 92.0	-	21.0, 92.0	18.0, 93.0	
≥ 65 years	140 (15.0%)	-	140 (15.0%)	351 (8.9%)	0.19
Sex					
Male	120 (12.9%)	-	120 (12.9%)	722 (18.3%)	0.15
Female	813 (87.1%)	-	813 (87.1%)	3,231 (81.7%)	0.15

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; vs = versus.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.1. Baseline Demographics, Unmatched [HealthVerity, PS20].docx

Table 4_PS20. Baseline Demographics Incident Serious Infections, Matched [HealthVerity, PS20]

	Baricitinib			TNFi (N=748)	Std. Diff. (Any vs TNFi)	Total (N=1,496)
	Any (N=748)	4-mg (N=0)	2-mg (N=748)			
Age [yrs]						
N	748	-	748	748		1,496
Mean (SD)	54.91 (11.10)	-	54.91 (11.10)	55.43 (12.01)	0.04	55.17 (11.56)
Median	56.00 [48.00, 62.00]	-	56.00 [48.00, 62.00]	57.00 [49.00, 63.00]		57.00 [48.00, 62.00]
Min, Max	21.0, 92.0	-	21.0, 92.0	18.0, 93.0		18.0, 93.0
≥ 65 years	114 (15.2%)	-	114 (15.2%)	128 (17.1%)	0.05	242 (16.2%)
Sex						
Male	106 (14.2%)	-	106 (14.2%)	99 (13.2%)	0.03	205 (13.7%)
Female	642 (85.8%)	-	642 (85.8%)	649 (86.8%)	0.03	1,291 (86.3%)

Abbreviations: N = number of patients in the specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.4 - Baseline Demographics Incident Serious Infections, Matched [HealthVerity, PS20].docx

Table 6_PS20. Clinical History at Baseline, Unmatched Cohorts [HealthVerity, PS20]

Characteristic[a,b]	Baricitinib[c] (N=933)	TNFi (N=3,953)	Std. Diff.
Clinical Conditions during baseline			
Cancer	74 (7.9%)	283 (7.2%)	0.03
NMSC	10 (1.1%)	23 (0.6%)	0.05
Chronic lung disease	177 (19.0%)	645 (16.3%)	0.07
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	26 (2.8%)	74 (1.9%)	0.06
Cardiovascular revascularization	0 (0.0%)	1 (0.0%)	0.02
Congestive heart failure, hospitalized	8 (0.9%)	7 (0.2%)	0.10
Coronary artery disease	51 (5.5%)	174 (4.4%)	0.05
Ischemic heart disease	51 (5.5%)	174 (4.4%)	0.05
Unstable angina	3 (0.3%)	18 (0.5%)	0.02
Ventricular arrhythmia	20 (2.1%)	111 (2.8%)	0.04
Diabetes Mellitus	180 (19.3%)	696 (17.6%)	0.04
Type I	18 (1.9%)	63 (1.6%)	0.03
Type II	172 (18.4%)	674 (17.1%)	0.04
Dyslipidaemia	335 (35.9%)	1,184 (30.0%)	0.13
Hypertension	402 (43.1%)	1,576 (39.9%)	0.07
Immune disorders	112 (12.0%)	354 (9.0%)	0.10
AIDS/HIV	1 (0.1%)	7 (0.2%)	0.02
Antiphospholipid syndrome	1 (0.1%)	8 (0.2%)	0.02
SLE	49 (5.3%)	141 (3.6%)	0.08
Primary Sjögren syndrome	69 (7.4%)	218 (5.5%)	0.08
Liver disorder	13 (1.4%)	75 (1.9%)	0.04
Obesity	263 (28.2%)	1,196 (30.3%)	0.05
Pregnancy	0 (0.0%)	34 (0.9%)	0.13
RA severity (CIRAS Index), mean (SD)	4.14 (1.23)	4.46 (1.28)	0.25
Smoking	137 (14.7%)	707 (17.9%)	0.09
Surgery, trauma & hospitalization, recent	57 (6.1%)	226 (5.7%)	0.02
TIA	4 (0.4%)	27 (0.7%)	0.03
DMARDs			
cDMARDs, during baseline			
n, total	450 (48.2%)	2,526 (63.9%)	0.32
Mean (SD)	0.70 (0.83)	0.87 (0.77)	0.22
Median	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-
Min, Max	0.0, 5.0	0.0, 4.0	-
>1 cDMARD concomitantly	148 (15.9%)	725 (18.3%)	0.07
Hydroxychloroquine	140 (15.0%)	754 (19.1%)	0.11
Leflunomide	119 (12.8%)	505 (12.8%)	0.00
Methotrexate	267 (28.6%)	1,563 (39.5%)	0.23
Minocycline	5 (0.5%)	36 (0.9%)	0.04
Sulfasalazine	51 (5.5%)	304 (7.7%)	0.09
bDMARDs, during baseline[a]			
n, total	446 (47.8%)	3,690 (93.3%)	1.15

Characteristic[a,b]	Baricitinib[c] (N=933)	TNFi (N=3,953)	Std. Diff.
Mean (SD)	0.57 (0.63)	1.08 (0.29)	1.04
Median	0.00 [0.00, 1.00]	1.00 [1.00, 1.00]	-
Min, Max	0.0, 3.0	1.0, 3.0	-
cDMARDs, concomitant	248 (26.6%)	2,105 (53.3%)	0.57
abatacept	75 (8.0%)	141 (3.6%)	0.19
adalimumab[d]	83 (8.9%)	1,327 (33.6%)	0.63
anakinra	5 (0.5%)	3 (0.1%)	0.08
certolizumab pegol[d]	31 (3.3%)	280 (7.1%)	0.17
etanercept[d]	77 (8.3%)	1,094 (27.7%)	0.52
golimumab[d]	48 (5.1%)	388 (9.8%)	0.18
infliximab[d]	22 (2.4%)	628 (15.9%)	0.48
rituximab	23 (2.5%)	12 (0.3%)	0.19
sarilumab	50 (5.4%)	28 (0.7%)	0.27
tocilizumab	83 (8.9%)	59 (1.5%)	0.34
Other Prescription Medications			
Antibiotics	358 (38.4%)	1,962 (49.6%)	0.23
Antidiabetic agents	114 (12.2%)	584 (14.8%)	0.08
Insulins	37 (4.0%)	179 (4.5%)	0.03
Non-insulins	105 (11.3%)	514 (13.0%)	0.05
Aspirin	22 (2.4%)	99 (2.5%)	0.01
Cardiovascular			
Anticoagulant	26 (2.8%)	113 (2.9%)	0.00
Antihypertensives	356 (38.2%)	1,829 (46.3%)	0.17
Antiplatelet	17 (1.8%)	66 (1.7%)	0.01
Nitrates	14 (1.5%)	65 (1.6%)	0.01
Hormonal			
HRT	61 (6.5%)	237 (6.0%)	0.02
Oral Contraceptives	21 (2.3%)	227 (5.7%)	0.18
SERMs	4 (0.4%)	15 (0.4%)	0.01
Lipid-lowering agents			
Bile acid binding	7 (0.8%)	42 (1.1%)	0.03
Cholesterol absorption inhibitor	9 (1.0%)	38 (1.0%)	0.00
Fibrates	11 (1.2%)	72 (1.8%)	0.05
Niacin	0 (0.0%)	1 (0.0%)	0.02
Omega-3 fatty acids	9 (1.0%)	19 (0.5%)	0.06
Statins	205 (22.0%)	847 (21.4%)	0.01
Rheumatoid arthritis-related			
Cox-2 Inhibitor	51 (5.5%)	265 (6.7%)	0.05
Glucocorticosteroid	454 (48.7%)	2,405 (60.8%)	0.25
Vaccinations	257 (27.5%)	1,100 (27.8%)	0.01

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = conventional disease-modifying antirheumatic drug; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy N = number of patients in the specified category; Std. Diff = standardised difference; NMSC = non-melanoma skin cancer; SD = standard deviation; RA = rheumatoid arthritis; SERM = selective estrogen receptor modifier; SLE = systemic lupus erythematosus; TIA= transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics, except for bDMARDs, are measured during the 6 months prior to initiation of study medication including the date at which the qualifying exposure of baricitinib or TNFi occurs (index date). bDMARDs are measured from the 6 months prior to the initiation of study medication until the day prior to baricitinib or the index TNFi exposure, excluding the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d TNF inhibitors.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.6. - Clinical History at Baseline, Unmatched Cohorts [HealthVerity, PS20]_.docx

Table 9_PS20. Clinical Characteristics Incident Serious Infection Cohorts, Matched [HealthVerity, PS20]

Characteristic[a,b]	Baricitinib[c] (N=748)	TNFi (N=748)	Std. Diff.
Clinical Conditions during baseline			
Cancer	59 (7.9%)	41 (5.5%)	0.10
NMSC	6 (0.8%)	6 (0.8%)	0.00
Chronic lung disease	141 (18.9%)	158 (21.1%)	0.06
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	25 (3.3%)	17 (2.3%)	0.07
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	-
Congestive heart failure, hospitalized	6 (0.8%)	2 (0.3%)	0.07
Coronary artery disease	44 (5.9%)	39 (5.2%)	0.03
Ischemic heart disease	44 (5.9%)	39 (5.2%)	0.03
Unstable angina	3 (0.4%)	3 (0.4%)	0.00
Ventricular arrhythmia	19 (2.5%)	16 (2.1%)	0.03
Diabetes Mellitus	146 (19.5%)	131 (17.5%)	0.05
Type I	17 (2.3%)	8 (1.1%)	0.09
Type II	138 (18.4%)	130 (17.4%)	0.03
Dyslipidaemia	271 (36.2%)	254 (34.0%)	0.05
Hypertension	325 (43.4%)	320 (42.8%)	0.01
Immune disorders	87 (11.6%)	90 (12.0%)	0.01
AIDS/HIV	1 (0.1%)	3 (0.4%)	0.05
Antiphospholipid syndrome	2 (0.3%)	2 (0.3%)	0.00
SLE	38 (5.1%)	37 (4.9%)	0.01
Primary Sjögren syndrome	54 (7.2%)	53 (7.1%)	0.01
Liver disorder	11 (1.5%)	12 (1.6%)	0.01
Obesity	214 (28.6%)	211 (28.2%)	0.01
Pregnancy	0 (0.0%)	2 (0.3%)	0.07
RA severity (CIRAS Index), mean (SD)	4.15 (1.21)	4.10 (1.25)	0.04
Smoking	116 (15.5%)	108 (14.4%)	0.03
Surgery, trauma & hospitalization, recent	41 (5.5%)	28 (3.7%)	0.08
TIA	4 (0.5%)	8 (1.1%)	0.06
DMARDs			
cDMARDs, during baseline			
n, total	364 (48.7%)	475 (63.5%)	0.30
Mean (SD)	0.70 (0.83)	0.84 (0.74)	0.18
Median	0.50 [0.00, 1.00]	1.00 [0.00, 1.00]	-
Min, Max	0.0, 5.0	0.0, 4.0	-
>1 cDMARD concomitantly	120 (16.0%)	127 (17.0%)	0.03
Hydroxychloroquine	111 (14.8%)	127 (17.0%)	0.06
Leflunomide	101 (13.5%)	94 (12.6%)	0.03
Methotrexate	215 (28.7%)	303 (40.5%)	0.25
Minocycline	5 (0.7%)	9 (1.2%)	0.06
Sulfasalazine	40 (5.3%)	51 (6.8%)	0.06
bDMARDs, during baseline[a]			

Characteristic[a,b]	Baricitinib[c] (N=748)	TNFi (N=748)	Std. Diff.
n, total	267 (35.7%)	714 (95.5%)	1.62
Mean (SD)	0.40 (0.54)	1.38 (0.53)	1.83
Median	0.00 [0.00, 1.00]	1.00 [1.00, 2.00]	-
Min, Max	0.0, 2.0	1.0, 3.0	-
cDMARDs, concomitant	162 (21.7%)	401 (53.6%)	0.70
abatacept	38 (5.1%)	122 (16.3%)	0.37
adalimumab[d]	47 (6.3%)	230 (30.7%)	0.66
anakinra	3 (0.4%)	3 (0.4%)	0.00
certolizumab pegol[d]	16 (2.1%)	55 (7.4%)	0.25
etanercept[d]	46 (6.1%)	236 (31.6%)	0.69
golimumab[d]	26 (3.5%)	84 (11.2%)	0.30
infliximab[d]	13 (1.7%)	122 (16.3%)	0.53
rituximab	12 (1.6%)	9 (1.2%)	0.03
sarilumab	35 (4.7%)	26 (3.5%)	0.06
tocilizumab	43 (5.7%)	51 (6.8%)	0.04
Other Prescription Medications			
Antibiotics	293 (39.2%)	291 (38.9%)	0.01
Antidiabetic agents	88 (11.8%)	105 (14.0%)	0.07
Insulins	31 (4.1%)	31 (4.1%)	0.00
Non-insulins	79 (10.6%)	96 (12.8%)	0.07
Aspirin	16 (2.1%)	12 (1.6%)	0.04
Cardiovascular			
Anticoagulant	31 (4.1%)	41 (5.5%)	0.06
Antihypertensives	267 (35.7%)	365 (48.8%)	0.27
Antiplatelet	14 (1.9%)	15 (2.0%)	0.01
Nitrates	14 (1.9%)	13 (1.7%)	0.01
Hormonal			
HRT	46 (6.1%)	58 (7.8%)	0.06
Oral Contraceptives	19 (2.5%)	33 (4.4%)	0.10
SERMs	2 (0.3%)	1 (0.1%)	0.03
Lipid-lowering agents			
Bile acid binding	4 (0.5%)	10 (1.3%)	0.08
Cholesterol absorption inhibitor	7 (0.9%)	10 (1.3%)	0.04
Fibrates	10 (1.3%)	14 (1.9%)	0.04
Niacin	0 (0.0%)	0 (0.0%)	-
Omega-3 fatty acids	8 (1.1%)	2 (0.3%)	0.10
Statins	155 (20.7%)	192 (25.7%)	0.12
Rheumatoid arthritis-related			
Cox-2 Inhibitor	40 (5.3%)	52 (7.0%)	0.07
Glucocorticosteroid	358 (47.9%)	336 (44.9%)	0.06
Vaccinations	201 (26.9%)	232 (31.0%)	0.09

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = conventional disease-modifying antirheumatic drug ; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy N = number of patients in the specified category; Std. Diff = standardised difference; NMSC = non-melanoma skin cancer; SD = standard deviation; RA = rheumatoid arthritis; SERM = selective estrogen receptor modifier; SLE = systemic lupus erythematosus; TIA= transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics, except for bDMARDs, are measured during the 6 months prior to initiation of study medication including the date at which the qualifying exposure of baricitinib or TNFi occurs (index date). bDMARDs are measured from the 6 months prior to the initiation of study medication until the day prior to baricitinib or the index TNFi exposure, excluding the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d TNF inhibitors.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.9. - Clinical Characteristics Incident Serious Infection Cohorts, Matched [HealthVerity, PS20].docx

Table 11A_PS20. Baseline Healthcare Resource Utilization, Unmatched [HealthVerity, PS20]

Type of Resource Use	Baricitinib (N=933)	TNFi (N=3,953)	Std. Diff.
Physician Office Visits			
n, patients	305 (32.7%)	1,536 (38.9%)	0.13
n, events	36490	173576	
Mean (SD)	39.11 (104.01)	43.91 (119.75)	0.04
Median	0.00 [0.00, 22.00]	0.00 [0.00, 43.00]	
Min, Max	0.0, 985.0	0.0, 3208.0	
Rheumatologist Visits			
n, patients	215 (23.0%)	1,068 (27.0%)	0.09
n, events	8061	49294	
Mean (SD)	8.64 (29.69)	12.47 (37.30)	0.11
Median	0.00 [0.00, 0.00]	0.00 [0.00, 5.00]	
Min, Max	0.0, 509.0	0.0, 787.0	
Other Outpatient Visits			
n, patients	794 (85.1%)	3,359 (85.0%)	0.00
n, events	141872	532311	
Mean (SD)	152.06 (463.69)	134.66 (447.27)	0.04
Median	44.00 [9.00, 119.00]	41.00 [9.00, 112.00]	
Min, Max	0.0, 9855.0	0.0, 14370.0	
Inpatient Visits			
n, patients	87 (9.3%)	369 (9.3%)	0.00
n, events	13529	41902	
Mean (SD)	14.50 (132.76)	10.60 (74.63)	0.04
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 3438.0	0.0, 2268.0	
ED Visits			
n, patients	193 (20.7%)	959 (24.3%)	0.09
n, events	9694	31545	
Mean (SD)	10.39 (87.85)	7.98 (41.92)	0.04
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 2450.0	0.0, 1342.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.11A. Baseline Healthcare Resource Utilization, Unmatched [HealthVerity, PS20].docx

Table 11B_PS20. Baseline Healthcare Resource Utilization, Unmatched [HealthVerity, PS20], count at most one visit per day[1]

Type of Resource Use	Baricitinib (N=933)	TNFi (N=3,953)	Std. Diff.
Physician Office Visits[1]			
n, patients	305 (32.7%)	1,536 (38.9%)	0.13
n, events	2,780	13,915	
Mean (SD)	2.98 (6.41)	3.52 (6.60)	0.08
Median	0.00 [0.00, 3.00]	0.00 [0.00, 5.00]	
Min, Max	0.0, 49.0	0.0, 90.0	
Rheumatologist Visits[1]			
n, patients	215 (23.0%)	1,068 (27.0%)	0.09
n, events	606	3,518	
Mean (SD)	0.65 (1.42)	0.89 (1.81)	0.15
Median	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	
Min, Max	0.0, 12.0	0.0, 15.0	
Other Outpatient Visits[1]			
n, patients	794 (85.1%)	3,359 (85.0%)	0.00
n, events	7,735	27,711	
Mean (SD)	8.29 (24.75)	7.01 (19.80)	0.06
Median	3.00 [1.00, 6.00]	3.00 [1.00, 6.00]	
Min, Max	0.0, 180.0	0.0, 180.0	
Inpatient Visits[1]			
n, patients	87 (9.3%)	369 (9.3%)	0.00
n, events	401	1,739	
Mean (SD)	0.43 (1.89)	0.44 (2.27)	0.00
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 22.0	0.0, 63.0	
ED Visits[1]			
n, patients	193 (20.7%)	959 (24.3%)	0.09
n, events	355	1,858	
Mean (SD)	0.38 (1.09)	0.47 (1.44)	0.07
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 17.0	0.0, 49.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

[1] In this table, results describe utilization of healthcare where a maximum of one event was allowed per day. In the PS matching analyses, multiple claims on the same day were allowed to capture additional information on the amount of services received in a given visit. These results are presented in table 6.11A.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.11B (count at most one visit per day). Baseline Healthcare Resource Utilization, Unmatched [HealthVerity, PS20].docx

Table 12A_PS20. Baseline Healthcare Resource Utilization Primary VTE Cohorts, Matched [HealthVerity, PS20]

Type of Resource Use	Baricitinib (N=748)	TNFi (N=748)	Std. Diff.
Physician Office Visits			
n, patients	252 (33.7%)	276 (36.9%)	0.07
n, events	31184	29441	
Mean (SD)	41.69 (110.31)	39.36 (90.65)	0.02
Median	0.00 [0.00, 26.00]	0.00 [0.00, 40.75]	
Min, Max	0.0, 985.0	0.0, 1062.0	
Rheumatologist Visits			
n, patients	177 (23.7%)	177 (23.7%)	0.00
n, events	6897	6650	
Mean (SD)	9.22 (32.00)	8.89 (24.63)	0.01
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 509.0	0.0, 283.0	
Other Outpatient Visits			
n, patients	641 (85.7%)	635 (84.9%)	0.02
n, events	108213	124288	
Mean (SD)	144.67 (358.57)	166.16 (707.66)	0.04
Median	42.50 [10.00, 116.75]	46.00 [10.00, 110.75]	
Min, Max	0.0, 3986.0	0.0, 14370.0	
Inpatient Visits			
n, patients	61 (8.2%)	71 (9.5%)	0.05
n, events	5782	9918	
Mean (SD)	7.73 (40.25)	13.26 (91.05)	0.08
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 555.0	0.0, 1322.0	
ED Visits			
n, patients	152 (20.3%)	163 (21.8%)	0.04
n, events	5894	5154	
Mean (SD)	7.88 (36.54)	6.89 (26.40)	0.03
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 456.0	0.0, 371.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.12A. Baseline Healthcare Resource Utilization, Primary VTE Cohorts, Matched [HealthVerity, PS20].docx

Table 13A_PS20. Baseline Healthcare Resource Utilization MACE Cohorts, Matched [HealthVerity, PS20]

Type of Resource Use	Baricitinib (N=743)	TNFi (N=743)	Std. Diff.
Physician Office Visits			
n, patients	246 (33.1%)	280 (37.7%)	0.10
n, events	30270	31904	
Mean (SD)	40.74 (109.99)	42.94 (101.15)	0.02
Median	0.00 [0.00, 27.00]	0.00 [0.00, 40.00]	
Min, Max	0.0, 985.0	0.0, 1141.0	
Rheumatologist Visits			
n, patients	180 (24.2%)	188 (25.3%)	0.03
n, events	6910	7712	
Mean (SD)	9.30 (31.24)	10.38 (29.46)	0.04
Median	0.00 [0.00, 0.00]	0.00 [0.00, 3.00]	
Min, Max	0.0, 509.0	0.0, 318.0	
Other Outpatient Visits			
n, patients	631 (84.9%)	626 (84.3%)	0.02
n, events	112401	106754	
Mean (SD)	151.28 (492.00)	143.68 (465.59)	0.02
Median	42.00 [9.00, 117.00]	40.00 [9.00, 109.00]	
Min, Max	0.0, 9855.0	0.0, 7949.0	
Inpatient Visits			
n, patients	63 (8.5%)	58 (7.8%)	0.03
n, events	5632	6650	
Mean (SD)	7.58 (35.99)	8.95 (63.24)	0.03
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 377.0	0.0, 1038.0	
ED Visits			
n, patients	150 (20.2%)	177 (23.8%)	0.09
n, events	5298	7029	
Mean (SD)	7.13 (34.09)	9.46 (60.37)	0.05
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 456.0	0.0, 1342.0	

Abbreviations: ED = emergency department; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.13A. Baseline Healthcare Resource Utilization MACE Cohorts, Matched [HealthVerity, PS20].docx

Table 14A_PS20. Baseline Healthcare Resource Utilization Serious Infection Cohorts, Matched [HealthVerity, PS20]

Type of Resource Use	Baricitinib (N=748)	TNFi (N=748)	Std. Diff.
Physician Office Visits			
n, patients	236 (31.6%)	260 (34.8%)	0.07
n, events	27541	28035	
Mean (SD)	36.82 (100.18)	37.48 (92.30)	0.01
Median	0.00 [0.00, 22.00]	0.00 [0.00, 32.00]	
Min, Max	0.0, 985.0	0.0, 862.0	
Rheumatologist Visits			
n, patients	167 (22.3%)	179 (23.9%)	0.04
n, events	6515	6926	
Mean (SD)	8.71 (31.63)	9.26 (30.64)	0.02
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 509.0	0.0, 524.0	
Other Outpatient Visits			
n, patients	639 (85.4%)	649 (86.8%)	0.04
n, events	115304	133249	
Mean (SD)	154.15 (493.13)	178.14 (873.29)	0.03
Median	44.50 [9.00, 117.75]	45.00 [11.00, 116.75]	
Min, Max	0.0, 9855.0	0.0, 15763.0	
Inpatient Visits			
n, patients	58 (7.8%)	62 (8.3%)	0.02
n, events	7817	6739	
Mean (SD)	10.45 (130.04)	9.01 (65.29)	0.01
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 3438.0	0.0, 1038.0	
ED Visits			
n, patients	153 (20.5%)	167 (22.3%)	0.05
n, events	7704	7113	
Mean (SD)	10.30 (95.14)	9.51 (56.39)	0.01
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 2450.0	0.0, 1099.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.14A. Baseline Healthcare Resource Utilization Incident Serious Infection Cohorts, Matched [HealthVerity, PS20].docx

Table 14B_PS20. Baseline Healthcare Resource Utilization Serious Infection Cohorts, Matched [HealthVerity, PS20], count at most one visit per day[1]

Type of Resource Use	Baricitinib (N=748)	TNFi (N=748)	Std. Diff.
Physician Office Visits[1]			
n, patients	236 (31.6%)	260 (34.8%)	0.07
n, events	2,147	2,356	
Mean (SD)	2.87 (6.11)	3.15 (6.42)	0.05
Median	0.00 [0.00, 3.00]	0.00 [0.00, 4.00]	
Min, Max	0.0, 46.0	0.0, 46.0	
Rheumatologist Visits[1]			
n, patients	167 (22.3%)	179 (23.9%)	0.04
n, events	449	576	
Mean (SD)	0.60 (1.34)	0.77 (1.66)	0.11
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 12.0	0.0, 9.0	
Other Outpatient Visits[1]			
n, patients	639 (85.4%)	649 (86.8%)	0.04
n, events	6,358	5,685	
Mean (SD)	8.50 (25.96)	7.60 (21.11)	0.04
Median	3.00 [1.00, 6.00]	3.00 [1.00, 6.00]	
Min, Max	0.0, 180.0	0.0, 180.0	
Inpatient Visits[1]			
n, patients	58 (7.8%)	62 (8.3%)	0.02
n, events	209	217	
Mean (SD)	0.28 (1.35)	0.29 (1.55)	0.00
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 22.0	0.0, 28.0	
ED Visits[1]			
n, patients	153 (20.5%)	167 (22.3%)	0.05
n, events	277	344	
Mean (SD)	0.37 (1.12)	0.46 (2.07)	0.06
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 17.0	0.0, 49.0	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

[1] In this table, results describe utilization of healthcare where a maximum of one event was allowed per day. In the PS matching analyses, multiple claims on the same day were allowed to capture additional information on the amount of services received in a given visit. These results are presented in table 6.14A.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.14B (count at most one visit per day). Baseline Healthcare Resource Utilization Serious Infection Cohorts, Matched [HealthVerity, PS20].docx

Table 16_PS20. Baseline Prevalence of Outcomes [HealthVerity, PS20]

Outcome in Each Matched Cohort[a,c,d]	Unmatched			Matched			
	Baricitinib[b]	TNFi	Std. Diff	Baricitinib[b]	TNFi	Std. Diff	Total
VTE	N=936	N=3,966	-	N=753	N=753	-	N=1,506
Main case definition in baseline	3 (0.3%)	13 (0.3%)	0.00	2 (0.3%)	3 (0.4%)	0.02	5 (0.3%)
Alternate case definition I in baseline	2 (0.2%)	12 (0.3%)	0.02	1 (0.1%)	3 (0.4%)	0.05	4 (0.3%)
Alternative case definition II in baseline	9 (1.0%)	24 (0.6%)	0.04	7 (0.9%)	8 (1.1%)	0.01	15 (1.0%)
MACE	N=936	N=3,966	-	N=742	N=742	-	N=1,484
MACE in baseline	4 (0.4%)	14 (0.4%)	0.01	4 (0.5%)	3 (0.4%)	0.02	7 (0.5%)
Serious Infection	N=949	N=4,042	-	N=761	N=761	-	N=1,522
Serious Infection in baseline	19 (2.0%)	66 (1.6%)	0.03	15 (2.0%)	11 (1.4%)	0.04	26 (1.7%)
Hospitalized Tuberculosis	N=949	N=4,042	-	N=761	N=761	-	N=1,522
Hospitalized Tuberculosis in baseline	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)	-	0 (0.0%)

Abbreviations: MACE = major adverse cardiovascular event, defined as hospital primary discharge diagnosis code of acute MI or hospital primary discharge diagnosis code of ischemic or hemorrhagic stroke; N = number of patients in specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism, defined based on the case definitions.

a Baseline prevalence was calculated for each distinct matched cohort for VTE, MACE, serious infection and hospitalized tuberculosis.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c Patients with the prevalent outcomes enumerated in this table are those excluded from the main analyses of each outcome, except for VTE alternative case definitions I and II. Only the VTE main case definition was used as an exclusion criterion in the main analyses.

d In the VTE and MACE analyses, cohorts additionally excluded the use of anticoagulants at the time of cohort entry (see protocol Section 8.7.7), resulting in a different N compared to the Serious Infection and Hospitalized Tuberculosis cohorts.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.16. Baseline Prevalence of Outcomes [HealthVerity, PS20]_.docx

Table 17_PS20. Duration of Follow-up Period (Days), Unmatched [HealthVerity, PS20]

	Baricitinib[a] (N=933)	TNFi (N=3,953)	Std. Diff.
N	933	3,953	
Mean (SD)	125.99 (124.86)	178.74 (156.27)	0.37
Median	79.00 [48.00, 166.00]	127.00 [61.00, 236.00]	
Min, Max	0.0, 718.0	0.0, 848.0	

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = Standarised difference; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be reported for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.17. Duration of Follow-up Period (Days), Unmatched [HealthVerity, PS20].docx

Table 18_PS20. Duration of Follow-up Period (Days) Primary VTE Cohorts, Matched [HealthVerity, PS20]

	Baricitinib[a,b] (N=748)	TNFi (N=748)	Std. Diff.
N	748	748	0
Mean (SD)	114.56 (111.77)	183.73 (164.08)	0.49
Median	68.50 [42.25, 149.25]	128.50 [60.25, 248.25]	
Min, Max	0.0, 718.0	0.0, 808	
Reasons for censoring [c]			
Incident event	6	4	-
Medication discontinued	204 (27.3%)	46 (6.1%)	-
Initiated b/tsDMARD	29 (3.9%)	38 (5.1%)	-
End of patient record	172 (23.0%)	242 (32.4%)	-
Death (where available)	0 (0.0%)	0 (0.0%)	-
End of study period (12/31/2020)	69 (9.2%)	99 (13.2%)	-

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = Standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b There were 0 patients with a baricitinib dose of 4 mg. Hence, 100% of the patients presented in this column have a baricitinib dose of 2 mg.

c A single patient can be censored on the same day for multiple reasons, e.g., medication discontinued could also be the same day as initiated b/tsDMARD. Further, additional censoring criteria (e.g., switching medication) were specified in the SAP. For these reasons, the total number of reasons for censoring may be less than or greater than the total number of patients.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.18. Duration of Follow-up Period (Days) Primary VTE Cohorts, Matched [HealthVerity].docx

Table 21_PS20. Duration of Follow-up Period (Days) MACE Cohorts, Matched [HealthVerity, PS20]

	Baricitinib[a,b] (N=743)	TNFi (N=743)	Std. Diff.
N	743	743	
Mean (SD)	119.71 (120.65)	173.91 (153.45)	0.39
Median	75.00 [46.00, 151.00]	124.00 [60.00, 229.00]	
Min, Max	0.0, 718.0	0.0, 826.0	
Reasons for censoring			
Incident event	2	4	-
Medication discontinued	489 (65.8%)	375 (50.5%)	-
Initiated b/tsDMARD	25 (3.4%)	46 (6.2%)	-
End of patient record	164 (22.1%)	240 (32.3%)	-
Death (where available)	0 (0.0%)	0 (0.0%)	-
End of study period (12/31/2020)	72 (9.7%)	102 (13.7%)	-

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = Standardised difference; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b There were 0 patients with a baricitinib dose of 4 mg. Hence, 100% of the patients presented in this column have a baricitinib dose of 2 mg.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.21. Duration of Follow-up Period (Days) MACE Cohorts, Matched [HV].docx

Table 22_PS20. Duration of Follow-up Period (Days) Incident Serious Infection Cohorts, Matched [HealthVerity, PS20]

	Baricitinib[a,b] (N=748)	TNFi (N=748)	Std. Diff.
N	748	748	
Mean (SD)	117.42 (118.27)	177.12 (156.17)	0.43
Median	68.00 [42.25, 151.75]	125.50 [60.00, 229.00]	
Min, Max	0.0, 718.0	0.0, 837.0	
Reasons for censoring			
Incident event	6	10	-
Medication discontinued	472 (63.1%)	380 (50.8%)	-
Initiated b/tsDMARD	29 (3.9%)	50 (6.7%)	-
End of patient record	174 (23.3%)	229 (30.6%)	-
Death (where available)	0 (0.0%)	0 (0.0%)	-
End of study period (07/05/2021)	76 (10.2%)	111 (14.8%)	-

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b There were 0 patients with a baricitinib dose of 4 mg. Hence, 100% of the patients presented in this column have a baricitinib dose of 2 mg.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.22. Duration of Follow-up Period (Days) Incident Serious Infection Cohorts, Matched [HealthVerity, PS20].docx

Table 39_PS20. Pattern of VTE and Related Diagnostic Codes in Patients with RA [HealthVerity, PS20]

Code	Total Patients (N=24)
Pulmonary Embolism	
I26.0 - Pulmonary embolism with acute cor pulmonale	0 (0.0%)
I26.02 - Saddle embolus of pulmonary artery with acute cor pulmonale	0 (0.0%)
I26.09 - Other pulmonary embolism with acute cor pulmonale	0 (0.0%)
I26.9 - Pulmonary embolism without acute cor pulmonale	0 (0.0%)
I26.92 - Saddle embolus of pulmonary artery without acute cor pulmonale	1 (4.2%)
I26.99 - Other pulmonary embolism without acute cor pulmonale	10 (41.7%)
Deep Vein Thrombosis, lower	
I80.10 - Phlebitis and thrombophlebitis of unspecified femoral vein	0 (0.0%)
I80.11 - Phlebitis and thrombophlebitis of right femoral vein	0 (0.0%)
I80.13 - Phlebitis and thrombophlebitis of femoral vein, bilateral	0 (0.0%)
I80.211 - Phlebitis and thrombophlebitis of right iliac vein	0 (0.0%)
I80.221 - Phlebitis and thrombophlebitis of right popliteal vein	0 (0.0%)
I80.223 - Phlebitis and thrombophlebitis of popliteal vein, bilateral	0 (0.0%)
I80.232 - Phlebitis and thrombophlebitis of left tibial vein	0 (0.0%)
I80.233 - Phlebitis and thrombophlebitis of tibial vein, bilateral	0 (0.0%)
I80.292 - Phlebitis and thrombophlebitis of other deep vessels of left lower extremity	0 (0.0%)
I80.293 - Phlebitis and thrombophlebitis of other deep vessels of lower extremity, bilateral	0 (0.0%)
I80.3 - Phlebitis and thrombophlebitis of lower extremities, unspecified	0 (0.0%)
I82.419 - Acute embolism and thrombosis of unspecified femoral vein	0 (0.0%)
I82.423 - Acute embolism and thrombosis of iliac vein, bilateral	0 (0.0%)
I82.431 - Acute embolism and thrombosis of right popliteal vein	0 (0.0%)
I82.432 - Acute embolism and thrombosis of left popliteal vein	0 (0.0%)
I82.433 - Acute embolism and thrombosis of popliteal vein, bilateral	0 (0.0%)
I82.441 - Acute embolism and thrombosis of right tibial vein	1 (4.2%)
I82.442 - Acute embolism and thrombosis of left tibial vein	1 (4.2%)
I82.443 - Acute embolism and thrombosis of tibial vein, bilateral	1 (4.2%)

Code	Total Patients (N=24)
I82.449 - Acute embolism and thrombosis of unspecified tibial vein	0 (0.0%)
I82.491 - Acute embolism and thrombosis of other specified deep vein of right lower extremity	0 (0.0%)
I82.4Y1 - Acute embolism and thrombosis of unspecified deep veins of right proximal lower extremity	0 (0.0%)
I82.4Y3 - Acute embolism and thrombosis of unspecified deep veins of proximal lower extremity, bilateral	0 (0.0%)
I82.4Y9 - Acute embolism and thrombosis of unspecified deep veins of unspecified proximal lower extremity	0 (0.0%)
I82.4Z1 - Acute embolism and thrombosis of unspecified deep veins of right distal lower extremity	1 (4.2%)
I82.4Z2 - Acute embolism and thrombosis of unspecified deep veins of left distal lower extremity	0 (0.0%)
I82.4Z3 - Acute embolism and thrombosis of unspecified deep veins of distal lower extremity, bilateral	0 (0.0%)
I80.12 - Phlebitis and thrombophlebitis of left femoral vein	0 (0.0%)
I80.201 - Phlebitis and thrombophlebitis of unspecified deep vessels of right lower extremity	0 (0.0%)
I80.202 - Phlebitis and thrombophlebitis of unspecified deep vessels of left lower extremity	0 (0.0%)
I80.203 - Phlebitis and thrombophlebitis of unspecified deep vessels of lower extremities, bilateral	0 (0.0%)
I80.209 - Phlebitis and thrombophlebitis of unspecified deep vessels of unspecified lower extremity	0 (0.0%)
I80.212 - Phlebitis and thrombophlebitis of left iliac vein	0 (0.0%)
I80.213 - Phlebitis and thrombophlebitis of iliac vein, bilateral	0 (0.0%)
I80.219 - Phlebitis and thrombophlebitis of unspecified iliac vein	0 (0.0%)
I80.222 - Phlebitis and thrombophlebitis of left popliteal vein	0 (0.0%)
I80.229 - Phlebitis and thrombophlebitis of unspecified popliteal vein	0 (0.0%)
I80.231 - Phlebitis and thrombophlebitis of right tibial vein	0 (0.0%)
I80.291 - Phlebitis and thrombophlebitis of other deep vessels of right lower extremity	0 (0.0%)
I80.299 - Phlebitis and thrombophlebitis of other deep vessels of unspecified lower extremity	0 (0.0%)
I82.401 - Acute embolism and thrombosis of unspecified deep veins of right lower extremity	0 (0.0%)
I82.402 - Acute embolism and thrombosis of unspecified deep veins of left lower extremity	0 (0.0%)
I82.403 - Acute embolism and thrombosis of unspecified deep veins of lower extremity, bilateral	0 (0.0%)
I82.409 - Acute embolism and thrombosis of unspecified deep veins of unspecified lower extremity	3 (12.5%)
I82.411 - Acute embolism and thrombosis of right femoral vein	1 (4.2%)
I82.412 - Acute embolism and thrombosis of left femoral vein	1 (4.2%)

Code	Total Patients (N=24)
I82.413 - Acute embolism and thrombosis of femoral vein, bilateral	0 (0.0%)
I82.421 - Acute embolism and thrombosis of right iliac vein	0 (0.0%)
I82.422 - Acute embolism and thrombosis of left iliac vein	0 (0.0%)
I82.429 - Acute embolism and thrombosis of unspecified iliac vein	1 (4.2%)
I82.439 - Acute embolism and thrombosis of unspecified popliteal vein	0 (0.0%)
I82.492 - Acute embolism and thrombosis of other specified deep vein of left lower extremity	1 (4.2%)
I82.493 - Acute embolism and thrombosis of other specified deep vein of lower extremity, bilateral	0 (0.0%)
I82.499 - Acute embolism and thrombosis of other specified deep vein of unspecified lower extremity	0 (0.0%)
I82.4Y2 - Acute embolism and thrombosis of unspecified deep veins of left proximal lower extremity	0 (0.0%)
Deep Vein Thrombosis, upper	
I82.210 - Acute embolism and thrombosis of superior vena cava	0 (0.0%)
I82.601 - Acute embolism and thrombosis of unspecified veins of right upper extremity	0 (0.0%)
I82.621 - Acute embolism and thrombosis of deep veins of right upper extremity	0 (0.0%)
I82.622 - Acute embolism and thrombosis of deep veins of left upper extremity	0 (0.0%)
I82.623 - Acute embolism and thrombosis of deep veins of upper extremity, bilateral	0 (0.0%)
I82.A12 - Acute embolism and thrombosis of left axillary vein	0 (0.0%)
I82.C11 - Acute embolism and thrombosis of right internal jugular vein	1 (4.2%)
I82.C13 - Acute embolism and thrombosis of internal jugular vein, bilateral	0 (0.0%)
I82.C19 - Acute embolism and thrombosis of unspecified internal jugular vein	0 (0.0%)
I82.602 - Acute embolism and thrombosis of unspecified veins of left upper extremity	0 (0.0%)
I82.603 - Acute embolism and thrombosis of unspecified veins of upper extremity, bilateral	0 (0.0%)
I82.609 - Acute embolism and thrombosis of unspecified veins of unspecified upper extremity	0 (0.0%)
I82.629 - Acute embolism and thrombosis of deep veins of unspecified upper extremity	0 (0.0%)
I82.A11 - Acute embolism and thrombosis of right axillary vein	0 (0.0%)
I82.A13 - Acute embolism and thrombosis of axillary vein, bilateral	0 (0.0%)
I82.A19 - Acute embolism and thrombosis of unspecified axillary vein	0 (0.0%)
I82.C12 - Acute embolism and thrombosis of left internal jugular vein	0 (0.0%)
Other Venous Thrombosis	

Code	Total Patients (N=24)
I81 - Portal vein thrombosis	0 (0.0%)
I82.0 - Budd-Chiari syndrome	0 (0.0%)
I82.1 - Thrombophlebitis migrans	0 (0.0%)
I82.3 - Embolism and thrombosis of renal vein	0 (0.0%)
I82.90 - Acute embolism and thrombosis of unspecified vein	0 (0.0%)
I82.B13 - Acute embolism and thrombosis of subclavian vein, bilateral	0 (0.0%)
I80.8 - Phlebitis and thrombophlebitis of other sites	1 (4.2%)
I80.9 - Phlebitis and thrombophlebitis of unspecified site	0 (0.0%)
I82.220 - Acute embolism and thrombosis of inferior vena cava	0 (0.0%)
I82.890 - Acute embolism and thrombosis of other specified veins	0 (0.0%)
I82.B11 - Acute embolism and thrombosis of right subclavian vein	0 (0.0%)
I82.B12 - Acute embolism and thrombosis of left subclavian vein	0 (0.0%)

Abbreviations: ICD-10 = International Classification of Disease, 10th Revision; N = number of patients in the specified category; RA = rheumatoid arthritis;
VTE = venous thromboembolism

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.39. Pattern of VTE and Related Diagnostic Codes in Patients with RA [HealthVerity, PS20].docx

Table 56_PS20. Clinical Characteristics of RA Patients with Incident Serious Infections [HealthVerity, PS20]

Characteristics[a,b]	Baricitinib[c] (N=6)	TNFi (N=10)	Total (N=16)
Age (mean) [SD]	59.00 (4.82)	55.00 (10.12)	56.50 (8.56)
Sex			
Female	6 (100.0%)	8 (80.0%)	14 (87.5%)
Male	0 (0.0%)	2 (20.0%)	2 (12.5%)
Clinical Conditions during baseline			
Cancer	3 (50.0%)	0 (0.0%)	3 (18.8%)
NMSC	1 (16.7%)	0 (0.0%)	1 (6.2%)
Chronic Lung disease	3 (50.0%)	3 (30.0%)	6 (37.5%)
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive Heart Failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	1 (16.7%)	1 (10.0%)	2 (12.5%)
Ischemic heart disease	1 (16.7%)	1 (10.0%)	2 (12.5%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	3 (50.0%)	0 (0.0%)	3 (18.8%)
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	3 (50.0%)	0 (0.0%)	3 (18.8%)
Dyslipidaemia	4 (66.7%)	3 (30.0%)	7 (43.8%)
Hypertension	5 (83.3%)	4 (40.0%)	9 (56.2%)
Immune disorders	1 (16.7%)	2 (20.0%)	3 (18.8%)
AIDS/HIV	0 (0.0%)	1 (10.0%)	1 (6.2%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	1 (16.7%)	0 (0.0%)	1 (6.2%)
Primary Sjögren Syndrome	0 (0.0%)	1 (10.0%)	1 (6.2%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	3 (50.0%)	3 (30.0%)	6 (37.5%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	3.59 (1.16)	3.69 (0.86)	3.65 (0.94)
Smoking	1 (16.7%)	4 (40.0%)	5 (31.2%)
Surgery, Trauma, & Hospitalization, recent	1 (16.7%)	2 (20.0%)	3 (18.8%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medications			
Antibiotics	5 (83.3%)	6 (60.0%)	11 (68.8%)
Antidiabetic agents	3 (50.0%)	0 (0.0%)	3 (18.8%)
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-insulins	3 (50.0%)	0 (0.0%)	3 (18.8%)
Aspirin	1 (16.7%)	0 (0.0%)	1 (6.2%)
Cardiovascular			
Anticoagulant	0 (0.0%)	0 (0.0%)	0 (0.0%)

Characteristics[a,b]	Baricitinib[c] (N=6)	TNFi (N=10)	Total (N=16)
Antihypertensives	6 (100.0%)	5 (50.0%)	11 (68.8%)
Antiplatelet	2 (33.3%)	0 (0.0%)	2 (12.5%)
Nitrates	1 (16.7%)	0 (0.0%)	1 (6.2%)
Hormonal			
HRT	0 (0.0%)	1 (10.0%)	1 (6.2%)
Oral Contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERMs	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	3 (50.0%)	1 (10.0%)	4 (25.0%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	1 (16.7%)	0 (0.0%)	1 (6.2%)
Glucocorticosteroid	5 (83.3%)	5 (50.0%)	10 (62.5%)
Vaccinations	2 (33.3%)	2 (20.0%)	4 (25.0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; CIRAS = claims-based index for RA severity; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; SD = standard deviation; RA = rheumatoid arthritis; SERM = selective estrogen receptor modifier; SLE = systemic lupus erythematosus; TIA= transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.56. Clinical Characteristics of RA Patients with Incident Serious Infections [HealthVerity, PS20].docx

Table 57_PS20. Pattern of RA Medication Use in Patients with Serious Infection Event [HealthVerity, PS20]

Characteristic[a]	Unmatched		Matched		
	Baricitinib[b] (N=7)	TNFi (N=47)	Baricitinib[b] (N=6)	TNFi (N=10)	Total (N=16)
Baseline Medication DMARDS					
cDMARDs, during baseline					
n, total	4 (57.1%)	38 (80.9%)	4 (66.7%)	9 (90.0%)	13 (81.2%)
Mean (SD)	1.29 (1.80)	1.21 (0.75)	1.50 (1.87)	1.10 (0.57)	1.25 (1.18)
Median	1.00 [0.00, 2.00]	1.00 [1.00, 2.00]	1.00 [0.00, 2.75]	1.00 [1.00, 1.25]	1.00 [1.00, 1.75]
Min, Max	0.0, 5.0	0.0, 3.0	0.0, 5.0	0.0, 2.0	0.0, 5.0
>1 cDMARD concomitantly	2 (28.6%)	15 (31.9%)	2 (33.3%)	2 (20.0%)	4 (25.0%)
Hydroxychloroquine	2 (28.6%)	14 (29.8%)	2 (33.3%)	3 (30.0%)	5 (31.3%)
Leflunomide	2 (28.6%)	9 (19.1%)	2 (33.3%)	1 (10.0%)	3 (18.8%)
Methotrexate	3 (42.9%)	22 (46.8%)	3 (50.0%)	6 (60.0%)	9 (56.3%)
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	1 (14.3%)	4 (8.5%)	1 (16.7%)	1 (10.0%)	2 (12.5%)
bDMARDs, during baseline					
n, total	3 (42.9%)	47 (100.0%)	2 (33.3%)	10 (100.0%)	12 (75.0%)
Mean (SD)	0.57 (0.79)	1.06 (0.32)	0.33 (0.52)	1.30 (0.67)	0.94 (0.77)
Median	0.00 [0.00, 1.00]	1.00 [1.00, 1.00]	0.00 [0.00, 1.00]	1.00 [1.00, 1.25]	1.00 [0.25, 1.00]
Min, Max	0.0, 2.0	1.0, 3.0	0.0, 1.0	1.0, 3.0	0.0, 3.0
cDMARDs, concomitant	1 (14.3%)	40 (85.1%)	1 (16.7%)	9 (90.0%)	10 (62.5%)
Abatacept	0 (0.0%)	1 (2.1%)	0 (0.0%)	1 (10.0%)	1 (6.3%)
Adalimumab[c]	0 (0.0%)	32 (68.1%)	0 (0.0%)	7 (70.0%)	7 (43.8%)
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	1 (14.3%)	8 (17.0%)	1 (16.7%)	3 (30.0%)	4 (25.0%)
Etanercept[c]	0 (0.0%)	24 (51.1%)	0 (0.0%)	5 (50.0%)	5 (31.3%)
Golimumab[c]	0 (0.0%)	12 (25.5%)	0 (0.0%)	4 (40.0%)	4 (25.0%)
Infliximab[c]	1 (14.3%)	16 (34.0%)	0 (0.0%)	1 (10.0%)	1 (6.3%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Medication					
Methotrexate, concomitant	3 (42.9%)	17 (36.2%)	3 (50.0%)	4 (40.0%)	7 (43.8%)
Other Concomitant cDMARD	4 (57.1%)	21 (44.7%)	4 (66.7%)	4 (40.0%)	8 (50.0%)
Dose change, baricitinib	NA	0 (0.0%)	NA	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c TNF inhibitors.

d Only baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked 'NA' as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.57. Pattern of RA Medication Use in Patients with Serious Infection Event [HealthVerity]].docx

Table 58_PS20. Time to First Serious Infection (Days) [HealthVerity PS20]

	Unmatched		Matched		
	Baricitinib[a,b] (N=930)	**TNFi (N=3,978)**	**Baricitinib[a,b] (N=748)**	**TNFi (N=748)**	**Total (N=1,496)**
n	930	3,978	748	748	1,496
Mean (SD)	174.71 (179.95)	133.91 (116.34)	203.50 (178.60)	82.50 (55.38)	127.88 (127.02)
Median	111.00 [11.00, 412.00]	94.00 [42.00, 213.00]	171.00 [35.00, 412.25]	88.50 [26.25, 114.50]	94.00 [32.50, 171.50]
Min, Max	2.0, 413.0	3.0, 393.0	11.0, 413.0	16.0, 175.0	11.0, 413.0

Abbreviations: MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis code of acute myocardial infarction or ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Only baricitinib 2-mg dose is available in the US

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.58. Time to First Seroius Infection (Days) [HealthVerity PS20].docx

Table 60_PS20. Serious Infection Events Per Patient During All Available Follow-up [HealthVerity, PS20]

Number of Infections per Person	Unmatched		Matched		
	Baricitinib (N=930)	TNFi (N=3,978)	Baricitinib (N=748)	TNFi (N=748)	Total (N=1,496)
0	898 (96.6%)	3,850 (96.8%)	720 (96.3%)	719 (96.1%)	1,439 (96.2%)
1	1 (0.1%)	8 (0.2%)	1 (0.1%)	3 (0.4%)	4 (0.3%)
2	1 (0.1%)	7 (0.2%)	1 (0.1%)	0 (0.0%)	1 (0.1%)
3	2 (0.2%)	13 (0.3%)	2 (0.3%)	5 (0.7%)	7 (0.5%)
4	4 (0.4%)	12 (0.3%)	2 (0.3%)	2 (0.3%)	4 (0.3%)
5	2 (0.2%)	2 (0.1%)	2 (0.3%)	0 (0.0%)	2 (0.1%)
6	1 (0.1%)	4 (0.1%)	1 (0.1%)	2 (0.3%)	3 (0.2%)
>6	17 (1.8%)	71 (1.8%)	15 (2.0%)	12 (1.6%)	27 (1.8%)
N/A[a]	4 (0.4%)	11 (0.3%)	4 (0.5%)	5 (0.7%)	9 (0.6%)

Abbreviations: N = number of patients in the specified category; N/A = not available; TNFi = tumour necrosis factor inhibitor.

[a] Patients who start their follow-up on the same day as the last day of available data are censored and have less than 1 day of follow-up. These patients are excluded from any of the Serious Infections count categories.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.60. Serious Infection Events Per Patient During All Available Follow-up [HealthVerity, PS20].docx

Table 64_PS20. Incidence Rate of Hospitalized TB Event [HealthVerity, PS20]

	Unmatched		Matched		
	Baricitinib (N=949)	**TNFi (N=4,042)**	**Baricitinib (N=761)**	**TNFi (N=761)**	**Total (N=1,522)**
Overall					
Person-Years	330.98	1,987.18	250.55	372.32	622.87
TB Events	0.0	0.0	0.0	0.0	0.0
TB Events/100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 1.12	0.00, 0.19	0.00, 1.47	0.00, 0.99	0.00, 0.59

Abbreviations: CI = confidence interval; N = number of patients in the specified category; PY = person-years; TB = tuberculosis; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.64. Incidence Rate of Hospitalized TB Event [HealthVerity].docx

II. Variable Ratio Matching

All prior tables presented in this annex were based on propensity score matched baricitinib:TNFi cohorts using a 1:1 matching strategy. In this section of the annex, the tables include results that are based on a variable ratio matching (VRM) approach as described in Section 9.9.6.1 of the final study report.

The main analysis was modified to use 1:1 matching, as this allows the results in the meta-analysis to be directly proportional to the amount of baricitinib exposure in each data source. For transparency, comparative results generated using VRM prior to the adoption of the 1:1 matching are included here.

Table 6.45_PS20_VRM. Incidence Rate of Event - VTE, Primary Definition [HealthVerity, PS20]

	Unmatched		Matched		
	Baricitinib[a] (N=933)	**TNFi (N=3,953)**	**Baricitinib[a] (N=643)**	**TNFi (N=1,532)**	**Total (N=2,175)**
Overall					
Person-Years	322.97	1,940.61	206.87	751.91	958.78
VTE Events	6	18	4	7	11
VTE Events/100 PY	1.86	0.93	1.93	0.93	1.15
95% CI	0.68, 4.04	0.50, 1.36	0.53, 4.95	0.37, 1.92	0.47, 1.83
Concomitant MTX Use[b]					
Total, n	146 (15.6%)	939 (23.8%)	96 (14.9%)	284 (18.5%)	380 (17.5%)
Person-Years	77.32	620.21	50.02	195.74	245.76
VTE Events	1	3	1	2	3
VTE Events/100 PY	1.29	0.48	2.00	1.02	1.22
95% CI	0.03, 7.21	0.10, 1.41	0.05, 11.14	0.12, 3.69	0.25, 3.57
No Concomitant MTX Use[b]					
Total, n	787 (84.4%)	3,014 (76.2%)	547 (85.1%)	1,248 (81.5%)	1,795 (82.5%)
Person-Years	245.65	1,320.40	156.85	556.17	713.02
VTE Events	5	15	3	5	8
VTE Events/100 PY	2.04	1.14	1.91	0.90	1.12
95% CI	0.66, 4.75	0.56, 1.71	0.39, 5.59	0.29, 2.10	0.48, 2.21

Abbreviations: CI = confidence intervals; MTX = methotrexate; N = number of patients in the specified category; PY = person-year; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available.

b Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period

c N (%) of subgroups may not always sum precisely to total group N (%) due to rounding

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.45. Incidence Rate of Event - VTE, Primary Definition [HealthVerity, PS20]_vrm.docx

Table 6.48_PS20_VRM. Comparative Risk of Incident VTE, Primary Definition [HealthVerity, PS20]

	TNFi	Baricitinib		p-value
		HR	95%CI	
Base Model	Ref	1.94	0.77, 4.90	0.16
Adjusted – Model [1][1]	Ref	2.57	0.70, 9.38	0.15

Abbreviations: CI = confidence interval; HR = Cox proportional hazard ratio; Ref = referent group; VTE = venous thromboembolism.

1 Model [1] - propensity score-matched model with outcome and baricitinib exposure, adjusted for any variables that remain unbalanced after PS matching.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.48. Comparative Risk of Incident VTE, Primary Definition [HealthVerity, PS20]_vrm.docx

Table 6.54_PS20_VRM. Incidence Rate of Event - MACE [HealthVerity, PS20]

Model	Unmatched		Matched		
	Baricitinib[a] (N=932)	TNFi (N=3,952)	Baricitinib[a] (N=643)	TNFi (N=1,556)	Total (N=2,199)
Overall					
Person-Years	324.73	1,942.05	206.18	777.51	983.69
MACE	4	10	2	6	8
MACE/100 PY	1.23	0.51	0.97	0.77	0.81
95% CI	0.34, 3.15	0.20, 0.83	0.12, 3.50	0.28, 1.68	0.35, 1.60
MI					
MI	2	4	1	2	3
Person-Years	325.12	1,943.83	206.43	779.09	985.52
IR per100 PY	0.62	0.21	0.48	0.26	0.30
95% CI	0.07, 2.22	0.06, 0.53	0.01, 2.70	0.03, 0.93	0.06, 0.89
Stroke, any					
Stroke	2	6	1	4	5
Person-Years	325.21	1,942.68	206.23	777.90	984.13
IR per 100 PY	0.61	0.31	0.48	0.51	0.51
95% CI	0.07, 2.22	0.11, 0.67	0.01, 2.70	0.14, 1.32	0.17, 1.19
Concomitant MTX Use[b]					

Model	Unmatched		Matched		
	Baricitinib[a] (N=932)	TNFi (N=3,952)	Baricitinib[a] (N=643)	TNFi (N=1,556)	Total (N=2,199)
MACE	1	3	0	0	0
Person-Years	77.57	623.24	46.00	248.91	294.91
IR per 100 PY	1.29	0.48	0.00	0.00	0.00
95% CI	0.03, 7.18	0.10, 1.41	0.00, 8.02	0.00, 1.48	0.00, 1.25
No Concomitant MTX Use[b]					
MACE	3	7	2	6	8
Person-Years	247.16	1,318.81	160.18	528.60	688.78
IR per 100 PY	1.21	0.53	1.25	1.14	1.16
95% CI	0.25, 3.55	0.21, 1.09	0.15, 4.51	0.42, 2.47	0.50, 2.29

Abbreviations: CI = confidence interval; IR = incidence rate; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; MI = Myocardial infarction; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

c N in subgroups may not always sum precisely to total group N due to rounding.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.54. Incidence Rate of Event - MACE [HealthVerity, PS20]_vrm.docx

Table 6.55_PS20_VRM. Comparative Risk of Incident MACE [HealthVerity, PS20]

	TNFi	Baricitinib		p-value
		HR	95%CI	
Base Model	Ref	2.33	0.73, 7.48	0.15
Adjusted – Model [1][1]	Ref	1.06	0.20, 5.57	0.95

Abbreviations: CI = confidence interval; HR = Cox proportional hazard ratio; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Ref = referent group; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

1 Model [1] - propensity score-matched model with outcome and baricitinib exposure, adjusted for any variables that remain unbalanced after PS matching.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.55. Comparative Risk of Incident MACE [HealthVerity, PS20]_vrm.docx

Table 6.59_PS20_VRM. Incidence Rate of Event - First Serious Infection [HealthVerity, PS20 RA]

	Unmatched		Matched		
	Baricitinib[a] (N=930)	TNFi (N=3,978)	Baricitinib[a] (N=667)	TNFi (N=1,597)	Total (N=2,264)
SI Events	7	47	5	20	25

	Unmatched		Matched		
	Baricitinib[a] (N=930)	TNFi (N=3,978)	Baricitinib[a] (N=667)	TNFi (N=1,597)	Total (N=2,264)
Person-years	320.63	1,937.44	211.53	774.45	985.98
IR per 100 PY	2.18	2.43	2.36	2.58	2.54
95% CI	0.88, 4.50	1.73, 3.12	0.77, 5.52	1.45, 3.71	1.54, 3.53

Abbreviations: CI = confidence interval; IR = incidence rate; N = number of patients in the specified category; PY = person-years; SI = serious infection; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\healthverity ps20_PS20\6. Table 6.59. Incidence Rate of Event - First Serious Infection [HealthVerity, PS20 RA]_vrm.docx

Annex 11. ARTIS – Additional Results

This annex includes information about results for the following analyses:

I. Additional analysis
These additional results were not presented in the body of the report. These results, like those included in the report body, are based on 1:1 baricitinib:TNFi propensity score matching. Specifically, this section of the annex includes:
- Descriptive tables for unmatched eligible patients.
- Descriptive tables for matched patient cohorts for the serious infection analyses

I. Additional analysis

Table 1_ARTIS Baseline Demographics, Unmatched [ARTIS]

	Baricitinib			TNFi (N=6230)	Std. Diff. (Any vs TNFi)
	Any (N=1737)	4-mg (n=1381)	2-mg (n=354)		
Age [yrs]					
N	1737	1381	354	6230	0.158
Mean (SD)	59 (13.7)	57 (12.9)	71 (10.4)	57 (14.7)	
Median	60	57	73	59	
Min, Max	18, 92	18, 89	30, 92	18, 91	
≥ 65 years	694 (40%)	425 (31%)	267 (75%)	2183 (35%)	
Sex					
Male	320 (18%)	258 (19%)	62 (18%)	1426 (23%)	-0.117
Female	1417 (82%)	1123 (81%)	292 (82%)	4804 (77%)	

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = standardised difference; TNFi = tumour necrosis factor inhibitor.
Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\Table1_demographics_08MAR22.xlsx

Table 4_ARTIS. Baseline Demographics Incident Serious Infections, Matched [ARTIS]

	Baricitinib			TNFi (N=1683)	Std. Diff. (Any vs TNFi)
	Any (N=1683)	4-mg (n=1343)	2-mg (n=339)		
Age [yrs]					
N	1683	1343	339	1683	-0.013
Mean (SD)	59 (13.7)	56 (12.9)	71 (10.3)	59 (13.7)	
Median	60	57	73	61	
Min, Max	18, 92	18, 89	32, 92	19, 88	
≥ 65 years	659 (39%)	403 (30%)	255 (75%)	672 (40%)	
Sex					
Male	303 (18%)	244 (18%)	59 (17%)	285 (17%)	0.027
Female	1380 (82%)	1099 (82%)	280 (83%)	1398 (83%)	

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = standardised difference; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\Table1_demographics_08MAR22.xlsx

Table 6_ARTIS. Clinical History at Baseline, Unmatched Cohorts [ARTIS]

Characteristic [a,b]	Baricitinib [c] (N=1737)	TNFi (N=6230)	Std. Diff.
Clinical Conditions during baseline			
Cancer	<5	10 (0%)	0.008
NMSC	<5	<5	0.022
Chronic lung disease	15 (1%)	39 (1%)	0.006
Cardiovascular conditions			
Atrial arrhythmia	<5	24 (0%)	0.002
Cardiovascular revascularization	<5	13 (0%)	-0.020
Congestive heart failure	<5	<5	0.012
Coronary artery disease	<5	<5	0.012
Ischemic heart disease	7 (0%)	12 (0%)	0.043
Unstable angina	<5	<5	0.022
Ventricular arrhythmia	9 (1%)	12 (0%)	0.063
Diabetes Mellitus	148 (9%)	507 (8%)	0.012
Type I	NA	NA	
Type II	NA	NA	
Dyslipidaemia	<5	<5	-
Hypertension	12 (1%)	15 (0%)	0.068
Immune disorders			
AIDS/HIV	NA	NA	
Antiphospholipid syndrome	NA	NA	
SLE	NA	NA	
Primary Sjögren syndrome	<5	20 (0%)	-0.017
Liver disorder	5 (0%)	15 (0%)	0.013
Obesity	NA	NA	
Pregnancy	5 (0%)	73 (1%)	-0.103
RA severity (DAS28) available	**949**	**3111**	
Mean (SD)	4.6 (1.28)	4.4 (1.36)	
DAS28 < 2.6 (remission)	61 (6%)	358 (12%)	-0.115
Mean	2.03	1.96	
DAS28 < 3.2 (low)	75 (8%)	252 (8%)	0.014
Mean	2.97	2.94	
DAS28 < 5.2 (moderate)	464 (49%)	1552 (50%)	0.045
Mean	4.26	4.20	
DAS28 5.2+ (high)	349 (37%)	949 (31%)	0.131
Mean	5.94	5.90	
Smoking	825 (47%)	2604 (42%)	0.121
Surgery	1388 (80%)	4496 (72%)	0.184
TIA	<5	<5	0.012
DMARDs			
cDMARDs, during baseline			
n, total	968 (56%)	4716 (76%)	-0.436
Mean (SD)	1 (0.6)	1 (0.7)	
Median	1	1	

Characteristic [a,b]	Baricitinib [c] (N=1737)	TNFi (N=6230)	Std. Diff.
Min, Max	0, 3	0, 4	
Hydroxychloroquine	93 (5%)	487 (8%)	-0.097
Leflunomide	75 (4%)	250 (4%)	0.018
Methotrexate	752 (43%)	4006 (64%)	-0.439
Minocycline	NA [e]	NA [e]	
Sulfasalazine	159 (9%)	896 (14%)	-0.165
bDMARDs, during baseline			
n, total	929 (53%)	2539 (41%)	0.268
Mean (SD)	1 (0.6)	0 (0.5)	
Median	1	0	
Min, Max	0, 3	0, 4	
abatacept	170 (10%)	112 (2%)	0.349
adalimumab[d]	192 (11%)	636 (10%)	0.038
anakinra	<5	<5	0.049
certolizumab pegol[d]	47 (3%)	135 (2%)	0.039
etanercept[d]	326 (19%)	1411 (23%)	-0.094
golimumab[d]	30 (2%)	130 (2%)	-0.020
infliximab[d]	59 (3%)	300 (5%)	-0.074
rituximab	74 (4%)	20 (0%)	0.267
sarilumab	27 (2%)	7 (0%)	0.164
tocilizumab	131 (8%)	70 (1%)	0.325
Other Prescription Medications			
Antibiotics	435 (25%)	1129 (18%)	0.166
Antidiabetic agents	148 (9%)	501 (8%)	0.015
Insulins	80 (5%)	260 (4%)	0.018
Non-insulins	104 (6%)	353 (6%)	0.008
Aspirin	159 (9%)	508 (8%)	0.040
Cardiovascular			
Anticoagulant	118 (7%)	291 (5%)	0.053
Antihypertensives	762 (44%)	2269 (36%)	0.144
Antiplatelet	184 (11%)	570 (9%)	0.053
Nitrates	54 (3%)	113 (2%)	0.085
Hormonal			
HRT	137 (8%)	454 (7%)	0.017
Oral Contraceptives	61 (4%)	264 (4%)	-0.036
SERMs	<5	<5	0.022
Lipid-lowering agents			
Bile acid binding	5 (0%)	18 (0%)	-0.011
Cholesterol absorption inhibitor	33 (2%)	54 (1%)	0.079
Fibrates	<5	6 (0%)	-0.014
Niacin	NA	NA	
Omega-3 fatty acids	NA	NA	
Statins	243 (14%)	883 (14%)	-0.013
Rheumatoid arthritis-related			
Cox-2 Inhibitor	122 (7%)	406 (7%)	0.024

Characteristic [a,b]	Baricitinib [c] (N=1737)	TNFi (N=6230)	Std. Diff.
Glucocorticosteroid	1108 (64%)	3763 (60%)	0.072
Vaccinations	NA	NA	

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; cDMARD = conventional disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff. = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort. Clinical conditions are defined based on the "main diagnosis" in the National Patient Register

[b] Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

[c] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

[d] TNF inhibitors. Unless otherwise noted, characteristics in this table and similar tables are measured during baseline, including on the index day.

[e] Minocycline is not used to treat RA in Sweden.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\Table2_clinical_16MAY22_update.xlsx

Table 9_ARTIS. Clinical Characteristics Incident Serious Infection Cohorts, Matched [ARTIS]

Characteristic[a,b]	Baricitinib[c] (N=1683)	TNFi (N=1683)	Std. Diff.
Clinical Conditions during baseline			
Cancer	<5	<5	0.000
NMSC	<5	<5	0.031
Chronic lung disease	14 (1%)	19 (1%)	-0.035
Cardiovascular conditions			
Atrial arrhythmia	<5	13 (1%)	-0.100
Cardiovascular revascularization	<5	6 (0%)	-0.059
Congestive heart failure	<5	<5	-0.028
Coronary artery disease	<5	<5	0.000
Ischemic heart disease	7 (0%)	5 (0%)	0.022
Unstable angina	<5	<5	0.000
Ventricular arrhythmia	9 (1%)	<5	0.060
Diabetes Mellitus	140 (8%)	125 (7%)	0.032
Type I	NA	NA	
Type II	NA	NA	
Dyslipidaemia	<5	<5	.
Hypertension	10 (1%)	<5	0.074
Immune disorders			
AIDS/HIV	NA	NA	
Antiphospholipid syndrome	NA	NA	
SLE	NA	NA	
Primary Sjögren syndrome	<5	5 (0%)	-0.011
Liver disorder	5 (0%)	5 (0%)	0.000
Obesity	NA	NA	
Pregnancy	5 (0%)	12 (1%)	-0.049
RA severity (DAS28) available	**922**	**782**	
Mean	4.6 (1.28)	4.3 (1.43)	
DAS28 < 2.6 (remission)	61 (7%)	99 (13%)	-0.107
Mean	2.03	1.86	
DAS28 < 3.2 (low)	75 (8%)	60 (8%)	0.044
Mean	2.97	2.89	
DAS28 < 5.2 (moderate)	450 (49%)	390 (50%)	0.081
Mean	4.26	4.23	
DAS28 5.2+ (high)	336 (36%)	233 (30%)	0.161
Mean	5.94	5.91	
Smoking	798 (47%)	735 (44%)	0.075
Surgery	1334 (79%)	1260 (75%)	0.103
TIA	<5	<5	0.000
DMARDs			
cDMARDs, during baseline			
n, total	942 (56%)	1227 (73%)	-0.365
Mean (SD)	1 (0.6)	1 (0.7)	

Characteristic[a,b]	Baricitinib[c] (N=1683)	TNFi (N=1683)	Std. Diff.
Median	1	1	
Min, Max	0, 3	0, 4	
Hydroxychloroquine	91 (5%)	120 (7%)	-0.069
Leflunomide	73 (4%)	70 (4%)	0.009
Methotrexate	731 (43%)	1016 (60%)	-0.347
Minocycline	NA [e]	NA [e]	
Sulfasalazine	157 (9%)	218 (13%)	-0.112
bDMARDs, during baseline			
n, total	899 (53%)	1021 (61%)	-0.146
Mean (SD)	1 (0.6)	1 (0.6)	
Median	1	1	
Min, Max	0, 3	0, 4	
abatacept	168 (10%)	70 (4%)	0.251
adalimumab [d]	187 (11%)	254 (15%)	-0.129
anakinra	<5	<5	0.049
certolizumab pegol [d]	42 (2%)	63 (4%)	-0.083
etanercept [d]	319 (19%)	566 (34%)	-0.362
golimumab [d]	29 (2%)	54 (3%)	-0.109
infliximab [d]	55 (3%)	129 (8%)	-0.223
rituximab	71 (4%)	13 (1%)	0.234
sarilumab	27 (2%)	<5	0.168
tocilizumab	124 (7%)	40 (2%)	0.251
Other Prescription Medications			
Antibiotics	396 (24%)	391 (23%)	0.007
Antidiabetic agents	140 (8%)	123 (7%)	0.037
Insulins	75 (4%)	68 (4%)	0.020
Non-insulins	97 (6%)	85 (5%)	0.031
Aspirin	150 (9%)	159 (9%)	-0.019
Cardiovascular			
Anticoagulant	106 (6%)	103 (6%)	0.008
Antihypertensives	726 (43%)	686 (41%)	0.049
Antiplatelet	173 (10%)	184 (11%)	-0.022
Nitrates	50 (3%)	45 (3%)	0.019
Hormonal			
HRT	132 (8%)	158 (9%)	-0.058
Oral Contraceptives	61 (4%)	47 (3%)	0.043
SERMs	<5	<5	0.031
Lipid-lowering agents			
Bile acid binding	5 (0%)	5 (0%)	0.000
Cholesterol absorption inhibitor	32 (2%)	23 (1%)	0.046
Fibrates	<5	<5	-0.021
Niacin	NA	NA	
Omega-3 fatty acids	NA	NA	
Statins	232 (14%)	261 (16%)	-0.050
Rheumatoid arthritis-related			

Characteristic[a,b]	Baricitinib[c] (N=1683)	TNFi (N=1683)	Std. Diff.
Cox-2 Inhibitor	116 (7%)	116 (7%)	0.000
Glucocorticosteroid	1065 (63%)	1068 (63%)	-0.004
Vaccinations	NA	NA	

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; cDMARD = conventional disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff. = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort. Clinical conditions are defined based on the "main diagnosis" in the National Patient Register.

[b] Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

[c] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

[d] TNF inhibitors.

[e] Minocycline is not used to treat RA in Sweden.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\Table2_clinical_16MAY22_update.xlsx

Table 11_ARTIS. Baseline Healthcare Resource Utilization, Unmatched [ARTIS]

Type of Resource Use	Baricitinib (N=1737)	TNFi (N=6230)	Std. Diff.
Physician Office Visits	NA	NA	
n, patients			
n, events			
Mean (SD)			
Median			
Min, Max			
Rheumatologist Visits			
n, patients	1399	4845	
n, events	3537	11,457	0.106
Mean (SD)	2 (1.9)	2 (1.8)	
Median	2	1	
Min, Max	0, 12	0, 20	
Other Outpatient Visits			
n, patients	1585	5475	
n, events	5927	18,455	0.155
Mean (SD)	3 (3.1)	3 (2.8)	
Median	3	2	
Min, Max	0, 27	0, 30	
Inpatient Visits			
n, patients	247	597	
n, events	365	876	0.121
Mean (SD)	0 (0.6)	0 (0.6)	
Median	0	0	
Min, Max	0, 9	0, 13	
ED Visits	NA	NA	
n, patients			
n, events			
Mean (SD)			
Median			
Min, Max			

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits. Other outpatient visits do not include physician office visits or rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\ Table3_HCRU_08MAR22.xlsx

Table 14_ARTIS. Baseline Healthcare Resource Utilization Incident Serious Infection Cohorts, Matched [ARTIS]

Type of Resource Use	Baricitinib (N=1683)	TNFi (N=1683)	Std. Diff.
Physician Office Visits	NA	NA	
n, patients			
n, events			
Mean (SD)			
Median			
Min, Max			
Rheumatologist Visits			
n, patients	1352	1348	
n, events	3380	3343	0.012
Mean (SD)	2 (1.9)	2 (1.9)	
Median	2	2	
Min, Max	0, 12	0, 15	
Other Outpatient Visits			
n, patients	1531	1509	
n, events	5589	5497	0.019
Mean (SD)	3 (3.0)	3 (2.8)	
Median	3	3	
Min, Max	0, 27	0, 22	
Inpatient Visits			
n, patients	194	199	
n, events	261	282	-0.026
Mean (SD)	0 (0.5)	0 (0.6)	
Median	0	0	
Min, Max	0, 6	0, 11	
ED Visits	NA	NA	
n, patients			
n, events			
Mean (SD)			
Median			
Min, Max			

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits. Other outpatient visits do not include physician office visits or rheumatologist visits.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\ Table3_HCRU_08MAR22.xlsx

Table 17_ARTIS. Duration of Follow-up Period (Days), Unmatched [ARTIS]

	Baricitinib[a] (N=1737)	TNFi (N=6230)	Std. Diff
N	1737	6230	
Mean (SD)	506 (347.4)	580 (419.3)	-0.197
Median	461	488	
Min, Max	1, 1310	3, 1460	

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\Table4_durationfup_08MAR22.xlsx

Table 18_ARTIS. Duration of Follow-up Period (Days) Primary VTE Cohorts, Matched [ARTIS]

	Baricitinib [a] (N=1685)	TNFi (N=1685)	Std. Diff. (N=n)
N	1685	1685	
Mean (SD)	502 (345.7)	565 (423.5)	-0.166
Median	454	454	
Min, Max	1, 1310	9, 1458	
Reasons for censoring			
Incident event	23 (1%)	14 (1%)	
Medication discontinued	270 (16%)	243 (14%)	
Initiated b/tsDMARD	322 (19%)	324 (19%)	
Death	33 (2%)	21 (1%)	
Migration	<5	<5	
End of study period (31 Dec 2020)	1035 (61%)	1081 (64%)	

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = Standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\Table4_durationfup_08MAR22.xlsx

Table 21_ARTIS. Duration of Follow-up Period (Days) MACE Cohorts, Matched [ARTIS]

	Baricitinib[a] (N=1681)	TNFi (N=1681)	Std. Diff.
N	1681	1681	
Mean (SD)	503 (346.4)	583 (425.6)	-0.209
Median	454	484	
Min, Max	1, 1310	3, 1460	
Reasons for censoring			
Incident event	13 (1%)	16 (1%)	
Medication discontinued	277 (16%)	211 (13%)	
Initiated b/tsDMARD	322 (19%)	317 (19%)	
Death	32 (2%)	17 (1%)	
Migration	<5	<5	
End of study period (31 Dec 2020)	1035 (62%)	1119 (67%)	

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; MACE =major adverse cardiovascular event; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\Table4_durationfup_08MAR22.xlsx

Table 22_ARTIS. Duration of Follow-up Period (Days) Incident Serious Infection Cohorts, Matched [ARTIS]

	Baricitinib[a] (N=1683)	TNFi (N=1683)	Std. Diff.
N	1683	1683	
Mean (SD)	485 (345.1)	562 (426.2)	-0.201
Median	428	453	
Min, Max	1, 1310	8, 1460	
Reasons for censoring			
Incident event	94 (6%)	66 (4%)	
Medication discontinued	251 (15%)	223 (13%)	
Initiated b/tsDMARD	318 (19%)	305 (18%)	
Death	24 (1%)	14 (1%)	
Migration	<5	<5	
End of study period (31 Dec 2020)	994 (59%)	1074 (64%)	

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\Table4_durationfup_08MAR22.xlsx

Table 56_ARTIS. Clinical Characteristics of RA Patients with Incident Serious Infections [ARTIS]

Characteristic [a,b]	Baricitinib[c] (N=94)	TNFi (N=66)	Total (N=160)
Age (mean) [SD]	66 (12.0)	65 (11.0)	65 (11.6)
Sex			
Female	28 (30%)	15 (23%)	43 (27%)
Male	66 (70%)	51 (77%)	117 (73%)
Clinical Conditions during baseline			
Cancer	<5	<5	<5
NMSC	<5	<5	<5
Chronic Lung disease Disease	<5	<5	<5
Cardiovascular conditions			
Atrial arrhythmia	<5	<5	<5
Cardiovascular revascularization	<5	<5	<5
Congestive heart failure	<5	<5	<5
Coronary artery disease	<5	<5	<5
Ischemic heart disease	<5	<5	<5
Unstable angina	<5	<5	<5
Ventricular arrhythmia	<5	<5	<5
Diabetes Mellitus	17 (18%)	7 (11%)	24 (15%)
Type I	NA	NA	NA
Type II	NA	NA	NA
Dyslipidaemia	<5	<5	<5
Hypertension	<5	<5	<5
Immune disorders			
AIDS/HIV	NA	NA	NA
Antiphospholipid syndrome	NA	NA	NA
SLE	NA	NA	NA
Primary Sjögren Syndrome	<5	<5	<5
Liver Disorder	<5	<5	<5
Obesity	NA	NA	NA
Pregnancy	<5	<5	<5
RA Severity (DAS28), mean (SD)	4.8 (1.23)	4.7 (1.63)	4.8 (1.39)
Smoking	51 (69%)	28 (53%)	79 (62%)
Surgery	81 (86%)	55 (83%)	136 (85%)
TIA	<5	<5	<5
Other Prescription Medication			
Antibiotics	35 (37%)	22 (33%)	57 (36%)
Antidiabetic agents	17 (18%)	7 (11%)	24 (15%)
Insulins	7 (7%)	<5	9 (6%)
Non-insulins	13 (14%)	5 (8%)	18 (11%)
Aspirin	19 (20%)	9 (14%)	28 (18%)
Cardiovascular			
Anticoagulant	14 (15%)	9 (14%)	23 (14%)

Characteristic [a,b]	Baricitinib[c] (N=94)	TNFi (N=66)	Total (N=160)
Antihypertensives	61 (64%)	45 (68%)	106 (66%)
Antiplatelet	23 (24%)	12 (18%)	35 (22%)
Nitrates	6 (6%)	<5	7 (4%)
Hormonal			
HRT	5 (5%)	7 (11%)	12 (8%)
Oral contraceptives	<5	<5	<5
SERMs	<5	<5	<5
Lipid-lowering agents			
Bile acid binding	<5	<5	<5
Cholesterol absorption inhibitor	6 (6%)	<5	7 (4%)
Fibrates	<5	<5	<5
Niacin	NA	NA	NA
Omega-3 fatty acids	NA	NA	NA
Statins	31 (33%)	12 (18%)	43 (27%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	6 (6%)	<5	10 (6%)
Glucocorticosteroid	82 (87%)	55 (83%)	137 (86%)
Vaccinations	NA	NA	NA

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; cDMARD = conventional disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff. = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort. Clinical conditions are defined based on the “main diagnosis” in the National Patient Register.

[b] Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

[c] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

[d] Except for cancer diagnosed within 90 days of VTE diagnosis, events in this category must have occurred in the 4 weeks immediately prior to VTE (Kline et al. 2017).

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Table 58_ARTIS. Time to First Serious Infection Event (Days) [ARTIS]

Time	Unmatched		Matched	
	Baricitinib [a] (N=1737)	TNFi (N=6230)	Baricitinib [a] (N=1683)	TNFi (N=1683)
n	1737	6230	1683	1683
Mean (SD)	483 (345.0)	565 (416.3)	485 (345.1)	562 (426.2)
Median	422	464	428	453
Min, Max	1, 1310	3, 1460	1, 1310	8, 1460

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; VTE = venous thromboembolism.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\ARTIS\ Table6_time_to_outcome_08MAR22.xlsx

Annex 12. BKK – Additional Results

This annex includes information about results for the following analyses:

I. Additional analysis

These are the additional results that were not presented in the body of this report. Like the results in the body, they are based on 1:1 baricitinib:TNFi propensity-score matching. Specifically, this includes the following:

a. Descriptive tables for unmatched eligible patients.
b. Descriptive tables for matched patient cohorts for the serious infection analyses

I. Additional analysis

Table 1_BKK. Baseline Demographics, Unmatched [BKK]

	Baricitinib			TNFi	Std. Diff.
	Any	4-mg	2-mg	(N=3332)	(Any vs TNFi)
	(N=851)	(n=699)	(n=152)		
Age [yrs]					
N	851	699	152	3332	39.6
Mean (SD)	57.1 (13)	54.8 (12)	67.6 (12)	51.6 (14)	
Median	57.0	56.0	71.0	53.0	
Min, Max	18.0, 92.0	18.0, 84.0	24.0, 92.0	18.0, 94.0	
≥ 65 years	232 (27%)	139 (20%)	93 (61%)	566 (17%)	
Sex					
Male	207 (24%)	173 (25%)	34 (22%)	1162 (35%)	-23.3
Female	644 (76%)	526 (75%)	118 (78%)	2170 (65%)	

Abbreviations: N = number of patients in the specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus; Max = maximum; Min = minimum.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\BKK\ Lilly Baricitinib Results_Top-Line_BKK_v2.0.docx -page 2

Table 4_BKK. Baseline Demographics Incident Serious Infections, Matched [BKK]

	Baricitinib			TNFi	Std. Diff.	Total
	Any (N=859)	4-mg (n=691)	2-mg (n=168)	(N=859)	(Any vs TNFi)	(N=1718)
Age [yrs]						
N	859	691	168	859	-1.5	1718
Mean (SD)	57.9 (14)	55.3 (13)	68.7 (12)	58.1 (14)		58.0 (14)
Median	58.0	56.0	72.0	58.0		58.0
Min, Max	18.0, 92.0	18.0, 84.0	24.0, 92.0	18.0, 90.0		18.0, 92.0
≥ 65 years	263 (31%)	151 (22%)	112 (67%)	274 (32%)		537 (31%)

Sex						
Male	224 (26%)	187 (27%)	37 (22%)	238 (28%)	-3.6	462 (27%)
Female	635 (74%)	504 (73%)	131 (78%)	621 (72%)		1256 (73%)

Abbreviations: N = number of patients in the specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus; Max = maximum; Min = minimum; SD = standard deviation.

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Table 5_BKK. Baseline Demographics Hospitalized Tuberculosis, Matched [BKK]

	Baricitinib			TNFi	Std. Diff.	Total
	Any	4-mg	2-mg	(N=868)	(Any vs TNFi)	(N=1736)
	(N=868)	(n=696)	(n=172)			
Age [yrs]						
N	868	696	172	868	-0.7	1736
Mean (SD)	58.0 (13)	55.4 (13)	68.8 (12)	58.1 (14)		58.1 (14)
Median	58.0	56.0	72.0	58.0		58.0
Min, Max	18.0, 92.0	18.0, 84.0	24.0, 92.0	18.0, 90.0		18.0, 92.0
≥ 65 years	266 (31%)	152 (22%)	114 (66%)	271 (31%)		537 (31%)
Sex						
Male	228 (26%)	192 (28%)	36 (21%)	233 (27%)	-1.3	461 (27%)
Female	640 (74%)	504 (72%)	136 (79%)	635 (73%)		1275 (73%)

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

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Table 6_BKK. Clinical History at Baseline, Unmatched Cohorts [BKK]

Characteristic[a,b]	Baricitinib[c]	4-mg	2-mg	TNFi	Std. Diff.
	(N=851)	(N=699)	(N=152)	(N=3332)	
Clinical Conditions during baseline					
Cancer	94 (11%)	70 (10%)	24 (16%)	299 (9%)	6.9
NMSC	11 (1%)	6 (1%)	5 (3%)	60 (2%)	-4.1
Chronic lung disease	133 (16%)	107 (15%)	26 (17%)	553 (17%)	-2.6
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	16 (2%)	10 (1%)	6 (4%)	33 (1%)	7.5
Cardiovascular revascularization	0 (0%)	0 (0%)	0 (0%)	0 (0%)	N/A
Congestive Heart Failure, hospitalized	9 (1%)	6 (1%)	3 (2%)	13 (0%)	7.9
Coronary artery disease	54 (6%)	37 (5%)	17 (11%)	162 (5%)	6.5
Ischemic heart disease	58 (7%)	40 (6%)	18 (12%)	174 (5%)	6.7
Unstable angina	1 (0%)	0 (0%)	1 (1%)	2 (0%)	1.9
Ventricular arrhythmia	40 (5%)	26 (4%)	14 (9%)	157 (5%)	-0.1
Diabetes Mellitus	137 (16%)	100 (14%)	37 (24%)	433 (13%)	8.8
Type I	21 (2%)	16 (2%)	5 (3%)	67 (2%)	3.1
Type II	122 (14%)	89 (13%)	33 (22%)	389 (12%)	7.9
Dyslipidaemia	228 (27%)	176 (25%)	52 (34%)	736 (22%)	11

Characteristic[a,b]	Baricitinib[c] (N=851)	4-mg (N=699)	2-mg (N=152)	TNFi (N=3332)	Std. Diff.
Hypertension	393 (46%)	297 (42%)	96 (63%)	1328 (40%)	12.8
Immune disorders	43 (5%)	34 (5%)	9 (6%)	132 (4%)	5.3
AIDS/HIV	0 (0%)	0 (0%)	0 (0%)	1 (0%)	-2.4
Antiphospholipid syndrome	1 (0%)	1 (0%)	0 (0%)	9 (0%)	-3.5
SLE	4 (0%)	4 (1%)	0 (0%)	21 (1%)	-2.2
Primary Sjögren Syndrome	41 (5%)	32 (5%)	9 (6%)	103 (3%)	8.9
Liver Disorder	19 (2%)	12 (2%)	7 (5%)	48 (1%)	5.9
Obesity	137 (16%)	115 (16%)	22 (14%)	575 (17%)	-3.1
Pregnancy	3 (0%)	3 (0%)	0 (0%)	33 (1%)	-7.8
RA Severity (CIRAS Index), mean (SD)	7.0 (2)	7.2 (2)	6.3 (2)	7.1 (2)	-5.6
Smoking	95 (11%)	72 (10%)	23 (15%)	350 (11%)	2.1
Surgery, trauma & hospitalization, recent	121 (14%)	96 (14%)	25 (16%)	456 (14%)	1.5
TIA	2 (0%)	1 (0%)	1 (1%)	20 (1%)	-5.7
Genetic Coagulopathies	3 (0%)	1 (0%)	2 (1%)	15 (0%)	-1.5
DMARDs					
cDMARDs, during baseline					
n, total	487 (57%)	403 (58%)	84 (55%)	1646 (49%)	15.7
Mean (SD)	0.7 (1)	0.7 (1)	0.7 (1)	0.6 (1)	10.1
Median	1.0	1.0	1.0	0.0	
Min, Max	0.0, 3.0	0.0, 3.0	0.0, 3.0	0.0, 4.0	
>1 cDMARD concomitantly	47 (6%)	41 (6%)	6 (4%)	220 (7%)	-4.5
Hydroxychloroquine	34 (4%)	25 (4%)	9 (6%)	120 (4%)	2.1
Leflunomide	142 (17%)	114 (16%)	28 (18%)	492 (15%)	5.3
Methotrexate	346 (41%)	291 (42%)	55 (36%)	1124 (34%)	14.4
Minocycline	0 (0%)	0 (0%)	0 (0%)	0 (0%)	N/A
Sulfasalazine	55 (6%)	40 (6%)	15 (10%)	250 (8%)	-4.1
bDMARDs, during baseline					
n, total	394 (46%)	336 (48%)	58 (38%)	401 (12%)	81.3
Mean (SD)	0.5 (1)	0.5 (1)	0.4 (1)	0.1 (0)	80.5
Median	0.0	0.0	0.0	0.0	
Min, Max	0.0, 2.0	0.0, 2.0	0.0, 2.0	0.0, 2.0	
cDMARDs, concomitant	139 (16%)	121 (17%)	18 (12%)	107 (3%)	45.3
abatacept	51 (6%)	40 (6%)	11 (7%)	31 (1%)	27.9
adalimumab[d]	70 (8%)	62 (9%)	8 (5%)	97 (3%)	23.3

Characteristic[a,b]	Baricitinib[c] (N=851)	4-mg (N=699)	2-mg (N=152)	TNFi (N=3332)	Std. Diff.
anakinra	2 (0%)	1 (0%)	1 (1%)	5 (0%)	1.9
certolizumab pegol[d]	46 (5%)	39 (6%)	7 (5%)	51 (2%)	21.3
etanercept[d]	119 (14%)	98 (14%)	21 (14%)	101 (3%)	40
golimumab[d]	29 (3%)	26 (4%)	3 (2%)	38 (1%)	15.2
infliximab[d]	3 (0%)	2 (0%)	1 (1%)	32 (1%)	-7.5
rituximab	19 (2%)	16 (2%)	3 (2%)	4 (0%)	19.7
sarilumab	15 (2%)	14 (2%)	1 (1%)	8 (0%)	15.3
tocilizumab	81 (10%)	74 (11%)	7 (5%)	46 (1%)	36.4
Other Prescription Medications					
Antibiotics	247 (29%)	195 (28%)	52 (34%)	979 (29%)	-0.8
Antidiabetic agents	82 (10%)	61 (9%)	21 (14%)	260 (8%)	6.5
Insulins	45 (5%)	34 (5%)	11 (7%)	123 (4%)	7.7
Non-insulins	62 (7%)	45 (6%)	17 (11%)	204 (6%)	4.7
Aspirin	3 (0%)	3 (0%)	0 (0%)	14 (0%)	-1.1
Cardiovascular					
Anticoagulant	23 (3%)	19 (3%)	4 (3%)	77 (2%)	2.5
Antihypertensives	371 (44%)	277 (40%)	94 (62%)	1205 (36%)	15.2
Antiplatelet	4 (0%)	3 (0%)	1 (1%)	21 (1%)	-2.2
Nitrates	1 (0%)	0 (0%)	1 (1%)	11 (0%)	-4.5
Hormonal					
HRT	44 (5%)	33 (5%)	11 (7%)	182 (5%)	-1.3
Oral Contraceptives	4 (0%)	4 (1%)	0 (0%)	18 (1%)	-1
SERMs	0 (0%)	0 (0%)	0 (0%)	1 (0%)	-2.4
Lipid-lowering agents					
Bile acid binding	10 (1%)	9 (1%)	1 (1%)	30 (1%)	2.7
Cholesterol absorption inhibitor	7 (1%)	5 (1%)	2 (1%)	18 (1%)	3.4
Fibrates	4 (0%)	3 (0%)	1 (1%)	5 (0%)	5.8
Niacin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	N/A
Omega-3 fatty acids	1 (0%)	1 (0%)	0 (0%)	0 (0%)	4.8
Statins	84 (10%)	61 (9%)	23 (15%)	279 (8%)	5.2
Rheumatoid arthritis-related					
Cox-2 Inhibitor	140 (16%)	117 (17%)	23 (15%)	513 (15%)	2.9
Glucocorticosteroid	622 (73%)	508 (73%)	114 (75%)	1844 (55%)	37.7
Vaccinations	11 (1%)	10 (1%)	1 (1%)	57 (2%)	-3.4

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; cDMARD = conventional disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = number of patients in the specified category; N/A = not applicable; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff. = standardisedstandardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

[a] All conditions and characteristics except for the use of bDMARD and concomitant cDMARD are measured during the 6 months prior to initiation of study medication until and including the index t date.

[b] Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

[c] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

[d] TNF inhibitors. Unless otherwise noted, characteristics in this table and similar tables are measured during baseline, including on the index day.

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Table 9_BKK. Clinical Characteristics Incident Serious Infection Cohorts, Matched [BKK]

Characteristic[a,b]	Baricitinib (N=859)	4-mg (N=691)	2-mg (N=168)	TNFi (N=859)	Std. Diff.
Clinical Conditions during baseline					
Cancer	105 (12%)	75 (11%)	30 (18%)	107 (12%)	-0.8
NMSC	14 (2%)	7 (1%)	7 (4%)	27 (3%)	-11.3
Chronic lung disease	154 (18%)	117 (17%)	37 (22%)	150 (17%)	1.2
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	55 (6%)	30 (4%)	25 (15%)	51 (6%)	2.2
Cardiovascular revascularization	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.0
Congestive Heart Failure, hospitalized	17 (2%)	8 (1%)	9 (5%)	9 (1%)	8.2
Coronary artery disease	88 (10%)	56 (8%)	32 (19%)	93 (11%)	-2.0
Ischemic heart disease	91 (11%)	59 (9%)	32 (19%)	95 (11%)	-1.6
Unstable angina	3 (0%)	0 (0%)	3 (2%)	2 (0%)	2.4
Ventricular arrhythmia	53 (6%)	34 (5%)	19 (11%)	62 (7%)	-4.5
Diabetes Mellitus	152 (18%)	105 (15%)	47 (28%)	166 (19%)	-4.4
Type I	28 (3%)	21 (3%)	7 (4%)	18 (2%)	7.1
Type II	137 (16%)	94 (14%)	43 (26%)	159 (19%)	-7.2
Dyslipidaemia	255 (30%)	188 (27%)	67 (40%)	239 (28%)	4.2
Hypertension	429 (50%)	313 (45%)	116 (69%)	457 (53%)	-6.5
Immune disorders	42 (5%)	32 (5%)	10 (6%)	38 (4%)	2.2

Characteristic[a,b]	Baricitinib (N=859)	4-mg (N=691)	2-mg (N=168)	TNFi (N=859)	Std. Diff.
AIDS/HIV	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.0
Antiphospholipid syndrome	4 (0%)	3 (0%)	1 (1%)	4 (0%)	0.0
SLE	4 (0%)	4 (1%)	0 (0%)	7 (1%)	-4.8
Primary Sjögren Syndrome	37 (4%)	27 (4%)	10 (6%)	28 (3%)	5.4
Liver Disorder	18 (2%)	12 (2%)	6 (4%)	16 (2%)	1.7
Obesity	152 (18%)	126 (18%)	26 (15%)	147 (17%)	1.5
Pregnancy	2 (0%)	2 (0%)	0 (0%)	7 (1%)	-7.4
RA Severity (CIRAS Index), mean (SD)	6.9 (2)	7.1 (2)	6.2 (2)	6.9 (2)	1.3
Smoking	108 (13%)	82 (12%)	26 (15%)	103 (12%)	1.8
Surgery, trauma & hospitalization, recent	140 (16%)	105 (15%)	35 (21%)	150 (17%)	-3.2
TIA	5 (1%)	3 (0%)	2 (1%)	5 (1%)	0.0
Genetic Coagulopathies	6 (1%)	3 (0%)	3 (2%)	6 (1%)	
DMARDs					
csDMARDs, during baseline					
n, total	508 (59%)	413 (60%)	95 (57%)	426 (50%)	19.2
Mean (SD)	0.7 (1)	0.7 (1)	0.7 (1)	0.6 (1)	14.9
Median	1.0	1.0	1.0	0.0	
Min, Max	0.0, 3.0	0.0, 3.0	0.0, 3.0	0.0, 3.0	
>1 csDMARD concomitantly	57 (7%)	49 (7%)	8 (5%)	56 (7%)	0.5
Hydroxychloroquine	43 (5%)	31 (4%)	12 (7%)	33 (4%)	5.9
Leflunomide	159 (19%)	128 (19%)	31 (18%)	123 (14%)	11.5
Methotrexate	345 (40%)	286 (41%)	59 (35%)	310 (36%)	8.5
Minocycline	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.0
Sulfasalazine	61 (7%)	43 (6%)	18 (11%)	51 (6%)	4.6
bDMARDs, during baseline					
n, total	330 (38%)	284 (41%)	46 (27%)	324 (38%)	1.7
Mean (SD)	0.4 (1)	0.4 (1)	0.3 (0)	0.4 (1)	2.0
Median	0.0	0.0	0.0	0.0	
Min, Max	0.0, 2.0	0.0, 2.0	0.0, 2.0	0.0, 2.0	
csDMARDs, concomitant	120 (14%)	104 (15%)	16 (10%)	95 (11%)	10.1
abatacept	41 (5%)	34 (5%)	7 (4%)	27 (3%)	9.0
adalimumab[c]	55 (6%)	50 (7%)	5 (3%)	75 (9%)	-10.4
anakinra	2 (0%)	1 (0%)	1 (1%)	5 (1%)	-8.4
certolizumab pegol[c]	34 (4%)	28 (4%)	6 (4%)	37 (4%)	-2.0
etanercept[c]	91 (11%)	76 (11%)	15 (9%)	88 (10%)	1.3
golimumab[c]	23 (3%)	20 (3%)	3 (2%)	31 (4%)	-6.4
infliximab[c]	2 (0%)	2 (0%)	0 (0%)	21 (2%)	-26.8

Characteristic[a,b]	Baricitinib (N=859)	4-mg (N=691)	2-mg (N=168)	TNFi (N=859)	Std. Diff.
rituximab	17 (2%)	15 (2%)	2 (1%)	2 (0%)	15.8
sarilumab	11 (1%)	10 (1%)	1 (1%)	8 (1%)	3.6
tocilizumab	68 (8%)	61 (9%)	7 (4%)	42 (5%)	13.5
Other Prescription Medications					
Antibiotics	254 (30%)	198 (29%)	56 (33%)	258 (30%)	-1.0
Antidiabetic agents	95 (11%)	68 (10%)	27 (16%)	91 (11%)	1.5
Insulins	53 (6%)	38 (5%)	15 (9%)	42 (5%)	5.7
Non-insulins	72 (8%)	50 (7%)	22 (13%)	74 (9%)	-0.9
Aspirin	40 (5%)	30 (4%)	10 (6%)	38 (4%)	1.2
Cardiovascular					
Anticoagulant	133 (15%)	93 (13%)	40 (24%)	116 (14%)	5.9
Antihypertensives	413 (48%)	299 (43%)	114 (68%)	429 (50%)	-3.8
Antiplatelet	50 (6%)	35 (5%)	15 (9%)	47 (5%)	1.6
Nitrates	2 (0%)	0 (0%)	2 (1%)	11 (1%)	-14.5
Hormonal					
HRT	42 (5%)	29 (4%)	13 (8%)	61 (7%)	-9.9
Oral Contraceptives	4 (0%)	4 (1%)	0 (0%)	1 (0%)	5.2
SERMs	0 (0%)	0 (0%)	0 (0%)	1 (0%)	-9.9
Lipid-lowering agents					
Bile acid binding	11 (1%)	9 (1%)	2 (1%)	8 (1%)	3.4
Cholesterol absorption inhibitor	11 (1%)	7 (1%)	4 (2%)	11 (1%)	0.0
Fibrates	4 (0%)	3 (0%)	1 (1%)	2 (0%)	4.3
Niacin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.0
Omega-3 fatty acids	1 (0%)	1 (0%)	0 (0%)	0 (0%)	4.5
Statins	119 (14%)	80 (12%)	39 (23%)	128 (15%)	-3.1
Rheumatoid arthritis-related					
Cox-2 Inhibitor	125 (15%)	103 (15%)	22 (13%)	127 (15%)	-0.6
Glucocorticosteroid	620 (72%)	493 (71%)	127 (76%)	629 (73%)	-2.2
Vaccinations	12 (1%)	11 (2%)	1 (1%)	13 (2%)	-1.0

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; csDMARD = conventional synthetic disease-modifying antirheumatic drugs; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff. = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics except for use of bDMARD and concomitant csDMARD are measured during the 6 months prior to initiation of study medication until and including the index date

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE

c TNF inhibitors

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Table 11_BKK. Baseline Healthcare Resource Utilization, Unmatched [BKK]

Type of Resource Use	Baricitinib (N=851)	4-mg (N=699)	2-mg (N=152)	TNFi (N=3332)	Std. Diff.
Physician Office Visits					
n, patients	849	697	152	3320	2.3
n, events	14689	11553	3136	57291	0.6
Mean (SD)	17.3 (10)	16.5 (9)	20.6 (13)	17.2 (11)	
Median	15.0	15.0	18.0	15.0	
Min, Max	0.0, 74.0	0.0, 61.0	1.0, 74.0	0.0, 106.0	
Rheumatologist Visits					
n, patients	653	549	104	2403	10.6
n, events	3264	2737	527	10313	21.8
Mean (SD)	3.8 (4)	3.9 (4)	3.5 (4)	3.1 (3)	
Median	3.0	3.0	3.0	2.0	
Min, Max	0.0, 22.0	0.0, 19.0	0.0, 22.0	0.0, 28.0	
Other Outpatient Visits					
n, patients	150	120	30	634	-3.6
n, events	264	204	60	1094	-2.4
Mean (SD)	0.3 (1)	0.3 (1)	0.4 (1)	0.3 (1)	
Median	0.0	0.0	0.0	0.0	
Min, Max	0.0, 5.0	0.0, 5.0	0.0, 4.0	0.0, 7.0	
Inpatient and ED Visits					
n, patients	199	158	41	726	3.8
n, events	266	207	59	932	5.1
Mean (SD)	0.3 (1)	0.3 (1)	0.4 (1)	0.3 (1)	

Median	0.0	0.0	0.0	0.0	
Min, Max	0.0, 7.0	0.0, 7.0	0.0, 4.0	0.0, 6.0	
ED Visits					
n, patients	NA	NA	NA	NA	
n, events	NA	NA	NA	NA	
Mean (SD)	NA	NA	NA	NA	
Median	NA	NA	NA	NA	
Min, Max	NA	NA	NA	NA	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits. Other outpatient visits do not include physician office visits or rheumatologist visits.

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Table 14_BKK. Baseline Healthcare Resource Utilization Incident Serious Infection Cohorts, Matched [BKK]

Type of Resource Use	Baricitinib (N=859)	4-mg (N=691)	2-mg (N=168)	TNFi (N=859)	Std. Diff.
Physician Office Visits					
n, patients	857	689	168	859	-4.5
n, events	15391	11804	3587	15437	-0.5
Mean (SD)	17.9 (10)	17.1 (10)	21.4 (12)	18.0 (11)	
Median	16.0	15.0	19.0	16.0	
Min, Max	0.0, 74.0	0.0, 61.0	2.0, 74.0	1.0, 80.0	
Rheumatologist Visits					
n, patients	652	535	117	664	-3.2
n, events	3144	2576	568	3052	3.2
Mean (SD)	3.7 (4)	3.7 (4)	3.4 (3)	3.6 (3)	
Median	3.0	3.0	3.0	3.0	
Min, Max	0.0, 22.0	0.0, 19.0	0.0, 22.0	0.0, 24.0	
Other Outpatient Visits					
n, patients	156	125	31	149	2.1
n, events	280	214	66	254	3.9
Mean (SD)	0.3 (1)	0.3 (1)	0.4 (1)	0.3 (1)	
Median	0.0	0.0	0.0	0.0	
Min, Max	0.0, 5.0	0.0, 5.0	0.0, 4.0	0.0, 4.0	
Inpatient and ED Visits					
n, patients	227	170	57	212	4
n, events	316	228	88	283	5.6

Mean (SD)	0.4 (1)	0.3 (1)	0.5 (1)	0.3 (1)	
Median	0.0	0.0	0.0	0.0	
Min, Max	0.0, 7.0	0.0, 7.0	0.0, 6.0	0.0, 5.0	
ED Visits					
n, patients	NA	NA	NA	NA	
n, events	NA	NA	NA	NA	
Mean (SD)	NA	NA	NA	NA	
Median	NA	NA	NA	NA	
Min, Max	NA	NA	NA	NA	

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = Not Applicable; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor

Note: Physician office visits do not include rheumatologist visits. Other outpatient visits do not include physician office visits or rheumatologist visits.

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Table 16_BKK. Baseline Prevalence of Outcomes [BKK]

Outcome in Each Matched Cohort[a, b]	Unmatched				
	Baricitinib (N=975)	4-mg (N=779)	2-mg (N=196)	TNFi (N=3675)	Std. Diff.
VTE					
Main case definition	23 (2%)	15 (2%)	8 (4%)	60 (2%)	5.2
Alternate case definition I	23 (2%)	15 (2%)	8 (4%)	60 (2%)	5.2
Alternative case definition II	31 (3%)	20 (3%)	11 (6%)	97 (3%)	3.2
MACE	2 (0%)	2 (0%)	0 (0%)	17 (0%)	-4.5
Serious Infection	10 (1%)	7 (1%)	3 (2%)	28 (1%)	2.8
Hospitalized Tuberculosis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.0

Abbreviations: MACE = major adverse cardiovascular event, defined as hospital primary discharge diagnosis code of acute MI or hospital primary discharge diagnosis code of ischemic or hemorrhagic stroke; N = number of patients in specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism, defined based on the case definitions.

a Baseline prevalence was calculated for each distinct matched cohort for VTE, MACE, serious infection, and hospitalized tuberculosis.

b Patients with the prevalent outcomes enumerated in this table are those excluded from the main analyses of each outcome.

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Table 17_BKK. Duration of Follow-up Period (Days), Unmatched [BKK]

	Baricitinib (N=851)	4-mg (N=699)	2-mg (N=152)	TNFi (N=3332)	Std. Diff.
N	851	699	152	3332	
Mean (SD)	254.2 (209)	255.9 (213)	246.4 (188)	237.7 (204)	8.0
Median	193.0	194.0	191.5	163.0	
Min, Max	2.0, 962.0	2.0, 962.0	7.0, 907.0	1.0, 1051.0	

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

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Table 18_BKK. Duration of Follow-up Period (Days) Primary VTE Cohorts, Matched [BKK]

	Baricitinib (N=765)	4-mg (N=628)	2-mg (N=137)	TNFi (N=765)	Std. Diff
N	765	628	137	765	
Mean (SD)	256.5 (211)	258.3 (215)	248.1 (191)	258.6 (214)	-1.1
Median	194.0	195.5	188.0	190.0	
Min, Max	2.0, 962.0	2.0, 962.0	7.0, 907.0	1.0, 1051.0	
Reasons for censoring					
Incident event	3 (0%)	3 (0%)	0 (0%)	6 (1%)	
Medication discontinued	331 (43%)	269 (43%)	62 (45%)	404 (53%)	
Initiated b/tsDMARD	120 (16%)	95 (15%)	25 (18%)	112 (15%)	
End of patient record	7 (1%)	6 (1%)	1 (1%)	7 (1%)	
Death (where available)	2 (0%)	1 (0%)	1 (1%)	3 (0%)	
End of study period (31 December 2019)	304 (40%)	255 (41%)	49 (36%)	236 (31%)	

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

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Table 21_BKK. Duration of Follow-up Period (Days) MACE Cohorts, Matched [BKK]

	Baricitinib (N=757)	4-mg (N=625)	2-mg (N=132)	TNFi (N=757)	Std. Diff
N	757	625	132	757	
Mean (SD)	250.2 (207)	253.5 (213)	234.4 (178)	257.8 (225)	-3.7
Median	185.0	187.0	170.0	175.0	
Min, Max	2.0, 962.0	2.0, 962.0	7.0, 816.0	1.0, 1051.0	
Reasons for censoring					
Incident event	8 (1%)	5 (1%)	3 (2%)	4 (1%)	
Medication discontinued	317 (42%)	259 (41%)	58 (44%)	405 (54%)	
Initiated b/tsDMARD	122 (16%)	99 (16%)	23 (17%)	115 (15%)	
End of patient record	7 (1%)	6 (1%)	1 (1%)	11 (1%)	
Death (where available)	2 (0%)	1 (0%)	1 (1%)	3 (0%)	
End of study period (31 December 2019)	303 (40%)	256 (41%)	47 (36%)	222 (29%)	

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; MACE = major adverse cardiovascular event; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std Diff = standardised difference; TNFi = tumour necrosis factor inhibitor

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Table 22_BKK. Duration of Follow-up Period (Days) Incident Serious Infection Cohorts, Matched [BKK]

	Baricitinib (N=859)	4-mg (N=691)	2-mg (N=168)	TNFi (N=859)	Std. Diff
N	859	691	168	859	
Mean (SD)	252.6 (210)	256.1 (214)	238.2 (192)	257.5 (224)	-2.4
Median	187.0	189.0	170.0	178.0	
Min, Max	2.0, 962.0	2.0, 962.0	7.0, 861.0	1.0, 1051.0	
Reasons for censoring					
Incident event	17 (2%)	14 (2%)	3 (2%)	12 (1%)	
Medication discontinued	342 (40%)	273 (40%)	69 (41%)	425 (49%)	
Initiated b/tsDMARD	139 (16%)	105 (15%)	34 (20%)	132 (15%)	
End of patient record	8 (1%)	6 (1%)	2 (1%)	12 (1%)	
Death (where available)	3 (0%)	1 (0%)	2 (1%)	4 (0%)	
End of study period (31 December 2019)	353 (41%)	293 (42%)	60 (36%)	278 (32%)	

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

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Table 39_BKK. Pattern of VTE and Related Diagnostic Codes in Patients with RA [BKK]

Code	Total Patients (N=1530)
ICD-10-GM (PE)	
I26	0 (0%)
I26.0	5 (0%)
I26.9	9 (1%)
ICD-10-GM (DVT lower extremities)	
I80.1	1 (0%)
I80.2	1 (0%)
I80.20	3 (0%)
I80.28	19 (1%)
I80.3	22 (1%)
ICD-10-GM (DVT upper extremities)	

Code	Total Patients (N=1530)
I80.81	1 (0%)
ICD-10-GM (Phlebitis and thrombophlebitis of lower extremity)	
no codes	0 (0%)
ICD-10-GM (Other venous thrombosis)	
I80.0	11 (1%)
I80.8	0 (0%)
I80.80	4 (0%)
I80.88	1 (0%)
I80.9	17 (1%)
I81	1 (0%)
I82.0	0 (0%)
I82.1	0 (0%)
I82.2	6 (0%)
I82.3	0 (0%)
I82.8	1 (0%)
I82.80	0 (0%)
I82.81	1 (0%)
I82.88	0 (0%)
I82.9	19 (1%)

Abbreviations: ICD-10-GM = International Classification of Disease, 10th Revision, German Modification; RA = rheumatoid arthritis; PE = pulmonary embolism; DVT = deep vein thrombosis; VTE = venous thromboembolism.

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Table 56_BKK. Clinical Characteristics of RA Patients with Incident Serious Infections [BKK]

Characteristics[a,b]	Baricitinib (N=17)	4-mg (N=14)	2-mg (N=3)	TNFi (N=12)	Total (N=29)
Age (mean) [SD]	67.4 (10)	67.4 (11)	67.3 (4)	61.8 (19)	65.1 (14)
Sex					
Female	8 (47%)	5 (36%)	3 (100%)	7 (58%)	15 (52%)
Male	9 (53%)	9 (64%)	0 (0%)	5 (42%)	14 (48%)
Clinical Conditions during baseline	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cancer	2 (12%)	1 (7%)	1 (33%)	3 (25%)	5 (17%)
NMSC	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Chronic Lung disease	8 (47%)	6 (43%)	2 (67%)	2 (17%)	10 (34%)

Characteristics[a,b]	Baricitinib (N=17)	4-mg (N=14)	2-mg (N=3)	TNFi (N=12)	Total (N=29)
Cardiovascular conditions	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Atrial arrhythmia/ fibrillation	7 (41%)	6 (43%)	1 (33%)	0 (0%)	7 (24%)
Cardiovascular revascularization	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Congestive Heart Failure, hospitalized	1 (6%)	1 (7%)	0 (0%)	0 (0%)	1 (3%)
Coronary artery disease	9 (53%)	7 (50%)	2 (67%)	4 (33%)	13 (45%)
Ischemic heart disease	9 (53%)	7 (50%)	2 (67%)	4 (33%)	13 (45%)
Unstable angina	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Ventricular arrhythmia	5 (29%)	5 (36%)	0 (0%)	1 (8%)	6 (21%)
Diabetes Mellitus	6 (35%)	4 (29%)	2 (67%)	6 (50%)	12 (41%)
Type I	3 (18%)	2 (14%)	1 (33%)	3 (25%)	6 (21%)
Type II	6 (35%)	4 (29%)	2 (67%)	6 (50%)	12 (41%)
Dyslipidaemia	9 (53%)	8 (57%)	1 (33%)	4 (33%)	13 (45%)
Hypertension	13 (76%)	11 (79%)	2 (67%)	8 (67%)	21 (72%)
Immune disorders	2 (12%)	1 (7%)	1 (33%)	0 (0%)	2 (7%)
AIDS/HIV	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Antiphospholipid syndrome	1 (6%)	0 (0%)	1 (33%)	0 (0%)	1 (3%)
SLE	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Primary Sjögren Syndrome	2 (12%)	1 (7%)	1 (33%)	0 (0%)	2 (7%)
Liver Disorder	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Obesity	5 (29%)	4 (29%)	1 (33%)	3 (25%)	8 (28%)
Pregnancy	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
RA Severity (CIRAS), mean (SD)	6.2 (2)	6.1 (2)	6.5 (1)	7.1 (2)	6.6 (2)
Smoking	4 (24%)	3 (21%)	1 (33%)	2 (17%)	6 (21%)
Surgery, trauma, & hospitalization, recent	6 (35%)	5 (36%)	1 (33%)	4 (33%)	10 (34%)
TIA	0 (0%)	0 (0%)	0 (0%)	1 (8%)	1 (3%)
Genetic Coagulopathies	1 (6%)	0 (0%)	1 (33%)	0 (0%)	1 (3%)
Other Prescription Medications					
Antibiotics	6 (35%)	5 (36%)	1 (33%)	5 (42%)	11 (38%)
Antidiabetic agents	4 (24%)	3 (21%)	1 (33%)	5 (42%)	9 (31%)
Insulins	3 (18%)	2 (14%)	1 (33%)	3 (25%)	6 (21%)
Non-insulins	4 (24%)	3 (21%)	1 (33%)	2 (17%)	6 (21%)
Aspirin	3 (18%)	3 (21%)	0 (0%)	3 (25%)	6 (21%)
Cardiovascular					
Anticoagulant	11 (65%)	9 (64%)	2 (67%)	5 (42%)	16 (55%)
Antihypertensives	13 (76%)	11 (79%)	2 (67%)	9 (75%)	22 (76%)
Antiplatelet	4 (24%)	4 (29%)	0 (0%)	4 (33%)	8 (28%)
Nitrates	0 (0%)	0 (0%)	0 (0%)	1 (8%)	1 (3%)
Hormonal					

Characteristics[a,b]	Baricitinib (N=17)	4-mg (N=14)	2-mg (N=3)	TNFi (N=12)	Total (N=29)
Oral contraceptives	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
HRT	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SERM	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Lipid-lowering agents	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Bile acid binding	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cholesterol absorption inhibitor	0 (0%)	0 (0%)	0 (0%)	2 (17%)	2 (7%)
Fibrates	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Niacin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Omega-3 fatty acids	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Statins	5 (29%)	4 (29%)	1 (33%)	5 (42%)	10 (34%)
Rheumatoid arthritis-related					
Cox-2 Inhibitor	2 (12%)	1 (7%)	1 (33%)	3 (25%)	5 (17%)
Glucocorticosteroid	15 (88%)	12 (86%)	3 (100%)	11 (92%)	26 (90%)
Vaccinations	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics except for use of bDMARD and concomitant csDMARD are measured during the 6 months prior to initiation of study medication until and including the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\BKK\Lilly Baricitinib Results_Serious Infection_BKK_v1.0.docx -pages 10-11

Table 57_BKK. Pattern of RA Medication Use in Patients with Serious Infection Event [BKK]

Characteristic[a]	Unmatched				Matched				
	Baricitinib	4-mg	2-mg	TNFi	Baricitinib	4-mg	2-mg	TNFi	Total
	(N=20)	(N=15)	(N=5)	(N=26)	(N=17)	(N=14)	(N=3)	(N=12)	(N=29)
Baseline Medication									
DMARDS									
csDMARDs, during baseline									

Characteristic[a]	Unmatched				Matched				
	Baricitinib	4-mg	2-mg	TNFi	Baricitinib	4-mg	2-mg	TNFi	Total
	(N=20)	(N=15)	(N=5)	(N=26)	(N=17)	(N=14)	(N=3)	(N=12)	(N=29)
n, total	9	7	2	15	8	7	1	9	17
Mean (SD)	0.5 (1)	0.5 (1)	0.4 (1)	0.8 (1)	0.5 (1)	0.6 (1)	0.3 (1)	1.1 (1)	0.8 (1)
Median	0.0	0.0	0.0	1.0	0.0	0.5	0.0	1.0	1.0
Min, Max	0.0, 2.0	0.0, 2.0	0.0, 1.0	0.0, 3.0	0.0, 2.0	0.0, 2.0	0.0, 1.0	0.0, 3.0	0.0, 3.0
>1 csDMARD, concomitantly	0 (0%)	0 (0%)	0 (0%)	2 (8%)	0 (0%)	0 (0%)	0 (0%)	1 (8%)	1 (3%)
Hydroxychloroquine	0 (0%)	0 (0%)	0 (0%)	1 (4%)	0 (0%)	0 (0%)	0 (0%)	1 (8%)	1 (3%)
Leflunomide	4 (20%)	3 (20%)	1 (20%)	6 (23%)	4 (24%)	3 (21%)	1 (33%)	3 (25%)	7 (24%)
Methotrexate	4 (20%)	3 (20%)	1 (20%)	10 (38%)	3 (18%)	3 (21%)	0 (0%)	8 (67%)	11 (38%)
Minocycline	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Sulfasalazine	1 (5%)	1 (7%)	0 (0%)	3 (12%)	1 (6%)	1 (7%)	0 (0%)	1 (8%)	2 (7%)
bDMARDs, during baseline									
n, total	6	4	2	5	3	3	0	5	8
Mean (SD)	0.3 (0)	0.3 (0)	0.4 (1)	0.2 (0)	0.2 (0)	0.2 (0)	0 (0)	0.4 (1)	0.3 (0)
Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Min, Max	0.0, 1.0	0.0, 1.0	0.0, 1.0	0.0, 1.0	0.0, 1.0	0.0, 1.0	0.0, 0.0	0.0, 1.0	0.0, 1.0
Concomitant csDMARDs	1 (5%)	0 (0%)	1 (20%)	2 (8%)	0 (0%)	0 (0%)	0 (0%)	2 (17%)	2 (7%)
Abatacept	1 (5%)	0 (0%)	1 (20%)	1 (4%)	0 (0%)	0 (0%)	0 (0%)	1 (8%)	1 (3%)
Adalimumab[b]	0 (0%)	0 (0%)	0 (0%)	1 (4%)	0 (0%)	0 (0%)	0 (0%)	1 (8%)	1 (3%)
Anakinra	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Certolizumab pegol[b]	1 (5%)	1 (7%)	0 (0%)	1 (4%)	1 (6%)	1 (7%)	0 (0%)	1 (8%)	2 (7%)

Characteristic[a]	Unmatched				Matched				
	Baricitinib	4-mg	2-mg	TNFi	Baricitinib	4-mg	2-mg	TNFi	Total
	(N=20)	(N=15)	(N=5)	(N=26)	(N=17)	(N=14)	(N=3)	(N=12)	(N=29)
Etanercept[b]	1 (5%)	0 (0%)	1 (20%)	1 (4%)	0 (0%)	0 (0%)	0 (0%)	1 (8%)	1 (3%)
Golimumab[b]	0 (0%)	0 (0%)	0 (0%)	1 (4%)	0 (0%)	0 (0%)	0 (0%)	1 (8%)	1 (3%)
Infliximab[b]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Rituximab	1 (5%)	1 (7%)	0 (0%)	0 (0%)	1 (6%)	1 (7%)	0 (0%)	0 (0%)	1 (3%)
Sarilumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Tocilizumab	2 (10%)	2 (13%)	0 (0%)	0 (0%)	1 (6%)	1 (7%)	0 (0%)	0 (0%)	1 (3%)
Post-index Medication									
Methotrexate, concomitant	4 (20%)	3 (20%)	1 (20%)	9 (35%)	3 (18%)	3 (21%)	0 (0%)	4 (33%)	7 (24%)
Other Concomitant csDMARD	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Dose change, baricitinib[c]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; csDMARD = conventional synthetic disease-modifying antirheumatic drug; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

a All conditions and characteristics except for use of bDMARD and concomitant csDMARD are measured during the 6 months prior to initiation of study medication until and including the index date.

b TNF inhibitors.

c Only baricitinib 2-mg dose is available in the US, so the baricitinib dose change should be marked 'NA' in US data.

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Table 58_BKK. Time to First Serious Infection Event (Days) [BKK]

	Unmatched				Matched				
	Baricitinib	4-mg	2-mg	TNFi	Baricitinib	4-mg	2-mg	TNFi	Total
	(N=20)	(N=15)	(N=5)	(N=26)	(N=17)	(N=14)	(N=3)	(N=12)	(N=29)
n	20	15	5	26	17	14	3	12	29
Mean (SD)	139.9 (148)	140.6 (167)	137.6 (78)	190.9 (188)	107.3 (72)	101.0 (69)	136.7 (95)	187.6 (195)	140.5 (140)

Median	109.5	100.0	125.0	110.5	100.0	92.0	125.0	96.0	97.0
Min, Max	14.0, 695.0	14.0, 695.0	48.0, 237.0	22.0, 648.0	14.0, 237.0	14.0, 221.0	48.0, 237.0	28.0, 648.0	14.0, 648.0

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

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Table 60_BKK. Serious Infection Events Per Patient During All Available Follow-up [BKK]

Number of Infections per Person	Unmatched				Matched				
	Baricitinib (N=965)	4-mg (N=772)	2-mg (N=193)	TNFi (N=3647)	Baricitinib (N=859)	4-mg (N=691)	2-mg (N=168)	TNFi (N=859)	Total (N=1718)
0	930 (96%)	749 (97%)	181 (94%)	3569 (98%)	831 (97%)	670 (97%)	161 (96%)	825 (96%)	1656 (96%)
1	27 (3%)	19 (2%)	8 (4%)	57 (2%)	21 (2%)	17 (2%)	4 (2%)	27 (3%)	48 (3%)
2	4 (0%)	1 (0%)	3 (2%)	17 (0%)	3 (0%)	1 (0%)	2 (1%)	6 (1%)	9 (1%)
3	4 (0%)	3 (0%)	1 (1%)	4 (0%)	4 (0%)	3 (0%)	1 (1%)	1 (0%)	5 (0%)
4	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
6	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
>6	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Abbreviations: N = number of patients in the specified category; TNFi = tumour necrosis factor inhibitor.

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Table 64_BKK. Incidence Rate of Hospitalized TB Event [BKK]

	Unmatched				Matched				
	Baricitinib	4-mg	2-mg	TNFi	Baricitinib	4-mg	2-mg	TNFi	Total
	(N=975)	(N=779)	(N=196)	(N=3675)	(N=868)	(N=696)	(N=172)	(N=868)	(N=1736)
Overall									
Person-Years	688	556	132	2424	605	491	114	634	1239
TB Events	0	0	0	0	0	0	0	0	0
TB Events/100 PY	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
95% CI	(0.0, 0.5)	(0.0, 0.7)	(0.0, 2.8)	(0.0, 0.2)	(0.0, 0.6)	(0.0, 0.8)	(0.0, 3.2)	(0.0, 0.6)	(0.0, 0.3)

Abbreviations: CI = confidence interval; N = number of patients in the specified category; PY = person-years; TB = tuberculosis; TNFi = tumour necrosis factor inhibitor

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Table 68_BKK. Incidence Rate of VTE (Primary Definition), by Dose and Unmatched [BKK]

	Baricitinib 2-mg (N=152)	Baricitinib 4-mg (N=699)	TNFi (N=3332)
Overall			
VTE Events	0	3	21
Person-years	102.9	491.7	2177.8
IR per 100 PY	0.0	0.6	1.0
95% CI	(0.0, 3.6)	(0.1, 1.8)	(0.6, 1.5)

Abbreviations: CI = confidence intervals; IR = incidence rate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

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Annex 13. French CEGEDIM THIN – Additional Results

I. Analysis

This annex includes all analysis results for this data source. French patients in this data were analysed in the SNDS data source instead. Analyses were based on 1:1 baricitinib:TNFi propensity score matching.

II. Variable Ratio Matching

These results are based on matching baricitinib:TNFi using Variable Ratio matching, i.e., as many matched 1:3 as possible, then the maximum number matched 1:2, then the remaining patients matched 1:1.

I. Analysis

Table 1_CGDM. Baseline Demographics, Unmatched [CGDM]

	Baricitinib			TNFi (N=814)	Std. Diff. (Any vs TNFi)
	Any (N=213)	4-mg (N=189)	2-mg (N=28)		
Age [yrs]					
N	213	189	28	814	
Mean (SD)	57.65 (12.72)	56.17 (11.97)	67.36 (12.74)	55.87 (13.97)	0.13
Median	59.00 [50.00, 66.50]	57.00 [50.00, 65.00]	71.00 [60.25, 75.75]	57.00 [47.00, 66.00]	
Min, Max	21.0, 88.0	21.0, 85.0	36.0, 88.0	18.0, 90.0	
≥ 65 years	66 (31.0%)	48 (25.4%)	18 (64.3%)	227 (27.9%)	0.07
Sex					
Male	33 (15.5%)	29 (15.3%)	4 (14.3%)	219 (26.9%)	0.28
Female	180 (84.5%)	160 (84.7%)	24 (85.7%)	595 (73.1%)	0.28

Abbreviations: CGDM = cegedim; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\ 4. Table 6.1. - Baseline Demographics, Unmatched [Cegedim THIN (FR) - France].docx

Table 2_CGDM. Baseline Demographics VTE Cohorts, Matched [CGDM]

	Baricitinib			TNFi (N=160)	Std. Diff. (Any vs TNFi)	Total (N=320)
	Any (N=160)	4-mg (n=147)	2-mg (n=14)			
Age [yrs]						
N	160	147	14	160		320
Mean (SD)	57.14 (12.43)	56.17 (12.00)	67.36 (12.30)	58.38 (12.02)	0.10	57.76 (12.23)
Median	58.00 [50.00, 66.00]	57.00 [50.00, 65.00]	71.00 [60.00, 74.50]	59.00 [53.00, 66.00]		59.00 [51.00, 66.00]
Min, Max	21.0, 85.0	21.0, 85.0	36.0, 83.0	19.0, 85.0		19.0, 85.0
≥ 65 years	46 (28.7%)	37 (25.2%)	9 (64.3%)	48 (30.0%)	0.03	94 (29.4%)
Sex						
Male	26 (16.2%)	23 (15.6%)	3 (21.4%)	26 (16.2%)	0.00	52 (16.2%)
Female	134 (83.8%)	124 (84.4%)	11 (78.6%)	134 (83.8%)	0.00	268 (83.8%)

Abbreviations: CGDM = cegedim; N = number of patients in the specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus; VTE = venous thromboembolism.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.2. - Baseline Demographics VTE Cohorts, Matched [Cegedim THIN (FR) - France].docx

Table 3_CGDM. Baseline Demographics MACE Cohorts, Matched [CGDM]

	Baricitinib			TNFi (N=162)	Std. Diff. (Any vs TNFi)	Total (N=324)
	Any (N=162)	4-mg (N=148)	2-mg (N=15)			
Age [yrs]						
N	162	148	15	162		324
Mean (SD)	57.49 (12.49)	56.37 (11.93)	68.53 (12.45)	56.43 (13.30)	0.08	56.96 (12.89)
Median	59.00 [50.00, 66.00]	58.00 [50.00, 65.00]	72.00 [61.00, 78.00]	57.50 [48.00, 66.25]		58.00 [49.00, 66.00]
Min, Max	21.0, 83.0	21.0, 81.0	36.0, 83.0	25.0, 86.0		21.0, 86.0
≥ 65 years	49 (30.2%)	39 (26.4%)	10 (66.7%)	44 (27.2%)	0.07	93 (28.7%)
Sex						
Male	28 (17.3%)	25 (16.9%)	3 (20.0%)	22 (13.6%)	0.10	50 (15.4%)
Female	134 (82.7%)	123 (83.1%)	12 (80.0%)	140 (86.4%)	0.10	274 (84.6%)

Abbreviations: CGDM = cegedim; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; N = number of patients in the specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.3. - Baseline Demographics MACE Cohorts, Matched [Cegedim THIN (FR) - France].docx

Table 4_CGDM. Baseline Demographics Incident Serious Infections, Matched [CGDM]

	Baricitinib			TNFi (N=169)	Std. Diff. (Any vs TNFi)	Total (N=338)
	Any (N=169)	4-mg (N=154)	2-mg (N=16)			
Age [yrs]						
N	169	154	16	169		338
Mean (SD)	57.36 (12.31)	56.18 (11.66)	68.62 (12.64)	57.20 (14.43)	0.01	57.28 (13.39)
Median	58.00 [50.00, 66.00]	56.50 [50.00, 64.25]	71.50 [60.25, 78.75]	59.00 [46.00, 67.00]		58.00 [49.75, 67.00]
Min, Max	21.0, 85.0	21.0, 85.0	36.0, 83.0	19.0, 90.0		19.0, 90.0
≥ 65 years	48 (28.4%)	38 (24.7%)	10 (62.5%)	58 (34.3%)	0.13	106 (31.4%)
Sex						
Male	30 (17.8%)	26 (16.9%)	4 (25.0%)	29 (17.2%)	0.02	59 (17.5%)
Female	139 (82.2%)	128 (83.1%)	12 (75.0%)	140 (82.8%)	0.02	279 (82.5%)

Abbreviations: CGDM = cegedim; N = number of patients in the specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.4. - Baseline Demographics Incident Serious Infections, Matched [Cegedim THIN (FR) - France].docx

Table 6_CGDM. Clinical History at Baseline, Unmatched Cohorts [CGDM]

Characteristic[a,b]	Baricitinib[c]			TNFi (N=814)	Std. Diff.
	Any (N=213)	2-mg (N=28)	4-mg (N=189)		
Clinical Conditions during baseline					
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	0.05
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Chronic lung disease	8 (3.8%)	2 (7.1%)	6 (3.2%)	18 (2.2%)	0.09
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	4 (1.9%)	3 (10.7%)	1 (0.5%)	1 (0.1%)	0.18
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Congestive heart failure, hospitalized	NA	N/A	N/A	NA	0.07
Coronary artery disease	2 (0.9%)	1 (3.6%)	1 (0.5%)	2 (0.2%)	0.09
Ischemic heart disease	2 (0.9%)	1 (3.6%)	1 (0.5%)	2 (0.2%)	0.09
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	0.05
Ventricular arrhythmia	3 (1.4%)	2 (7.1%)	1 (0.5%)	0 (0.0%)	0.17
Diabetes Mellitus	4 (1.9%)	0 (0.0%)	4 (2.1%)	19 (2.3%)	0.03
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (0.5%)	0.10
Type II	4 (1.9%)	0 (0.0%)	4 (2.1%)	15 (1.8%)	0.00
Dyslipidaemia	1 (0.5%)	0 (0.0%)	1 (0.5%)	19 (2.3%)	0.16
Hypertension	11 (5.2%)	4 (14.3%)	7 (3.7%)	63 (7.7%)	0.11
Immune disorders	2 (0.9%)	1 (3.6%)	1 (0.5%)	3 (0.4%)	0.07
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
SLE	1 (0.5%)	0 (0.0%)	1 (0.5%)	2 (0.2%)	0.04
Primary Sjögren syndrome	1 (0.5%)	1 (3.6%)	0 (0.0%)	1 (0.1%)	0.06
Liver disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (0.4%)	0.09
Obesity	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
RA severity (CIRAS Index), mean (SD)	4.12 (1.09)	3.42 (0.80)	4.22 (1.08)	4.05 (1.13)	0.06
Smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	0.05
Surgery, trauma & hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	0.05
DMARDs					
cDMARDs, during baseline					
n, total	131 (61.5%)	16 (57.1%)	117 (61.9%)	560 (68.8%)	0.15
Mean (SD)	0.71 (0.56)	0.64 (0.49)	0.72 (0.57)	0.74 (0.52)	0.04
Median	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-
Min, Max	0.0, 2.0	0.00, 1.00	0.00, 2.00	0.0, 3.0	-
>1 cDMARD concomitantly	12 (5.6%)	0 (0.0%)	12 (6.3%)	25 (3.1%)	0.13

Characteristic[a,b]	Baricitinib[c]			TNFi (N=814)	Std. Diff.
	Any (N=213)	2-mg (N=28)	4-mg (N=189)		
Hydroxychloroquine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Leflunomide	30 (14.1%)	4 (14.3%)	26 (13.8%)	76 (9.3%)	0.15
Methotrexate	99 (46.5%)	9 (32.1%)	91 (48.1%)	485 (59.6%)	0.27
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Sulfasalazine	6 (2.8%)	1 (3.6%)	5 (2.6%)	22 (2.7%)	0.01
bDMARDs, during baseline[a]					
n, total	80 (37.6%)	15 (53.6%)	68 (36.0%)	48 (5.9%)	0.83
Mean (SD)	0.44 (0.60)	0.61 (0.63)	0.42 (0.60)	0.07 (0.26)	0.80
Median	0.00 [0.00, 1.00]	1.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 0.00]	-
Min, Max	0.0, 3.0	0.00, 2.00	0.00, 3.00	0.0, 2.0	-
cDMARDs, concomitant	30 (14.1%)	6 (21.4%)	25 (13.2%)	28 (3.4%)	0.38
abatacept	21 (9.9%)	8 (28.6%)	16 (8.5%)	15 (1.8%)	0.35
adalimumab[d]	11 (5.2%)	2 (7.1%)	9 (4.8%)	8 (1.0%)	0.24
anakinra	1 (0.5%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0.10
certolizumab pegol[d]	7 (3.3%)	1 (3.6%)	6 (3.2%)	0 (0.0%)	0.26
etanercept[d]	18 (8.5%)	2 (7.1%)	17 (9.0%)	9 (1.1%)	0.35
golimumab[d]	5 (2.3%)	0 (0.0%)	5 (2.6%)	2 (0.2%)	0.19
infliximab[d]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
sarilumab	4 (1.9%)	1 (3.6%)	3 (1.6%)	1 (0.1%)	0.18
tocilizumab	24 (11.3%)	2 (7.1%)	22 (11.6%)	15 (1.8%)	0.39
Other Prescription Medications					
Antibiotics	73 (34.3%)	12 (42.9%)	62 (32.8%)	192 (23.6%)	0.24
Antidiabetic agents	15 (7.0%)	2 (7.1%)	13 (6.9%)	43 (5.3%)	0.07
Insulins	1 (0.5%)	0 (0.0%)	1 (0.5%)	11 (1.4%)	0.09
Non-insulins	14 (6.6%)	2 (7.1%)	12 (6.3%)	37 (4.5%)	0.09
Aspirin	14 (6.6%)	3 (10.7%)	11 (5.8%)	56 (6.9%)	0.01
Cardiovascular					
Anticoagulant	8 (3.8%)	1 (3.6%)	7 (3.7%)	17 (2.1%)	0.10
Antihypertensives	54 (25.4%)	11 (39.3%)	45 (23.8%)	173 (21.3%)	0.10
Antiplatelet	4 (1.9%)	1 (3.6%)	3 (1.6%)	18 (2.2%)	0.02
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (0.4%)	0.09
Hormonal					
HRT	10 (4.7%)	2 (7.1%)	8 (4.2%)	27 (3.3%)	0.07
Oral Contraceptives	6 (2.8%)	0 (0.0%)	6 (3.2%)	29 (3.6%)	0.04
SERMs	2 (0.9%)	0 (0.0%)	2 (1.1%)	5 (0.6%)	0.04
Lipid-lowering agents					
Bile acid binding	2 (0.9%)	0 (0.0%)	2 (1.1%)	1 (0.1%)	0.11
Cholesterol absorption inhibitor	7 (3.3%)	2 (7.1%)	5 (2.6%)	12 (1.5%)	0.12
Fibrates	2 (0.9%)	1 (3.6%)	1 (0.5%)	8 (1.0%)	0.00
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-

Characteristic[a,b]	Baricitinib[c]			TNFi (N=814)	Std. Diff.
	Any (N=213)	2-mg (N=28)	4-mg (N=189)		
Statins	22 (10.3%)	4 (14.3%)	18 (9.5%)	73 (9.0%)	0.05
Rheumatoid arthritis-related					
Cox-2 Inhibitor	6 (2.8%)	1 (3.6%)	6 (3.2%)	37 (4.5%)	0.09
Glucocorticosteroid	145 (68.1%)	19 (67.9%)	128 (67.7%)	391 (48.0%)	0.42
Vaccinations	51 (23.9%)	4 (14.3%)	48 (25.4%)	186 (22.9%)	0.03

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CGDM = cegedim; CIRAS = claims-based index for RA severity; cDMARD = conventional disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = number of patients in the specified category; N/A = not applicable; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff. = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism

a All conditions and characteristics, except for bDMARDs, are measured during the 6 months prior to initiation of study medication including the date at which the qualifying exposure of baricitinib or TNFi occurs (index date). bDMARDs are measured from the 6 months prior to the initiation of study medication until the day prior to baricitinib or the index TNFi exposure, excluding the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d TNF inhibitors.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.6. - Clinical History at Baseline, Unmatched Cohorts [Cegedim THIN (FR) - France].docx

Table 7_CGDM. Clinical Characteristics Primary VTE Cohorts, Matched [CGDM]

Characteristic[a,b]	Baricitinib[c]			TNFi (N=160)	Std. Diff.
	Any (N=160)	2-mg (N=14)	4-mg (N=147)		
Clinical Conditions during baseline					
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Chronic lung disease	2 (1.3%)	0 (0.0%)	2 (1.4%)	3 (1.9%)	0.05
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	1 (0.6%)	1 (7.1%)	0 (0.0%)	1 (0.6%)	0.00
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Congestive heart failure, hospitalized	0 (0.0%)	N/A	N/A	1 (0.6%)	0.11
Coronary artery disease	2 (1.2%)	1 (7.1%)	1 (0.7%)	1 (0.6%)	0.07
Ischemic heart disease	2 (1.2%)	1 (7.1%)	1 (0.7%)	1 (0.6%)	0.07
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Ventricular arrhythmia	1 (0.6%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0.11
Diabetes Mellitus	3 (1.9%)	0 (0.0%)	3 (2.0%)	5 (3.1%)	0.08
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.2%)	0.16
Type II	3 (1.9%)	0 (0.0%)	3 (2.0%)	3 (1.9%)	0.00
Dyslipidaemia	1 (0.6%)	0 (0.0%)	1 (0.7%)	3 (1.9%)	0.11
Hypertension	6 (3.8%)	2 (14.3%)	4 (2.7%)	18 (11.2%)	0.29
Immune disorders	2 (1.2%)	1 (7.1%)	1 (0.7%)	2 (1.2%)	0.00
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
SLE	1 (0.6%)	0 (0.0%)	1 (0.7%)	2 (1.2%)	0.07
Primary Sjögren syndrome	1 (0.6%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0.11
Liver disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Obesity	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
RA severity (CIRAS Index), mean (SD)	4.15 (1.08)	3.29 (0.80)	4.23 (1.07)	3.95 (1.08)	0.19
Smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Surgery, trauma & hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.10
DMARDs					
cDMARDs, during baseline					
n, total	107 (66.9%)	8 (57.1%)	99 (67.3%)	114 (71.2%)	0.10
Mean (SD)	0.78 (0.56)	0.64 (0.50)	0.79 (0.56)	0.75 (0.51)	0.06
Median	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-
Min, Max	0.0, 2.0	0.00, 1.00	0.00, 2.00	0.0, 2.0	-
>1 cDMARD concomitantly	11 (6.9%)	0 (0.0%)	11 (7.5%)	6 (3.8%)	0.14
Hydroxychloroquine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-

Characteristic[a,b]	Baricitinib[c]			TNFi (N=160)	Std. Diff.
	Any (N=160)	2-mg (N=14)	4-mg (N=147)		
Leflunomide	22 (13.8%)	3 (21.4%)	19 (12.9%)	20 (12.5%)	0.04
Methotrexate	85 (53.1%)	4 (28.6%)	81 (55.1%)	94 (58.8%)	0.11
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Sulfasalazine	6 (3.8%)	1 (7.1%)	5 (3.4%)	6 (3.8%)	0.00
bDMARDs, during baseline[a]					
n, total	34 (21.3%)	2 (14.3%)	32 (21.8%)	34 (21.3%)	0.00
Mean (SD)	0.22 (0.41)	0.14 (0.36)	0.22 (0.42)	0.23 (0.44)	0.03
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	-
Min, Max	0.0, 1.0	0.00, 1.00	0.00, 1.00	0.0, 2.0	-
cDMARDs, concomitant	15 (9.4%)	2 (14.3%)	13 (8.8%)	20 (12.5%)	0.10
abatacept	9 (5.6%)	1 (7.1%)	8 (5.4%)	12 (7.5%)	0.08
adalimumab[d]	6 (3.8%)	1 (7.1%)	5 (3.4%)	4 (2.5%)	0.07
anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
certolizumab pegol[d]	3 (1.9%)	0 (0.0%)	3 (2.0%)	0 (0.0%)	0.20
etanercept[d]	8 (5.0%)	0 (0.0%)	8 (5.4%)	6 (3.8%)	0.06
golimumab[d]	1 (0.6%)	0 (0.0%)	1 (0.7%)	2 (1.3%)	0.07
infliximab[d]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
sarilumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.6%)	0.11
tocilizumab	7 (4.4%)	0 (0.0%)	7 (4.8%)	10 (6.3%)	0.08
Other Prescription Medications					
Antibiotics	46 (28.7%)	5 (35.7%)	41 (27.9%)	48 (30.0%)	0.03
Antidiabetic agents	10 (6.2%)	1 (7.1%)	9 (6.1%)	8 (5.0%)	0.05
Insulins	1 (0.6%)	0 (0.0%)	1 (0.7%)	4 (2.5%)	0.15
Non-insulins	9 (5.6%)	1 (7.1%)	8 (5.4%)	6 (3.8%)	0.09
Aspirin	11 (6.9%)	1 (7.1%)	10 (6.8%)	12 (7.5%)	0.02
Cardiovascular					
Anticoagulant	6 (3.8%)	1 (7.1%)	5 (3.4%)	4 (2.5%)	0.07
Antihypertensives	36 (22.5%)	4 (28.6%)	33 (22.4%)	44 (27.5%)	0.12
Antiplatelet	2 (1.2%)	0 (0.0%)	2 (1.4%)	4 (2.5%)	0.09
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Hormonal					
HRT	7 (4.4%)	0 (0.0%)	7 (4.8%)	5 (3.1%)	0.07
Oral Contraceptives	4 (2.5%)	0 (0.0%)	4 (2.7%)	2 (1.2%)	0.09
SERMs	2 (1.2%)	0 (0.0%)	2 (1.4%)	4 (2.5%)	0.09
Lipid-lowering agents					
Bile acid binding	2 (1.2%)	0 (0.0%)	2 (1.4%)	0 (0.0%)	0.16
Cholesterol absorption inhibitor	5 (3.1%)	1 (7.1%)	4 (2.7%)	2 (1.2%)	0.13
Fibrates	1 (0.6%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0.11
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Statins	15 (9.4%)	1 (7.1%)	14 (9.5%)	17 (10.6%)	0.04
Rheumatoid arthritis-related					

Characteristic[a,b]	Baricitinib[c]			TNFi (N=160)	Std. Diff.
	Any (N=160)	2-mg (N=14)	4-mg (N=147)		
Cox-2 Inhibitor	4 (2.5%)	0 (0.0%)	4 (2.7%)	7 (4.4%)	0.10
Glucocorticosteroid	98 (61.3%)	7 (50.0%)	91 (61.9%)	105 (65.6%)	0.09
Vaccinations	35 (21.9%)	1 (7.1%)	34 (23.1%)	39 (24.4%)	0.06

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CGDM = cegedim; CIRAS = claims-based index for RA severity; cDMARD = conventional disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = number of patients in the specified category; N/A = not applicable; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff. = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics, except for bDMARDs, are measured during the 6 months prior to initiation of study medication including the date at which the qualifying exposure of baricitinib or TNFi occurs (index date). bDMARDs are measured from the 6 months prior to the initiation of study medication until the day prior to baricitinib or the index TNFi exposure, excluding the index date.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d TNF inhibitors.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.7. – Clinical Characteristics Primary VTE Cohorts, Matched [Cegedim THIN].docx

Table 8_CGDM. Clinical Characteristics MACE Cohorts, Matched [CGDM]

Characteristic[a,b]	Baricitinib[c]			TNFi (N=162)	Std. Diff.
	Any (N=162)	2-mg (N=15)	4-mg (N=148)		
Clinical Conditions during baseline					
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.6%)	0.111
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Chronic lung disease	6 (3.7%)	1 (6.7%)	5 (3.4%)	4 (2.5%)	0.07
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	3 (1.9%)	2 (13.3%)	1 (0.7%)	0 (0.0%)	0.19
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Congestive heart failure, hospitalized	0 (0.0%)	N/A	N/A	2 (1.2%)	0.16
Coronary artery disease	2 (1.2%)	1 (6.7%)	1 (0.7%)	0 (0.0%)	0.16
Ischemic heart disease	2 (1.2%)	1 (6.7%)	1 (0.7%)	0 (0.0%)	0.16
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Ventricular arrhythmia	2 (1.2%)	1 (6.7%)	1 (0.7%)	0 (0.0%)	0.16
Diabetes Mellitus	4 (2.5%)	0 (0.0%)	4 (2.7%)	0 (0.0%)	0.23
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Type II	4 (2.5%)	0 (0.0%)	4 (2.7%)	0 (0.0%)	0.23
Dyslipidaemia	1 (0.6%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0.11
Hypertension	8 (4.9%)	2 (13.3%)	6 (4.1%)	7 (4.3%)	0.039
Immune disorders	1 (0.6%)	0 (0.0%)	1 (0.7%)	2 (1.2%)	0.06
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
SLE	1 (0.6%)	0 (0.0%)	1 (0.7%)	2 (1.2%)	0.06
Primary Sjögren syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Liver disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.6%)	0.11
Obesity	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
RA severity (CIRAS Index), mean (SD)	4.09 (1.09)	3.28 (0.80)	4.16 (1.08)	4.16 (1.10)	0.06
Smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Surgery, trauma & hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.22
DMARDs					
cDMARDs, during baseline					
n, total	105 (64.8%)	8 (53.3%)	97 (65.5%)	121 (74.7%)	0.22
Mean (SD)	0.77 (0.57)	0.67 (0.49)	0.77 (0.58)	0.77 (0.45)	0.01
Median	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	1.00 [1.00, 1.00]	-
Min, Max	0.0, 2.0	0.00, 1.00	0.00, 2.00	0.0, 2.0	-

Characteristic[a,b]	Baricitinib[c]			TNFi (N=162)	Std. Diff.
	Any (N=162)	2-mg (N=15)	4-mg (N=148)		
>1 cDMARD concomitantly	12 (7.4%)	0 (0.0%)	12 (8.1%)	2 (1.2%)	0.31
Hydroxychloroquine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Leflunomide	24 (14.8%)	2 (13.3%)	22 (14.9%)	18 (11.1%)	0.11
Methotrexate	81 (50.0%)	5 (33.3%)	76 (51.4%)	102 (63.0%)	0.26
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Sulfasalazine	6 (3.7%)	1 (6.7%)	5 (3.4%)	3 (1.9%)	0.11
bDMARDs, during baseline[a]					
n, total	33 (20.4%)	4 (26.7%)	29 (19.6%)	31 (19.1%)	0.03
Mean (SD)	0.22 (0.44)	0.27 (0.46)	0.21 (0.44)	0.21 (0.42)	0.01
Median	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	-
Min, Max	0.0, 2.0	0.00, 2.00	0.00, 2.00	0.0, 2.0	-
cDMARDs, concomitant	14 (8.6%)	3 (20.0%)	11 (7.4%)	22 (13.6%)	0.16
abatacept	6 (3.7%)	1 (6.7%)	5 (3.4%)	9 (5.6%)	0.09
adalimumab[d]	5 (3.1%)	1 (6.7%)	4 (2.7%)	5 (3.1%)	0.00
anakinra	1 (0.6%)	1 (6.7%)	0 (0.0%)	0 (0.0%)	0.11
certolizumab pegol[d]	3 (1.9%)	0 (0.0%)	3 (2.0%)	0 (0.0%)	0.19
etanercept[d]	9 (5.6%)	0 (0.0%)	9 (6.1%)	7 (4.3%)	0.06
golimumab[d]	2 (1.2%)	0 (0.0%)	2 (1.4%)	1 (0.6%)	0.06
infliximab[d]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
sarilumab	1 (0.6%)	1 (6.7%)	0 (0.0%)	0 (0.0%)	0.11
tocilizumab	8 (4.9%)	0 (0.0%)	8 (5.4%)	10 (6.2%)	0.05
Other Prescription Medications					
Antibiotics	53 (32.7%)	6 (40.0%)	47 (31.8%)	42 (25.9%)	0.15
Antidiabetic agents	12 (7.4%)	1 (6.7%)	11 (7.4%)	4 (2.5%)	0.23
Insulins	1 (0.6%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0.11
Non-insulins	11 (6.8%)	1 (6.7%)	10 (6.8%)	4 (2.5%)	0.21
Aspirin	11 (6.8%)	1 (6.7%)	10 (6.8%)	8 (4.9%)	0.08
Cardiovascular					
Anticoagulant	6 (3.7%)	0 (0.0%)	6 (4.1%)	4 (2.5%)	0.07
Antihypertensives	41 (25.3%)	5 (33.3%)	37 (25.0%)	34 (21.0%)	0.10
Antiplatelet	3 (1.9%)	0 (0.0%)	3 (2.0%)	1 (0.6%)	0.11
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Hormonal					
HRT	8 (4.9%)	1 (6.7%)	7 (4.7%)	3 (1.9%)	0.17
Oral Contraceptives	4 (2.5%)	0 (0.0%)	4 (2.7%)	5 (3.1%)	0.04
SERMs	2 (1.2%)	0 (0.0%)	2 (1.4%)	2 (1.2%)	0.00
Lipid-lowering agents					
Bile acid binding	2 (1.2%)	0 (0.0%)	2 (1.4%)	0 (0.0%)	0.16
Cholesterol absorption inhibitor	6 (3.7%)	1 (6.7%)	5 (3.4%)	1 (0.6%)	0.21
Fibrates	1 (0.6%)	0 (0.0%)	1 (0.7%)	2 (1.2%)	0.06
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-

Characteristic[a,b]	Baricitinib[c]			TNFi (N=162)	Std. Diff.
	Any (N=162)	2-mg (N=15)	4-mg (N=148)		
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Statins	17 (10.5%)	2 (13.3%)	15 (10.1%)	12 (7.4%)	0.11
Rheumatoid arthritis-related					
Cox-2 Inhibitor	5 (3.1%)	0 (0.0%)	5 (3.4%)	4 (2.5%)	0.04
Glucocorticosteroid	101 (62.3%)	8 (53.3%)	93 (62.8%)	104 (64.2%)	0.04
Vaccinations	38 (23.5%)	2 (13.3%)	36 (24.3%)	43 (26.5%)	0.07

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CGDM = cegedim; CIRAS = claims-based index for RA severity; cDMARD = conventional disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; N/A = not applicable; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff. = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

A All conditions and characteristics, except for bDMARDs, are measured during the 6 months prior to initiation of study medication including the date at which the qualifying exposure of baricitinib or TNFi occurs (index date). bDMARDs are measured from the 6 months prior to the initiation of study medication until the day prior to baricitinib or the index TNFi exposure, excluding the index date.

B Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

C Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

D TNF inhibitors.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.8. – Clinical Characteristics MACE Cohorts, Matched [Cegedim THIN (FR) – France].docx

Table 9_CGDM. Clinical Characteristics Incident Serious Infection Cohorts, Matched [CGDM]

Characteristic[a,b]	Baricitinib[c]			TNFi (N=169)	Std. Diff.
	Any (N=169)	2-mg (N=16)	4-mg (N=154)		
Clinical Conditions during baseline					
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Chronic lung disease	4 (2.4%)	1 (6.3%)	3 (1.9%)	3 (1.8%)	0.04
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	5 (3.0%)	2 (12.5%)	3 (1.9%)	1 (0.6%)	0.18
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Congestive heart failure, hospitalized	0 (0.0%)	N/A	N/A	2 (1.2%)	0.16
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.2%)	0.16
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.2%)	0.16
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Ventricular arrhythmia	3 (1.8%)	2 (12.5%)	1 (0.6%)	0 (0.0%)	0.19
Diabetes Mellitus	1 (0.6%)	0 (0.0%)	1 (0.6%)	1 (0.6%)	0.00
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.6%)	0.11
Type II	1 (0.6%)	0 (0.0%)	1 (0.6%)	0 (0.0%)	0.11
Dyslipidaemia	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (2.4%)	0.22
Hypertension	7 (4.1%)	2 (12.5%)	5 (3.2%)	15 (8.9%)	0.19
Immune disorders	1 (0.6%)	0 (0.0%)	1 (0.6%)	1 (0.6%)	0.00
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
SLE	1 (0.6%)	0 (0.0%)	1 (0.6%)	0 (0.0%)	0.11
Primary Sjögren syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.6%)	0.11
Liver disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Obesity	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
RA severity (CIRAS Index), mean (SD)	4.10 (1.07)	3.20 (0.72)	4.19 (1.05)	4.12 (1.17)	0.02
Smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Surgery, trauma & hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
DMARDs					
cDMARDs, during baseline					
n, total	108 (63.9%)	7 (43.8%)	101 (65.6%)	116 (68.6%)	0.10
Mean (SD)	0.76 (0.57)	0.56 (0.51)	0.77 (0.58)	0.73 (0.51)	0.06
Median	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	-

Characteristic[a,b]	Baricitinib[c]			TNFi (N=169)	Std. Diff.
	Any (N=169)	2-mg (N=16)	4-mg (N=154)		
Min, Max	0.0, 2.0	0.00, 1.00	0.00, 2.00	0.0, 3.0	-
>1 cDMARD concomitantly	12 (7.1%)	0 (0.0%)	12 (7.8%)	3 (1.8%)	0.26
Hydroxychloroquine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Leflunomide	25 (14.8%)	2 (12.5%)	23 (14.9%)	18 (10.7%)	0.13
Methotrexate	84 (49.7%)	5 (31.3%)	79 (51.3%)	97 (57.4%)	0.16
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Sulfasalazine	5 (3.0%)	0 (0.0%)	5 (3.2%)	3 (1.8%)	0.08
bDMARDs, during baseline[a]					
n, total	35 (20.7%)	3 (18.8%)	32 (20.8%)	35 (20.7%)	0.00
Mean (SD)	0.22 (0.43)	0.19 (0.40)	0.22 (0.43)	0.22 (0.43)	0.01
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	-
Min, Max	0.0, 2.0	0.00, 1.00	0.00, 2.00	0.0, 2.0	-
cDMARDs, concomitant	10 (5.9%)	0 (0.0%)	10 (6.5%)	20 (11.8%)	0.21
abatacept	9 (5.3%)	1 (6.3%)	8 (5.2%)	11 (6.5%)	0.05
adalimumab[d]	3 (1.8%)	1 (6.3%)	2 (1.3%)	5 (3.0%)	0.08
anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
certolizumab pegol[d]	4 (2.4%)	0 (0.0%)	4 (2.6%)	0 (0.0%)	0.22
etanercept[d]	9 (5.3%)	1 (6.3%)	8 (5.2%)	8 (4.7%)	0.03
golimumab[d]	2 (1.2%)	0 (0.0%)	2 (1.3%)	2 (1.2%)	0.00
infliximab[d]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
sarilumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.6%)	0.11
tocilizumab	9 (5.3%)	0 (0.0%)	9 (5.8%)	9 (5.3%)	0.00
Other Prescription Medications					
Antibiotics	50 (29.6%)	5 (31.3%)	45 (29.2%)	48 (28.4%)	0.03
Antidiabetic agents	9 (5.3%)	1 (6.3%)	8 (5.2%)	6 (3.6%)	0.09
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.6%)	0.11
Non-insulins	9 (5.3%)	1 (6.3%)	8 (5.2%)	5 (3.0%)	0.12
Aspirin	10 (5.9%)	1 (6.3%)	9 (5.8%)	12 (7.1%)	0.05
Cardiovascular					
Anticoagulant	12 (7.1%)	2 (12.5%)	10 (6.5%)	8 (4.7%)	0.10
Antihypertensives	38 (22.5%)	5 (31.3%)	34 (22.1%)	48 (28.4%)	0.14
Antiplatelet	2 (1.2%)	0 (0.0%)	2 (1.3%)	3 (1.8%)	0.05
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Hormonal					
HRT	9 (5.3%)	1 (6.3%)	8 (5.2%)	8 (4.7%)	0.03
Oral Contraceptives	3 (1.8%)	0 (0.0%)	3 (1.9%)	2 (1.2%)	0.05
SERMs	2 (1.2%)	0 (0.0%)	2 (1.3%)	0 (0.0%)	0.16
Lipid-lowering agents					
Bile acid binding	2 (1.2%)	0 (0.0%)	2 (1.3%)	0 (0.0%)	0.16
Cholesterol absorption inhibitor	2 (1.2%)	0 (0.0%)	2 (1.3%)	1 (0.6%)	0.06
Fibrates	1 (0.6%)	1 (6.3%)	0 (0.0%)	1 (0.6%)	0.00
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-

Characteristic[a,b]	Baricitinib[c]			TNFi (N=169)	Std. Diff.
	Any (N=169)	2-mg (N=16)	4-mg (N=154)		
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Statins	13 (7.7%)	1 (6.3%)	12 (7.8%)	23 (13.6%)	0.19
Rheumatoid arthritis-related					
Cox-2 Inhibitor	5 (3.0%)	0 (0.0%)	5 (3.2%)	6 (3.6%)	0.03
Glucocorticosteroid	107 (63.3%)	9 (56.3%)	98 (63.6%)	111 (65.7%)	0.05
Vaccinations	38 (22.5%)	2 (12.5%)	36 (23.4%)	40 (23.7%)	0.03

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CGDM = cegedim; CIRAS = claims-based index for RA severity; cDMARD = conventional disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = number of patients in the specified category; N/A = not applicable; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff. = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism

a All conditions and characteristics, except for bDMARDs, are measured during the 6 months prior to initiation of study medication including the date at which the qualifying exposure of baricitinib or TNFi occurs (index date). bDMARDs are measured from the 6 months prior to the initiation of study medication until the day prior to baricitinib or the index TNFi exposure, excluding the index date.

B Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, and may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

C Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

D TNF inhibitors.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.9. - Clinical Characteristics Incident Serious Infection Cohorts, Matched [Cegedim THIN].docx

Table 11A_CGDM. Baseline Healthcare Resource Utilization, Unmatched [CGDM]

Type of Resource Use	Baricitinib (N=213)	TNFi (N=814)	Std. Diff.
Physician Office Visits			
n, patients	67 (31.5%)	296 (36.4%)	0.10
n, events	530	2190	
Mean (SD)	2.49 (5.03)	2.69 (5.10)	0.04
Median	0.00 [0.00, 3.50]	0.00 [0.00, 4.00]	
Min, Max	0.0, 30.0	0.0, 32.0	
Rheumatologist Visits			
n, patients	132 (62.0%)	414 (50.9%)	0.23
n, events	1067	2165	
Mean (SD)	5.01 (5.75)	2.66 (4.02)	0.47
Median	4.00 [0.00, 8.00]	1.50 [0.00, 4.00]	
Min, Max	0.0, 26.0	0.0, 28.0	
Other Outpatient Visits			
n, patients	44 (20.7%)	186 (22.9%)	0.05
n, events	262	977	
Mean (SD)	1.23 (3.14)	1.20 (3.07)	0.01
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 22.0	0.0, 34.0	
Inpatient Visits*			
n, patients	-	-	-
n, events	-	-	-
Mean (SD)	- (-)	- (-)	
Median	- [-, -]	- [-, -]	
Min, Max	-, -	-, -	
ED Visits*			
n, patients	-	-	-
n, events	-	-	-
Mean (SD)	- (-)	- (-)	
Median	- [-, -]	- [-, -]	
Min, Max	-, -	-, -	

Abbreviations: CGDM = cegedim; ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

*Not Applicable

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.11A. Baseline Healthcare Resource Utilization, Unmatched [Cegedim THIN (FR) - France].docx

Table 11B_CGDM. Baseline Healthcare Resource Utilization, Unmatched [CGDM], count at most one visit per day

Type of Resource Use	Baricitinib (N=213)	TNFi (N=814)	Std. Diff.
Physician Office Visits[1]			
n, patients	67 (31.5%)	296 (36.4%)	0.10
n, events	245	1,058	
Mean (SD)	1.15 (2.33)	1.30 (2.42)	0.06
Median	0.00 [0.00, 2.00]	0.00 [0.00, 2.00]	
Min, Max	0.0, 14.0	0.0, 15.0	
Rheumatologist Visits[1]			
n, patients	132 (62.0%)	414 (50.9%)	0.23
n, events	511	1,050	
Mean (SD)	2.40 (2.63)	1.29 (1.85)	0.49
Median	2.00 [0.00, 4.00]	1.00 [0.00, 2.00]	
Min, Max	0.0, 12.0	0.0, 13.0	
Other Outpatient Visits[1]			
n, patients	44 (20.7%)	186 (22.9%)	0.05
n, events	132	513	
Mean (SD)	0.62 (1.55)	0.63 (1.54)	0.00
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 11.0	0.0, 15.0	
Inpatient Visits[2]			
n, patients	-	-	-
n, events	-	-	-
Mean (SD)	- (-)	- (-)	
Median	- [-, -]	- [-, -]	
Min, Max	-, -	-, -	
ED Visits[2]			
n, patients	-	-	-
n, events	-	-	-
Mean (SD)	- (-)	- (-)	
Median	- [-, -]	- [-, -]	
Min, Max	-, -	-, -	

Abbreviations: CGDM = cegedim; ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

1 In this table, results describe utilization of healthcare where a maximum of one event was allowed per day. In the PS matching analyses, multiple claims on the same day were allowed to capture additional information on the amount of services received in a given visit. These results are presented in table 6.11A.

2 Type(s) of healthcare encounter not applicable to the Cegedim THIN (France) database.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.11B (count at most one visit per day). Baseline Healthcare Resource Utilization, Unmatched [Cegedim THIN (FR) - France].docx

Table 12A_CGDM. Baseline Healthcare Resource Utilization Primary VTE Cohorts, Matched [CGDM]

Type of Resource Use	Baricitinib (N=160)	TNFi (N=160)	Std. Diff.
Physician Office Visits			
n, patients	47 (29.4%)	59 (36.9%)	0.16
n, events	406	494	
Mean (SD)	2.54 (5.37)	3.09 (6.03)	0.10
Median	0.00 [0.00, 2.00]	0.00 [0.00, 4.00]	
Min, Max	0.0, 30.0	0.0, 32.0	
Rheumatologist Visits			
n, patients	101 (63.1%)	88 (55.0%)	0.17
n, events	730	653	
Mean (SD)	4.56 (5.13)	4.08 (5.36)	0.09
Median	4.00 [0.00, 7.00]	2.00 [0.00, 6.00]	
Min, Max	0.0, 22.0	0.0, 22.0	
Other Outpatient Visits			
n, patients	35 (21.9%)	33 (20.6%)	0.03
n, events	214	166	
Mean (SD)	1.34 (3.37)	1.04 (2.65)	0.10
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 22.0	0.0, 18.0	
Inpatient Visits*			
n, patients	-	-	-
n, events	-	-	-
Mean (SD)	- (-)	- (-)	
Median	- [-, -]	- [-, -]	
Min, Max	-, -	-, -	
ED Visits*			
n, patients	-	-	-
n, events	-	-	-
Mean (SD)	- (-)	- (-)	
Median	- [-, -]	- [-, -]	
Min, Max	-, -	-, -	

Abbreviations: CGDM = Cegedim; ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

*Not Applicable

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.12A. Baseline Healthcare Resource Utilization Primary VTE Cohorts, Matched [Cegedim THIN (FR) - France].docx

Table 12B_CGDM. Baseline Healthcare Resource Utilization Primary VTE Cohorts, Matched [CGDM], count at most one visit per day

Type of Resource Use	Baricitinib (N=160)	TNFi (N=160)	Std. Diff.
Physician Office Visits[1]			
n, patients	47 (29.4%)	59 (36.9%)	0.16
n, events	186	245	
Mean (SD)	1.16 (2.46)	1.53 (2.88)	0.14
Median	0.00 [0.00, 1.00]	0.00 [0.00, 2.00]	
Min, Max	0.0, 14.0	0.0, 15.0	
Rheumatologist Visits[1]			
n, patients	101 (63.1%)	88 (55.0%)	0.17
n, events	366	298	
Mean (SD)	2.29 (2.51)	1.86 (2.38)	0.18
Median	2.00 [0.00, 3.00]	1.00 [0.00, 3.00]	
Min, Max	0.0, 11.0	0.0, 10.0	
Other Outpatient Visits[1]			
n, patients	35 (21.9%)	33 (20.6%)	0.03
n, events	109	86	
Mean (SD)	0.68 (1.66)	0.54 (1.33)	0.10
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 11.0	0.0, 8.0	
Inpatient Visits[2]			
n, patients	-	-	-
n, events	-	-	-
Mean (SD)	- (-)	- (-)	
Median	- [-, -]	- [-, -]	
Min, Max	-, -	-, -	
ED Visits[2]			
n, patients	-	-	-
n, events	-	-	-
Mean (SD)	- (-)	- (-)	
Median	- [-, -]	- [-, -]	
Min, Max	-, -	-, -	

Abbreviations: CGDM = Cegedim; ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

1 In this table, results describe utilization of healthcare where a maximum of one event was allowed per day. In the PS matching analyses, multiple claims on the same day were allowed to capture additional information on the amount of services received in a given visit. These results are presented in table 6.12A.

2 Type(s) of healthcare encounter not applicable to the Cegedim THIN (France) database.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.12B (count at most one visit per day). Baseline Healthcare Resource Utilization Primary VTE Cohorts, Matched [Cegedim THIN (FR) - France].docx

Table 13A_CGDM. Baseline Healthcare Resource Utilization MACE Cohorts, Matched [CGDM]

Type of Resource Use	Baricitinib (N=162)	TNFi (N=162)	Std. Diff.
Physician Office Visits			
n, patients	55 (34.0%)	50 (30.9%)	0.07
n, events	446	403	
Mean (SD)	2.75 (5.35)	2.49 (5.19)	0.05
Median	0.00 [0.00, 4.00]	0.00 [0.00, 2.00]	
Min, Max	0.0, 30.0	0.0, 30.0	
Rheumatologist Visits			
n, patients	95 (58.6%)	99 (61.1%)	0.05
n, events	677	664	
Mean (SD)	4.18 (4.99)	4.10 (5.55)	0.02
Median	3.00 [0.00, 6.00]	2.00 [0.00, 6.00]	
Min, Max	0.0, 22.0	0.0, 28.0	
Other Outpatient Visits			
n, patients	34 (21.0%)	37 (22.8%)	0.05
n, events	203	181	
Mean (SD)	1.25 (3.04)	1.12 (3.07)	0.04
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 18.0	0.0, 24.0	
Inpatient Visits*			
n, patients	-	-	-
n, events	-	-	-
Mean (SD)	- (-)	- (-)	
Median	- [-, -]	- [-, -]	
Min, Max	-, -	-, -	
ED Visits*			
n, patients	-	-	-
n, events	-	-	-
Mean (SD)	- (-)	- (-)	
Median	- [-, -]	- [-, -]	
Min, Max	-, -	-, -	

Abbreviations: CGDM = Cegedim; ED = emergency department; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

*Not Applicable

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.13A. Baseline Healthcare Resource Utilization MACE Cohorts, Matched [Cegedim THIN (FR) - France].docx

Table 13B_CGDM. Baseline Healthcare Resource Utilization MACE Cohorts, Matched [CGDM], count at most one visit per day.

Type of Resource Use	Baricitinib (N=162)	TNFi (N=162)	Std. Diff.
Physician Office Visits[1]			
n, patients	55 (34.0%)	50 (30.9%)	0.07
n, events	206	199	
Mean (SD)	1.27 (2.46)	1.23 (2.57)	0.02
Median	0.00 [0.00, 2.00]	0.00 [0.00, 1.00]	
Min, Max	0.0, 14.0	0.0, 14.0	
Rheumatologist Visits[1]			
n, patients	95 (58.6%)	99 (61.1%)	0.05
n, events	335	304	
Mean (SD)	2.07 (2.39)	1.88 (2.43)	0.08
Median	2.00 [0.00, 3.00]	1.00 [0.00, 3.00]	
Min, Max	0.0, 10.0	0.0, 13.0	
Other Outpatient Visits[1]			
n, patients	34 (21.0%)	37 (22.8%)	0.05
n, events	100	98	
Mean (SD)	0.62 (1.47)	0.61 (1.57)	0.01
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 9.0	0.0, 12.0	
Inpatient Visits[2]			
n, patients	-	-	-
n, events	-	-	-
Mean (SD)	- (-)	- (-)	
Median	- [-, -]	- [-, -]	
Min, Max	-, -	-, -	
ED Visits[2]			
n, patients	-	-	-
n, events	-	-	-
Mean (SD)	- (-)	- (-)	
Median	- [-, -]	- [-, -]	
Min, Max	-, -	-, -	

Abbreviations: CGDM = Cegedim; ED = emergency department; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

1 In this table, results describe utilization of healthcare where a maximum of one event was allowed per day. In the PS matching analyses, multiple claims on the same day were allowed to capture additional information on the amount of services received in a given visit. These results are presented in table 6.13A.

2 Type(s) of healthcare encounter not applicable to the Cegedim THIN (France) database.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.13B (count at most one visit per day). Baseline Healthcare Resource Utilization MACE Cohorts, Matched [Cegedim THIN (FR) - France].docx

Table 14A_CGDM. Baseline Healthcare Resource Utilization Serious Infection Cohorts, Matched [CGDM]

Type of Resource Use	Baricitinib (N=169)	TNFi (N=169)	Std. Diff.
Physician Office Visits			
n, patients	52 (30.8%)	56 (33.1%)	0.05
n, events	395	465	
Mean (SD)	2.34 (4.76)	2.75 (5.59)	0.08
Median	0.00 [0.00, 2.50]	0.00 [0.00, 2.00]	
Min, Max	0.0, 26.0	0.0, 30.0	
Rheumatologist Visits			
n, patients	103 (60.9%)	95 (56.2%)	0.10
n, events	744	647	
Mean (SD)	4.40 (5.20)	3.83 (5.23)	0.11
Median	4.00 [0.00, 6.00]	2.00 [0.00, 6.00]	
Min, Max	0.0, 26.0	0.0, 28.0	
Other Outpatient Visits			
n, patients	36 (21.3%)	37 (21.9%)	0.01
n, events	204	235	
Mean (SD)	1.21 (2.95)	1.39 (3.52)	0.06
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 18.0	0.0, 24.0	
Inpatient Visits*			
n, patients	-	-	-
n, events	-	-	-
Mean (SD)	- (-)	- (-)	
Median	- [-, -]	- [-, -]	
Min, Max	-, -	-, -	
ED Visits*			
n, patients	-	-	-
n, events	-	-	-
Mean (SD)	- (-)	- (-)	
Median	- [-, -]	- [-, -]	
Min, Max	-, -	-, -	

Abbreviations: CGDM = Cegedim; ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

*Not Applicable

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.14A. Baseline Healthcare Resource Utilization Serious Infection Cohorts, Matched [Cegedim THIN (FR) - France].docx

Table 14B_CGDM. Baseline Healthcare Resource Utilization Serious Infection Cohorts, Matched [CGDM], count at most one visit per day

Type of Resource Use	Baricitinib (N=169)	TNFi (N=169)	Std. Diff.
Physician Office Visits[1]			
n, patients	52 (30.8%)	56 (33.1%)	0.05
n, events	188	232	
Mean (SD)	1.11 (2.22)	1.37 (2.71)	0.11
Median	0.00 [0.00, 1.50]	0.00 [0.00, 1.50]	
Min, Max	0.0, 13.0	0.0, 14.0	
Rheumatologist Visits[1]			
n, patients	103 (60.9%)	95 (56.2%)	0.10
n, events	368	303	
Mean (SD)	2.18 (2.49)	1.79 (2.35)	0.16
Median	2.00 [0.00, 3.00]	1.00 [0.00, 3.00]	
Min, Max	0.0, 12.0	0.0, 13.0	
Other Outpatient Visits[1]			
n, patients	36 (21.3%)	37 (21.9%)	0.01
n, events	103	120	
Mean (SD)	0.61 (1.44)	0.71 (1.74)	0.06
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Min, Max	0.0, 9.0	0.0, 12.0	
Inpatient Visits[2]			
n, patients	-	-	-
n, events	-	-	-
Mean (SD)	- (-)	- (-)	
Median	- [-, -]	- [-, -]	
Min, Max	-, -	-, -	
ED Visits[2]			
n, patients	-	-	-
n, events	-	-	-
Mean (SD)	- (-)	- (-)	
Median	- [-, -]	- [-, -]	
Min, Max	-, -	-, -	

Abbreviations: CGDM = Cegedim; ED = emergency department; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

1 In this table, results describe utilization of healthcare where a maximum of one event was allowed per day. In the PS matching analyses, multiple claims on the same day were allowed to capture additional information on the amount of services received in a given visit. These results are presented in table 6.14A.

2 Type(s) of healthcare encounter not applicable to the Cegedim THIN (France) database.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.14B (count at most one visit per day). Baseline Healthcare Resource Utilization Serious Infection Cohorts, Matched [Cegedim THIN (FR) - France].docx

Table 16_CGDM. Baseline Prevalence of Outcomes [CGDM]

Outcome in Each Matched Cohort[a,c,d]	Unmatched					Matched					
	Baricitinib[b]			TNFi	Std. Diff	Baricitinib[b]			TNFi	Std. Diff	Total
	Any	2mg	4mg			Any	2mg	4mg			
VTE	**N=213**	**N=28**	**N=189**	**N=814**	**-**	**N=160**	**N=15**	**N=146**	**N=160**	**-**	**N=320**
Main case definition in baseline	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	0.05	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)
Alternate case definition I in baseline	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	0.05	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)
Alternative case definition II in baseline	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	0.05	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)
MACE	**N=213**	**N=28**	**N=189**	**N=814**	**-**	**N=163**	**N=17**	**N=147**	**N=163**	**-**	**N=326**
MACE in baseline	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	0.05	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.6%)	0.11	1 (0.3%)
Serious Infection	**N=218**	**N=29**	**N=193**	**N=825**	**-**	**N=169**	**N=16**	**N=154**	**N=169**	**-**	**N=338**
Serious Infection in baseline	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.2%)	0.07	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)
Hospitalized Tuberculosis	**N=218**	**N=29**	**N=193**	**N=825**	**-**	**N=169**	**N=16**	**N=154**	**N=169**	**-**	**N=338**
Hospitalized Tuberculosis in baseline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)

Abbreviations: CGDM = Cegedim; MACE = major adverse cardiovascular event, defined as hospital primary discharge diagnosis code of acute MI or hospital primary discharge diagnosis code of ischemic or hemorrhagic stroke; N = number of patients in specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism, defined based on the case definitions.

a Baseline prevalence was calculated for each distinct matched cohort for VTE, MACE, serious infection and hospitalized tuberculosis.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c Patients with the prevalent outcomes enumerated in this table are those excluded from the main analyses of each outcome, except for VTE alternative case definitions I and II. Only the VTE main case definition was used as an exclusion criterion in the main analyses.

d In the VTE and MACE analyses, cohorts additionally excluded the use of anticoagulants at the time of cohort entry (see protocol Section 8.7.7), resulting in a different N compared to the Serious Infection and Hospitalized Tuberculosis cohorts.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.16. Baseline Prevalence of Outcomes [Cegedim THIN (FR) - France]_.docx

Table 17_CGDM. Duration of Follow-up Period (Days), Unmatched [CGDM]

	Baricitinib[a]			TNFi (N=814)	Std. Diff
	Any (N=213)	4-mg (N= 189)	2-mg (N= 28)		
N	213	189	28	814	
Mean (SD)	87.83 (103.63)	87.72 (105.97)	81.50 (80.41)	164.71 (177.32)	0.21
Median	50.00 [30.00, 95.00]	49.00 [30.00, 91.00]	54.50 [30.00, 95.50]	99.50 [30.00, 223.25]	
Min, Max	10.0, 641.0	10.0, 641.0	22.0, 329.0	2.0, 966.0	

Abbreviations: CGDM = cegedim; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = standardised difference; TNFi = tumour necrosis factor inhibitor.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be reported for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.17. Duration of Follow-up Period (Days), Unmatched [Cegedim THIN (FR) - France].docx

Table 18_CGDM. Duration of Follow-up Period (Days) Primary VTE Cohorts, Matched [CGDM]

	Baricitinib[a]				
	Any (N=160)	**4mg[b] (N=147)**	**2mg[b] (N=14)**	**TNFi (N=160)**	**Std. Diff.**
N	160	147	14	160	0
Mean (SD)	84.27 (96.89)	83.86 (98.08)	86.64 (82.69)	183.48 (187.67)	0.66
Median	50.50 [30.00, 90.00]	50.00 [30.00, 90.00]	57.50 [30.00, 112.00]	115.00 [42.25, 244.00]	
Min, Max	10.0, 641.0	10.0, 641.0	30.0, 288.0	7.0, 924.0	
Reasons for censoring[c]					
Incident event	0	0	0	0	-
Medication discontinued	140 (87.5%)	127 (86.4%)	14 (100.0%)	116 (72.5%)	-
Initiated b/tsDMARD	4 (2.5%)	4 (2.7%)	0 (0.0%)	6 (3.8%)	-
End of patient record	13 (8.1%)	13 (8.8%)	0 (0.0%)	30 (18.8%)	-
Death (where available)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
End of study period (12/31/2020)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.6%)	-

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; CGD = Cegedim; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = standardised difference; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be reported for each dose where numbers of patients are sufficient to warrant separate reporting.

b Patients may have claims for both the 4mg dose and 2mg dose on the index date. Thus, the total of 4mg and 2mg baricitinib users may be greater than or equal to the number of baricitinib users of any dose.

c A single patient can be censored on the same day for multiple reasons, e.g., medication discontinued could also be the same day as initiated b/tsDMARD. Further, additional censoring criteria (e.g., switching medication) were specified in the SAP. For these reasons, the total number of reasons for censoring may be less than or greater than the total number of patients.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.18. Duration of Follow-up Period (Days) Primary VTE Cohorts, Matched [Cegedim THIN (FR) - France].docx

Table 21_CGDM. Duration of Follow-up Period (Days) MACE Cohorts, Matched [CGDM]

	Baricitinib[a]				
	Any (N=162)	**4mg (N=148)**	**2mg (N=15)**	**TNFi (N=162)**	**Std. Diff.**
N	162	148	15	162	
Mean (SD)	84.42 (100.95)	85.49 (102.70)	72.07 (79.57)	155.75 (166.38)	0.28
Median	49.00 [30.00, 87.25]	49.50 [30.00, 89.50]	49.00 [30.00, 60.00]	103.50 [30.00, 197.00]	
Min, Max	10.0, 641.0	10.0, 641.0	30.0, 288.0	7.0, 751.0	
Reasons for censoring					
Incident event	1	1	0	0	-
Medication discontinued	145 (89.5%)	131 (88.5%)	15 (100.0%)	129 (79.6%)	-
Initiated b/tsDMARD	2 (1.2%)	2 (1.4%)	0 (0.0%)	6 (3.7%)	-
End of patient record	12 (7.4%)	12 (8.1%)	0 (0.0%)	22 (13.6%)	-
Death (where available)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
End of study period (12/31/2020)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.6%)	-

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; CGDM = Cegedim; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = standardised difference; TNFi = tumour necrosis factor inhibitor.

[a] Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be reported for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.21. Duration of Follow-up Period (Days) MACE Cohorts, Matched [Cegedim THIN (FR) - France].docx

Table 22_CGDM. Duration of Follow-up Period (Days) Incident Serious Infection Cohorts, Matched [CGDM]

	Baricitinib[a]			TNFi (N=169)	Std. Diff.
	Any (N=169)	4-mg (N=154)	2-mg (N=16)		
N	169	154	16	169	
Mean (SD)	88.82 (100.59)	87.68 (101.66)	97.81 (88.71)	169.49 (166.54)	0.59
Median	52.00 [30.00, 100.00]	51.50 [30.00, 93.50]	57.50 [30.00, 131.50]	106.00 [43.00, 249.00]	
Min, Max	10.0, 641.0	10.0, 641.0	30.0, 288.0	2.0, 741.0	
Reasons for censoring					
Incident event	0	0	0	0	-
Medication discontinued	147 (87.0%)	133 (86.4%)	15 (93.8%)	124 (73.4%)	-
Initiated b/tsDMARD	4 (2.4%)	4 (2.6%)	0 (0.0%)	5 (3.0%)	-
End of patient record	14 (8.3%)	13 (8.4%)	1 (6.3%)	32 (18.9%)	-
Death (where available)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
End of study period (12/31/2020)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-

Abbreviations: b/tsDMARD = biologic or targeted synthetic disease-modifying antirheumatic drug; CGDM = cegedim; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; Std. Diff. = standardised difference; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.22. Duration of Follow-up Period (Days) Incident Serious Infection Cohorts, Matched [Cegedim THIN (FR) - France].docx

Table 39_CGDM. Pattern of VTE and Related Diagnostic Codes in Patients with RA [CGDM]

Code	Total Patients (N=1)
Deep Vein Thrombosis, lower	
I80.10 - Phlebitis and thrombophlebitis of unspecified femoral vein	0 (0.0%)
I80.11 - Phlebitis and thrombophlebitis of right femoral vein	0 (0.0%)
I80.201 - Phlebitis and thrombophlebitis of unspecified deep vessels of right lower extremity	0 (0.0%)
I80.213 - Phlebitis and thrombophlebitis of iliac vein, bilateral	0 (0.0%)
I80.219 - Phlebitis and thrombophlebitis of unspecified iliac vein	0 (0.0%)
I80.221 - Phlebitis and thrombophlebitis of right popliteal vein	0 (0.0%)
I80.222 - Phlebitis and thrombophlebitis of left popliteal vein	0 (0.0%)
I80.223 - Phlebitis and thrombophlebitis of popliteal vein, bilateral	0 (0.0%)
I80.229 - Phlebitis and thrombophlebitis of unspecified popliteal vein	0 (0.0%)
I80.232 - Phlebitis and thrombophlebitis of left tibial vein	0 (0.0%)
I80.233 - Phlebitis and thrombophlebitis of tibial vein, bilateral	0 (0.0%)
I80.293 - Phlebitis and thrombophlebitis of other deep vessels of lower extremity, bilateral	0 (0.0%)
I80.3 - Phlebitis and thrombophlebitis of lower extremities, unspecified	0 (0.0%)
I82.402 - Acute embolism and thrombosis of unspecified deep veins of left lower extremity	0 (0.0%)
I82.409 - Acute embolism and thrombosis of unspecified deep veins of unspecified lower extremity	0 (0.0%)
I82.411 - Acute embolism and thrombosis of right femoral vein	0 (0.0%)
I82.431 - Acute embolism and thrombosis of right popliteal vein	0 (0.0%)
I82.432 - Acute embolism and thrombosis of left popliteal vein	0 (0.0%)

Code	Total Patients (N=1)
I82.433 - Acute embolism and thrombosis of popliteal vein, bilateral	0 (0.0%)
I82.441 - Acute embolism and thrombosis of right tibial vein	0 (0.0%)
I82.442 - Acute embolism and thrombosis of left tibial vein	0 (0.0%)
I82.449 - Acute embolism and thrombosis of unspecified tibial vein	0 (0.0%)
I82.491 - Acute embolism and thrombosis of other specified deep vein of right lower extremity	0 (0.0%)
I82.492 - Acute embolism and thrombosis of other specified deep vein of left lower extremity	0 (0.0%)
I82.493 - Acute embolism and thrombosis of other specified deep vein of lower extremity, bilateral	0 (0.0%)
I82.499 - Acute embolism and thrombosis of other specified deep vein of unspecified lower extremity	0 (0.0%)
I82.4Y2 - Acute embolism and thrombosis of unspecified deep veins of left proximal lower extremity	0 (0.0%)
I82.4Y3 - Acute embolism and thrombosis of unspecified deep veins of proximal lower extremity, bilateral	0 (0.0%)
I82.4Y9 - Acute embolism and thrombosis of unspecified deep veins of unspecified proximal lower extremity	0 (0.0%)
I82.4Z1 - Acute embolism and thrombosis of unspecified deep veins of right distal lower extremity	0 (0.0%)
I80.12 - Phlebitis and thrombophlebitis of left femoral vein	0 (0.0%)
I80.13 - Phlebitis and thrombophlebitis of femoral vein, bilateral	0 (0.0%)
I80.202 - Phlebitis and thrombophlebitis of unspecified deep vessels of left lower extremity	0 (0.0%)
I80.203 - Phlebitis and thrombophlebitis of unspecified deep vessels of lower extremities, bilateral	0 (0.0%)
I80.209 - Phlebitis and thrombophlebitis of unspecified deep vessels of unspecified lower extremity	0 (0.0%)
I80.211 - Phlebitis and thrombophlebitis of right iliac vein	0 (0.0%)
I80.212 - Phlebitis and thrombophlebitis of left iliac vein	0 (0.0%)
I80.231 - Phlebitis and thrombophlebitis of right tibial vein	0 (0.0%)
I80.291 - Phlebitis and thrombophlebitis of other deep vessels of right lower extremity	0 (0.0%)

Code	Total Patients (N=1)
I80.292 - Phlebitis and thrombophlebitis of other deep vessels of left lower extremity	0 (0.0%)
I80.299 - Phlebitis and thrombophlebitis of other deep vessels of unspecified lower extremity	0 (0.0%)
I82.401 - Acute embolism and thrombosis of unspecified deep veins of right lower extremity	0 (0.0%)
I82.403 - Acute embolism and thrombosis of unspecified deep veins of lower extremity, bilateral	0 (0.0%)
I82.412 - Acute embolism and thrombosis of left femoral vein	0 (0.0%)
I82.413 - Acute embolism and thrombosis of femoral vein, bilateral	0 (0.0%)
I82.419 - Acute embolism and thrombosis of unspecified femoral vein	0 (0.0%)
I82.421 - Acute embolism and thrombosis of right iliac vein	0 (0.0%)
I82.422 - Acute embolism and thrombosis of left iliac vein	0 (0.0%)
I82.423 - Acute embolism and thrombosis of iliac vein, bilateral	0 (0.0%)
I82.429 - Acute embolism and thrombosis of unspecified iliac vein	0 (0.0%)
I82.439 - Acute embolism and thrombosis of unspecified popliteal vein	0 (0.0%)
I82.443 - Acute embolism and thrombosis of tibial vein, bilateral	0 (0.0%)
I82.4Y1 - Acute embolism and thrombosis of unspecified deep veins of right proximal lower extremity	0 (0.0%)
I82.4Z2 - Acute embolism and thrombosis of unspecified deep veins of left distal lower extremity	0 (0.0%)
I82.4Z3 - Acute embolism and thrombosis of unspecified deep veins of distal lower extremity, bilateral	0 (0.0%)
Deep Vein Thrombosis, upper	
I82.602 - Acute embolism and thrombosis of unspecified veins of left upper extremity	0 (0.0%)
I82.603 - Acute embolism and thrombosis of unspecified veins of upper extremity, bilateral	0 (0.0%)
I82.609 - Acute embolism and thrombosis of unspecified veins of unspecified upper extremity	0 (0.0%)
I82.622 - Acute embolism and thrombosis of deep veins of left upper extremity	0 (0.0%)

Code	Total Patients (N=1)
I82.623 - Acute embolism and thrombosis of deep veins of upper extremity, bilateral	0 (0.0%)
I82.A11 - Acute embolism and thrombosis of right axillary vein	0 (0.0%)
I82.A12 - Acute embolism and thrombosis of left axillary vein	0 (0.0%)
I82.A19 - Acute embolism and thrombosis of unspecified axillary vein	0 (0.0%)
I82.C19 - Acute embolism and thrombosis of unspecified internal jugular vein	0 (0.0%)
I82.210 - Acute embolism and thrombosis of superior vena cava	0 (0.0%)
I82.601 - Acute embolism and thrombosis of unspecified veins of right upper extremity	0 (0.0%)
I82.621 - Acute embolism and thrombosis of deep veins of right upper extremity	0 (0.0%)
I82.629 - Acute embolism and thrombosis of deep veins of unspecified upper extremity	0 (0.0%)
I82.A13 - Acute embolism and thrombosis of axillary vein, bilateral	0 (0.0%)
I82.C11 - Acute embolism and thrombosis of right internal jugular vein	0 (0.0%)
I82.C12 - Acute embolism and thrombosis of left internal jugular vein	0 (0.0%)
I82.C13 - Acute embolism and thrombosis of internal jugular vein, bilateral	0 (0.0%)
Other Venous Thrombosis	
I80.8 - Phlebitis and thrombophlebitis of other sites	0 (0.0%)
I80.9 - Phlebitis and thrombophlebitis of unspecified site	1 (100.0%)
I81 - Portal vein thrombosis	0 (0.0%)
I82.0 - Budd-Chiari syndrome	0 (0.0%)
I82.3 - Embolism and thrombosis of renal vein	0 (0.0%)
I82.90 - Acute embolism and thrombosis of unspecified vein	0 (0.0%)
I82.1 - Thrombophlebitis migrans	0 (0.0%)

Code	Total Patients (N=1)
I82.220 - Acute embolism and thrombosis of inferior vena cava	0 (0.0%)
I82.890 - Acute embolism and thrombosis of other specified veins	0 (0.0%)
I82.B11 - Acute embolism and thrombosis of right subclavian vein	0 (0.0%)
I82.B12 - Acute embolism and thrombosis of left subclavian vein	0 (0.0%)
I82.B13 - Acute embolism and thrombosis of subclavian vein, bilateral	0 (0.0%)

Abbreviations: CGDM = Cegedim; ICD-10 = International Classification of Disease, 10th Revision; N = number of patients in the specified category; RA = rheumatoid arthritis; VTE = venous thromboembolis

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.39. Pattern of VTE and Related Diagnostic Codes in Patients with RA [Cegedim THIN (FR) - France].docx

Table 40_CGDM. Clinical Characteristics of RA Patients with VTE, Primary Definition [CGDM]

Characteristic[a,b]	Baricitinibc (N=0)	TNFi (N=0)	Total (N=0)
Age (mean) [SD]	- (-)	- (-)	- (-)
Sex			
Female	0 (0.0%)	0 (0.0%)	0 (0.0%)
Male	0 (0.0%)	0 (0.0%)	0 (0.0%)
Clinical Conditions during baseline			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic Lung disease Disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular conditions			
Atrial arrhythmia/ fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dyslipidaemia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertension	0 (0.0%)	0 (0.0%)	0 (0.0%)
Immune disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Primary Sjögren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)

Characteristic[a,b]	Baricitinibc (N=0)	TNFi (N=0)	Total (N=0)
RA Severity (CIRAS Index), mean (SD)	- (-)	- (-)	- (-)
Smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)
Surgery, trauma, & hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medication			
Antibiotics	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antidiabetic agents	0 (0.0%)	0 (0.0%)	0 (0.0%)
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			
Antihypertensives	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anticoagulant	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiplatelet	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			
Oral contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERM	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucocorticosteroid	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vaccinations	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Occurrence[d]			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)

Characteristic[a,b]	Baricitinibc (N=0)	TNFi (N=0)	Total (N=0)
Hospitalization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Surgery	0 (0.0%)	0 (0.0%)	0 (0.0%)
Trauma	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CGDM = Cegedim; CIRAS = claims-based index for RA severity; cDMARD = conventional disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = number of patients in the specified category; N/A = not applicable; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff. = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d Except for cancer diagnosed within 90 days of VTE diagnosis, events in this category must have occurred in the 4 weeks immediately prior to VTE (Kline et al. 2017).

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.40. - Clinical Characteristics of RA Patients with VTE, Primary Definition [Cegedim THIN (FR) - France].docx

Table 41_CGDM. Pattern of RA Medication Use in Patients with VTE, Primary Definition [CGDM]

Characteristic[a]	Unmatched				Matched		
	Baricitinib[b]						
	Any (N=1)	4 mg (N=1)	2mg (N=0)	TNFi (N=0)	Baricitinib[b] (N=0)	TNFi (N=0)	Total (N=0)
Baseline Medication							
cDMARDs, during baseline							
n, total	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	0.00 (0.00)	0.00 (0.00)	- (-)	- (-)	- (-)	- (-)	- (-)
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	- [-, -]	- [-, -]	- [-, -]	- [-, -]	- [-, -]
Min, Max	0.0, 0.0	0.0, 0.0	-, -	-, -	-, -	-, -	-, -
>1 cDMARD concomitantly	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hydroxychloroquine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Leflunomide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
bDMARDs, during baseline							
n, total	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	0.00 (0.00)	0.00 (0.00)	- (-)	- (-)	- (-)	- (-)	- (-)
Median	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	- [-, -]	- [-, -]	- [-, -]	- [-, -]	- [-, -]
Min, Max	0.0, 0.0	0.0, 0.0	-, -	-, -	-, -	-, -	-, -
cDMARDs, concomitant	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abatacept	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adalimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Etanercept[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Golimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infliximab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Medication[d]							

Methotrexate, concomitant	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Concomitant cDMARD	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dose change, baricitinib	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; CGDM = Cegedim; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c TNF inhibitors.

d Only baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked ‘NA’ as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.41. - Pattern of RA Medication Use in Patients with VTE, Primary Definition [Cegedim THIN (FR) - France].docx

Table 42_CGDM. Time to First Event Outcome (days) - VTE, Primary Definition [CGDM]

Time	Unmatched				Matched				
	Baricitinib[a]			TNFi	Baricitinib[a]			TNFi	Total
	Any (N=213)	4mg (N= 189)	2mg (N= 28)	(N=814)	Any (N=160)	4mg (N= 147)	2mg (N= 14)	(N=160)	(N=320)
n	213	189	28	814	160			160	320
Mean (SD)	36.00 (0.00)	36.00 (0.00)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
Median	36.00 [36.00, 36.00]	36.00 [36.00, 36.00]	- [-, -]	- [-, -]	- [-, -]	- [-, -]	- [-, -]	- [-, -]	- [-, -]
Min, Max	36.0, 36.0	36.0, 36.0	-,-	-,-	-,-	-,-	-,-	-,-	-,-

Abbreviations: CGDM = Cegedim; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; VTE = venous thromboembolism.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.42. Time to First Event Outcome (days) - VTE, Primary Definition [Cegedim].docx

Table 45_CGDM. Incidence Rate of Event - VTE, Primary Definition [CGDM]

	Unmatched		Matched[a]		
	Baricitinib[a] (N=213)	TNFi (N=814)	Baricitinib[a] (N=160)	TNFi (N=160)	Total (N=320)
Overall					
Person-Years	51.25	367.33	36.94	80.43	117.37
VTE Events	1	0	0	0	0
VTE Events/100 PY	1.95	0.00	0.00	0.00	0.00
95% CI	0.05, 10.87	0.00, 1.00	0.00, 9.99	0.00, 4.59	0.00, 3.14
Concomitant MTX Use[c]					
Total, n	36 (16.9%)	301 (37.0%)	31 (19.4%)	63 (39.4%)	94 (29.4%)
Person-Years	15.69	207.30	12.70	43.32	56.01
VTE Events	0	0	0	0	0
VTE Events/100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 23.51	0.00, 1.78	0.00, 29.05	0.00, 8.52	0.00, 6.59
No Concomitant MTX Use[c]					
Total, n	177 (83.1%)	513 (63.0%)	129 (80.6%)	97 (60.6%)	226 (70.6%)
Person-Years	35.56	160.04	24.24	37.12	61.36
VTE Events	1	0	0	0	0
VTE Events/100 PY	2.81	0.00	0.00	0.00	0.00
95% CI	0.07, 15.67	0.00, 2.31	0.00, 15.22	0.00, 9.94	0.00, 6.01

Abbreviations: CGDM = Cegedim; CI = confidence intervals; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a Hospitalized congestive heart failure cannot be identified due to the lack of data for inpatient diagnoses in Cegedim THIN (France). As a result, the cardiovascular disease category used in the PS calculation includes only atrial fibrillation and ventricular arrhythmia, and does not include hospitalized congestive heart failure.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.45. Incidence Rate of Event - VTE, Primary Definition [Cegedim THIN (FR) - France].docx

Table 48_CGDM. Comparative Risk of Incident VTE, Primary Definition [CGDM]

	TNFi	Baricitinib		p-value
		HR	95%CI	
Base Model[1,2]	Ref	-	-	-

Abbreviations: cDMARD = conventional disease-modifying antirheumatic drug; CI = confidence interval; HR = Cox proportional hazard ratio; Ref = referent group; VTE = venous thromboembolism.

1 Base model - propensity score-matched model with confounders, outcome and baricitinib exposure.

2 Zero outcome events in both the exposed and referent groups preclude the calculation of the HR.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.48. Comparative Risk of Incident VTE, Primary Definition [Cegedim THIN (FR) - France], updated base model = PS matched.docx

Table 51_CGDM. Clinical Characteristics of RA Patients with MACE [CGDM]

Characteristic[a,b]	Baricitinibc (N=0)	TNFi (N=0)	Total (N=0)
Age (mean) [SD]	- (-)	- (-)	- (-)
Sex			
Female	0 (0.0%)	0 (0.0%)	0 (0.0%)
Male	0 (0.0%)	0 (0.0%)	0 (0.0%)
Clinical Conditions during baseline			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic lung disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive heart failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dyslipidaemia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertension	0 (0.0%)	0 (0.0%)	0 (0.0%)
Immune disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Primary Sjögren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)
RA Severity (CIRAS Index), mean (SD)	- (-)	- (-)	- (-)

Characteristic[a,b]	Baricitinibc (N=0)	TNFi (N=0)	Total (N=0)
Smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)
Surgery, Trauma, & Hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medications			
Antibiotics	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antidiabetic agents	0 (0.0%)	0 (0.0%)	0 (0.0%)
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			
Anticoagulant	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antihypertensives	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiplatelet	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			
Oral contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERM	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucocorticosteroid	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vaccinations	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Occurrence[d]			
Methotrexate, concomitant	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CGDM = Cegedim; CIRAS = claims-based index for RA severity; cDMARD = conventional disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; MACE = major adverse cardiovascular event; Max = maximum; Min = minimum; N = number of patients in the specified category; N/A = not applicable; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff. = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

d Events in this category must have occurred in the 7 days immediately prior to MACE.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.51. - Clinical Characteristics of RA Patients with MACE [Cegedim THIN (FR) - France]_.docx

Table 52_CGDM. Pattern of RA Medication Use in Patients with MACE [CGDM]

Characteristic[a]	Unmatched		Matched		
	Baricitinib[b] (N=0)	TNFi (N=0)	Baricitinib[b] (N=0)	TNFi (N=0)	Total (N=0)
Baseline Medication					
cDMARDs, during baseline					
n, total	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	- (-)	- (-)	- (-)	- (-)	- (-)
Median	- [-, -]	- [-, -]	- [-, -]	- [-, -]	- [-, -]
Min, Max	-, -	-, -	-, -	-, -	-, -
>1 cDMARD concomitantly	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hydroxychloroquine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Leflunomide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
bDMARDs, during baseline					
n, total	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	- (-)	- (-)	- (-)	- (-)	- (-)
Median	- [-, -]	- [-, -]	- [-, -]	- [-, -]	- [-, -]
Min, Max	-, -	-, -	-, -	-, -	-, -
cDMARDs, concomitant	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abatacept	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adalimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Etanercept[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Golimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infliximab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Medication[d]					
Methotrexate, concomitant	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Other Concomitant cDMARD	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dose change, baricitinib	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; MACE = major adverse cardiovascular event; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c TNF inhibitors.

d Only baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked ‘NA’ as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim_CGDM\4. Table 6.52. - Pattern of RA Medication Use in Patients with MACE [Cegedim THIN (FR) - France].docx

Table 6.53. Time to First Event Outcome (days) - MACE [Cegedim THIN (FR) - France]

Time	Unmatched				Matched				
	Baricitinib[a]			TNFi	Baricitinib[a]			TNFi	Total
	Any (N=213)	4mg (N= 145)	2mg (N=28)	(N=813)	Any (N=162)	4mg (N= 148)	2mg (N= 15)	(N=162)	(N=324)
n	213	189	28	813	162	148	15	162	324
Mean (SD)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
Median	- [-, -]	- [-, -]	- [-, -]	- [-, -]	- [-, -]	- [-, -]	- [-, -]	- [-, -]	- [-, -]
Min, Max	-,-	-,-	-,-	-,-	-,-	-,-	-,-	-,-	-,-

Abbreviations: CGDM = Cegedim; MACE = major adverse cardiovascular event; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; VTE = venous thromboembolism.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.53. Time to First Event Outcome (days) - MACE [Cegedim].docx

Table 54_CGDM. Incidence Rate of Event - MACE [CGCM]

Model	Unmatched		Matched		
	Baricitinib[a] (N=213)	TNFi (N=813)	Baricitinib[a] (N=162)	TNFi (N=162)	Total (N=324)
Overall					
Person-Years	51.27	366.33	37.47	69.13	106.60
MACE	0	0	0	0	0
MACE/100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 7.20	0.00, 1.01	0.00, 9.85	0.00, 5.34	0.00, 3.46
MI					
MI	0	0	0	0	0
Person-Years	51.27	366.33	37.47	69.13	106.60
IR per100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 7.20	0.00, 1.01	0.00, 9.85	0.00, 5.34	0.00, 3.46
Stroke, any					
Stroke	0	0	0	0	0
Person-Years	51.27	366.33	37.47	69.13	106.60
IR per 100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 7.20	0.00, 1.01	0.00, 9.85	0.00, 5.34	0.00, 3.46
Concomitant MTX Use[b]					
MACE	0	0	0	0	0
Person-Years	15.69	206.37	12.30	38.07	50.36
IR per 100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 23.51	0.00, 1.79	0.00, 30.00	0.00, 9.69	0.00, 7.32
No Concomitant MTX Use[b]					
MACE	0	0	0	0	0

Person-Years	35.58	159.96	25.17	31.06	56.23
IR per 100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 10.37	0.00, 2.31	0.00, 14.65	0.00, 11.88	0.00, 6.56

Abbreviations: CGCM = Cegedim; CI = confidence interval; IR = incidence rate; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; MI = myocardial infarction; MTX = methotrexate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

b Concomitant MTX (methotrexate) use is defined as greater than or equal to 2 dispensings of MTX over the follow-up period.

c N in subgroups may not always sum precisely to total group N due to rounding

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.54. Incidence Rate of Event - MACE [Cegedim THIN (FR) - France].docx

Table 55_CGDM, Comparative Risk of MACE [Cegedim THIN (FR) - France]

	TNFi	Baricitinib		p-value
		HR	95%CI	
Base Model[1,2]	Ref	-	-	-

Abbreviations: CGDM = Cegedim; CI = confidence interval; HR = Cox proportional hazard ratio; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Ref = referent group; TNFi = tumor necrosis factor inhibitor.

1 Base model - propensity score-matched model with confounders, outcome and baricitinib exposure.

2 Zero events in the TNFi group preclude analyzing models with additional parameters. The model did not converge.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.55. - Comparative Risk of MACE [Cegedim THIN (FR) - France].docx

Table 56_CGDM. Clinical Characteristics of RA Patients with Incident Serious Infections [CGDM]

Characteristics[a,b]	Baricitinib[c] (N=0)	TNFi (N=0)	Total (N=0)
Age (mean) [SD]	- (-)	- (-)	- (-)
Sex			
Female	0 (0.0%)	0 (0.0%)	0 (0.0%)
Male	0 (0.0%)	0 (0.0%)	0 (0.0%)
Clinical Conditions during baseline			
Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)
NMSC	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic Lung disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular revascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Congestive Heart Failure, hospitalized	0 (0.0%)	0 (0.0%)	0 (0.0%)
Coronary artery disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ischemic heart disease	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unstable angina	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ventricular arrhythmia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitus	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type I	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dyslipidaemia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertension	0 (0.0%)	0 (0.0%)	0 (0.0%)
Immune disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiphospholipid syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
SLE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Primary Sjögren Syndrome	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obesity	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pregnancy	0 (0.0%)	0 (0.0%)	0 (0.0%)

Characteristics[a,b]	Baricitinib[c] (N=0)	TNFi (N=0)	Total (N=0)
RA Severity (CIRAS Index), mean (SD)	- (-)	- (-)	- (-)
Smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)
Surgery, Trauma, & Hospitalization, recent	0 (0.0%)	0 (0.0%)	0 (0.0%)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Prescription Medications			
Antibiotics	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antidiabetic agents	0 (0.0%)	0 (0.0%)	0 (0.0%)
Insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-insulins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aspirin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular			
Anticoagulant	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antihypertensives	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antiplatelet	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nitrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hormonal			
HRT	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oral Contraceptives	0 (0.0%)	0 (0.0%)	0 (0.0%)
SERMs	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lipid-lowering agents			
Bile acid binding	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesterol absorption inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibrates	0 (0.0%)	0 (0.0%)	0 (0.0%)
Niacin	0 (0.0%)	0 (0.0%)	0 (0.0%)
Omega-3 fatty acids	0 (0.0%)	0 (0.0%)	0 (0.0%)
Statins	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rheumatoid arthritis-related			
Cox-2 Inhibitor	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucocorticosteroid	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vaccinations	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CGDM = Cegedim; CIRAS = claims-based index for RA severity; cDMARD = conventional disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; Max = maximum; Min = minimum; N = number of patients in the specified category; N/A = not applicable; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulators; SLE = systemic lupus erythematosus; Std. Diff. = standardised difference; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Many characteristics of the cohort are included in this table, but propensity score matching is only expected to balance those risk factors listed in Table 4 in protocol Section 8.3.3 (Annex 19) for each outcome, e.g., hospitalized congestive heart failure for VTE. Other factors are included for descriptive purposes only, may not be balanced across treatment groups but do not contribute to confounding bias, e.g., Type I diabetes for VTE.

c Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.56. Clinical Characteristics of RA Patients with Incident Serious Infections [Cegedim THIN (FR) - France].docx

Table 57_CGDM. Pattern of RA Medication Use in Patients with Serious Infection Event [CGDM]

Characteristic[a]	Unmatched		Matched		
	Baricitinib[b] (N=0)	TNFi (N=1)	Baricitinib[b] (N=0)	TNFi (N=0)	Total (N=0)
Baseline Medication DMARDS					
cDMARDs, during baseline					
n, total	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	- (-)	0.00 (0.00)	- (-)	- (-)	- (-)
Median	- [-, -]	0.00 [0.00, 0.00]	- [-, -]	- [-, -]	- [-, -]
Min, Max	-, -	0.0, 0.0	-, -	-, -	-, -
>1 cDMARD concomitantly	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hydroxychloroquine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Leflunomide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Methotrexate	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Minocycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sulfasalazine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
bDMARDs, during baseline					
n, total	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mean (SD)	- (-)	0.00 (0.00)	- (-)	- (-)	- (-)
Median	- [-, -]	0.00 [0.00, 0.00]	- [-, -]	- [-, -]	- [-, -]
Min, Max	-, -	0.0, 0.0	-, -	-, -	-, -
cDMARDs, concomitant	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abatacept	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adalimumab[c]	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anakinra	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Certolizumab pegol[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Etanercept[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Golimumab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infliximab[c]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tocilizumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-index Medication					

Methotrexate, concomitant	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Concomitant cDMARD	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dose change, baricitinib	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; CGDM = Cegedim; Max = maximum; Min = minimum; N = number of patients in the specified category; NA = not applicable; RA = rheumatoid arthritis; SD = standard deviation; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 6 months prior to initiation of study medication until and including the day prior to baricitinib or the index TNFi exposure that qualifies the patient for the cohort.

b Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

c TNF inhibitors.

d Only baricitinib 2-mg dose is available in the US, so the baricitinib cells should be marked ‘NA’ as necessary.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.57. Pattern of RA Medication Use in Patients with Serious Infection Event [Cegedim THIN (FR) - France].docx

Table 58_CGDM. Time to First Serious Infection (Days) [CGDM]

Time	Unmatched				Matched				
	Baricitinib[a]			TNFi	Baricitinib[a]			TNFi	Total
	Any (N=218)	4mg (N= 193)	2mg (N=29)	(N=823)	Any (N=169)	4mg (N=131)	2mg (N= 89)	(N=169)	(N=338)
n	218	193	29	823	169	131	89	169	338
Mean (SD)	- (-)	- (-)	- (-)	333.00 (0.00)	- (-)	- (-)	- (-)	- (-)	- (-)
Median	- [-, -]	- [-, -]	- [-, -]	333.00 [333.00, 333.00]	- [-, -]	- [-, -]	- [-, -]	- [-, -]	- [-, -]
Min, Max	-,-	-,-	-,-	333.0, 333.0	-,-	-,-	-,-	-,-	-,-

Abbreviations: CGDM = Cegedim; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor.

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available. Alternatively, additional columns may be added for each dose where numbers of patients are sufficient to warrant separate reporting.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.58. Time to First Serious Infection (Days) [Cegedim THIN (FR) - France].docx

Table 59_CGDM. Incidence Rate of Event - First Serious Infection [CGDM]

	Unmatched		Matched		
	Baricitinib[a] (N=218)	**TNFi (N=823)**	**Baricitinib[a] (N=169)**	**TNFi (N=169)**	**Total (N=338)**
SI Events	0	1	0	0	0
Person-years	53.86	371.15	41.13	78.47	119.60
IR per 100 PY	0.00	0.27	0.00	0.00	0.00
95% CI	0.00, 6.85	0.01, 1.50	0.00, 8.97	0.00, 4.70	0.00, 3.08

Abbreviations: CGDM = Cegedim; CI = confidence interval; IR = incidence rate; N = number of patients in the specified category; PY = person-years; SI = serious infection; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.59. Incidence Rate of Event - First Serious Infection [Cegedim THIN (FR) RA].docx

Table 60_CGDM. Serious Infection Events Per Patient During All Available Follow-up [CGDM]

Number of Infections per Person	Unmatched		Matched		
	Baricitinib (N=218)	TNFi (N=823)	Baricitinib (N=169)	TNFi (N=169)	Total (N=338)
0	215 (98.6%)	810 (98.4%)	166 (98.2%)	166 (98.2%)	332 (98.2%)
1	2 (0.9%)	1 (0.1%)	2 (1.2%)	0 (0.0%)	2 (0.6%)
2	1 (0.5%)	4 (0.5%)	1 (0.6%)	1 (0.6%)	2 (0.6%)
3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
4	0 (0.0%)	5 (0.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
5	0 (0.0%)	2 (0.2%)	0 (0.0%)	2 (1.2%)	2 (0.6%)
6	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
>6	0 (0.0%)	1 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviations: CGDM = Cegedim; N = number of patients in the specified category; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.60. Serious Infection Events Per Patient During All Available Follow-up [Cegedim THIN (FR) - France].docx

Table 61_CGDM. Comparative Risk of First Serious Infection Event [CGDM]

	TNFi	Baricitinib		p-value
		HR	95%CI	
Base Model[1,2]	Ref	-	-	-

Abbreviations: CGDM = Cegedim; CI = confidence interval; HR = Cox proportional hazard ratio; Ref = referent group; TNFi = tumor necrosis factor inhibitor.

1 Base model = propensity score-matched model with confounders, outcome and baricitinib exposure.

2 Zero events in the TNFi group and Baricitinib group preclude analyzing models with additional parameters. The model did not converge.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\Table 6.61. Comparative Risk of First Serious Infection Event [Cegedim THIN (FR) - France].docx

Table 68_CGDM. Incidence Rate of VTE (Primary Definition), by Dose and Unmatched [CGDM]

	Baricitinib 2mg (N=28)	Baricitinib 4mg (N=189)	TNFi (N=814)
VTE Events	0	1	0
Person-Years	6.25	45.41	367.33
IR per 100 PY	0.00	2.20	0.00
95% CI	0.00, 59.00	0.06, 12.27	0.00, 1.00

Abbreviations: CGDM = Cegedim; CI = confidence intervals; IR = incidence rate; N = number of patients in the specified category; PY = person-years; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\cegedim\4. Table 6.68. Incidence Rate of VTE (Primary Definition), by Dose and Unmatched [Cegedim THIN (FR) - France].docx

II. Variable Ratio Matching

All prior tables presented were based on propensity score matched baricitinib:TNFi cohorts using a 1:1 matching strategy. In this section, the tables include results that are based on a variable ratio matching (VRM) approach as described in Section 9.9.6.1 of the final study report.

The main analysis was modified to use 1:1 matching, as this allows the results in the meta-analysis to be directly proportional to the amount of baricitinib exposure in each data source. For transparency, comparative results generated using VRM prior to the adoption of the 1:1 matching are included here.

Table 45_CGDM_VRM. Incidence Rate of Event - VTE, Primary Definition [CGDM]

	Unmatched		Matched		
	Baricitinib[a] (N=213)	TNFi (N=814)	Baricitinib[a] (N=35)	TNFi (N=45)	Total (N=80)
Overall					
Person-Years	51.25	367.33	8.52	20.82	29.34
VTE Events	1	0	1	0	1
VTE Events/100 PY	1.95	0.00	11.74	0.00	3.41
95% CI	0.05, 10.87	0.00, 1.00	0.30, 65.39	0.00, 17.72	0.09, 18.99
Concomitant MTX Use[b]					
Total, n	36 (16.9%)	301 (37.0%)	8 (22.9%)	14 (31.1%)	22 (27.5%)
Person-Years	15.69	207.30	3.49	9.51	13.00
VTE Events	0	0	0	0	0
VTE Events/100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 23.51	0.00, 1.78	0.00, 105.77	0.00, 38.78	0.00, 28.38
No Concomitant MTX Use[b]					
Total, n	177 (83.1%)	513 (63.0%)	27 (77.1%)	31 (68.9%)	58 (72.5%)
Person-Years	35.56	160.04	5.03	11.31	16.34
VTE Events	1	0	1	0	1