Characteristics[b]	bDMARD-Experienced					bDMARD naïve				
	Bari. Any[e] n = 1643	Bari. 4 mg n = 1376	Bari. 2 mg n = 264	TNFi n = 1643	Std. Diff. (Any vs TNFi)	Bari. Any n = 1319	Bari. 4 mg n = 985	Bari. 2 mg n = 334	TNFi n = 1319	Std. Diff. (Any vs TNFi)
Antibiotics	713 (43.4)	591 (43.0)	120 (45.5)	720 (43.8)	-0.009	534 (40.5)	366 (37.2)	168 (50.3)	530 (40.2)	0.006
Antidiabetic agents	163 (9.9)	126 (9.2)	36 (13.6)	158 (9.6)	0.01	118 (8.9)	76 (7.7)	42 (12.6)	124 (9.4)	-0.016
Insulins	64 (3.9)	49 (3.6)	15 (5.7)	56 (3.4)	0.026	44 (3.3)	29 (2.9)	15 (4.5)	43 (3.3)	0.004
Non-insulins	128 (7.8)	101 (7.3)	26 (9.8)	130 (7.9)	-0.005	101 (7.7)	66 (6.7)	35 (10.5)	107 (8.1)	-0.017
Cardiovascular										
Antithrombotic agents	286 (17.4)	195 (14.2)	90 (34.1)	297 (18.1)	-0.018	274 (20.8)	164 (16.6)	110 (32.9)	253 (19.2)	0.04
Anticoagulant	114 (6.9)	76 (5.5)	38 (14.4)	116 (7.1)	-0.005	137 (10.4)	71 (7.2)	66 (19.8)	121 (9.2)	0.041
Antiplatelet	194 (11.8)	132 (9.6)	61 (23.1)	205 (12.5)	-0.021	164 (12.4)	105 (10.7)	59 (17.7)	141 (10.7)	0.055
Antihypertensives	570 (34.7)	423 (30.7)	146 (55.3)	606 (36.9)	-0.046	474 (35.9)	279 (28.3)	195 (58.4)	491 (37.2)	-0.027
Angiotensin converting enzyme inhibitors (ACE)	164 (10.0)	127 (9.2)	37 (14.0)	161 (9.8)	0.006	114 (8.6)	65 (6.6)	49 (14.7)	136 (10.3)	-0.057
Angiotensin receptor blockers (ARB)	212 (12.9)	151 (11.0)	61 (23.1)	254 (15.5)	-0.073	187 (14.2)	114 (11.6)	73 (21.9)	201 (15.2)	-0.03
Beta blocker	245 (14.9)	175 (12.7)	69 (26.1)	267 (16.3)	-0.037	232 (17.6)	130 (13.2)	102 (30.5)	211 (16.0)	0.043
Calcium channel blocker	155 (9.4)	109 (7.9)	45 (17.0)	184 (11.2)	-0.058	139 (10.5)	70 (7.1)	69 (20.7)	136 (10.3)	0.007

	bDMARD-Experienced					bDMARD naïve				
Characteristics[b]	**Bari. Any[e] n = 1643**	**Bari. 4 mg n = 1376**	**Bari. 2 mg n = 264**	**TNFi n = 1643**	**Std. Diff. (Any vs TNFi)**	**Bari. Any n = 1319**	**Bari. 4 mg n = 985**	**Bari. 2 mg n = 334**	**TNFi n = 1319**	**Std. Diff. (Any vs TNFi)**
Nitrates	16 (1.0)	≤ 10	11 (4.2)	22 (1.3)	-0.034	13 (1.0)	≤ 10	≤ 10	≤ 10	0.033
Acyclovir	≤ 10	≤ 10	≤ 10	16 (1.0)	-0.084	≤ 10	≤ 10	≤ 10	≤ 10	0
ValAcyclovir	73 (4.4)	58 (4.2)	15 (5.7)	76 (4.6)	-0.009	37 (2.8)	26 (2.6)	11 (3.3)	46 (3.5)	-0.039
Hormonal	230 (14.0)	208 (15.1)	22 (8.3)	236 (14.4)	-0.011	136 (10.3)	111 (11.3)	25 (7.5)	138 (10.5)	-0.005
HRT	126 (7.7)	112 (8.1)	14 (5.3)	135 (8.2)	-0.02	84 (6.4)	67 (6.8)	17 (5.1)	81 (6.1)	0.009
Oral Contraceptives	100 (6.1)	92 (6.7)	≤ 10	102 (6.2)	-0.005	48 (3.6)	42 (4.3)	≤ 10	55 (4.2)	-0.027
SERMs	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.011	≤ 10	≤ 10	≤ 10	≤ 10	0.032
Topic with progestogens and/or estrogens	≤ 10	≤ 10	≤ 10	≤ 10	0.035	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.017
Lipid-lowering agents	273 (16.6)	201 (14.6)	71 (26.9)	298 (18.1)	-0.04	234 (17.7)	150 (15.2)	84 (25.1)	215 (16.3)	0.038
HMG CoA reductase inhibitors	220 (13.4)	159 (11.6)	60 (22.7)	246 (15.0)	-0.045	191 (14.5)	121 (12.3)	70 (21.0)	178 (13.5)	0.028
Fibrates	28 (1.7)	22 (1.6)	≤ 10	24 (1.5)	0.02	13 (1.0)	≤ 10	≤ 10	17 (1.3)	-0.029
Bile acid sequestrants	≤ 10	≤ 10	≤ 10	≤ 10	0.025	≤ 10	≤ 10	≤ 10	≤ 10	0.025
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Other lipid modifying agents	12 (0.7)	≤ 10	≤ 10	19 (1.2)	-0.044	13 (1.0)	≤ 10	≤ 10	16 (1.2)	-0.022

Characteristics[b]	bDMARD-Experienced					bDMARD naïve				
	Bari. Any[e] n = 1643	Bari. 4 mg n = 1376	Bari. 2 mg n = 264	TNFi n = 1643	Std. Diff. (Any vs TNFi)	Bari. Any n = 1319	Bari. 4 mg n = 985	Bari. 2 mg n = 334	TNFi n = 1319	Std. Diff. (Any vs TNFi)
Lipid modifying agents, combinations	18 (1.1)	15 (1.1)	≤ 10	23 (1.4)	-0.027	24 (1.8)	19 (1.9)	≤ 10	14 (1.1)	0.064
Rheumatoid arthritis-related										
Aspirin	25 (1.5)	17 (1.2)	≤ 10	21 (1.3)	0.021	≤ 10	≤ 10	≤ 10	15 (1.1)	-0.039
Cox-2 Inhibitor	90 (5.5)	81 (5.9)	≤ 10	97 (5.9)	-0.018	64 (4.9)	53 (5.4)	11 (3.3)	81 (6.1)	-0.057
NSAIDs	574 (34.9)	509 (37.0)	65 (24.6)	612 (37.2)	-0.048	478 (36.2)	391 (39.7)	87 (26.0)	485 (36.8)	-0.011
Glucocorticosteroid	1144 (69.6)	951 (69.1)	191 (72.3)	1123 (68.4)	0.028	981 (74.4)	719 (73.0)	262 (78.4)	990 (75.1)	-0.016
Vaccines	462 (28.1)	355 (25.8)	107 (40.5)	419 (25.5)	0.059	451 (34.2)	322 (32.7)	129 (38.6)	493 (37.4)	-0.067
Antineoplastic agents	≤ 10	≤ 10	≤ 10	≤ 10	-0.061	≤ 10	≤ 10	≤ 10	≤ 10	0.059

Abbreviations: N = number of patients in the specified category; Std. Diff = standardized difference; TNFi = tumor necrosis factor inhibitor; VTE = venous thrombotic event, HRT = hormone replacement therapy.

[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] TNF inhibitors.

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

[e] n=3 subjects were dispensed both baricitinib 4mg and 2mg at index date, are included in the overall « Baricitinib Any » group but not in the strata according to the dosage

Table 6.87. bDMARD-Experienced and bDMARD naïve: Clinical history at baseline - Incident Serious Infection cohort, Matched [SNDS]

bDMARD-experienced and bDMARD naïve are grouped in the table above

Table 6.88. bDMARD-Experienced: Clinical history at baseline - Hospitalized tuberculosis, Matched [SNDS]

Not applicable for SNDS data: no event

Table 6.89. bDMARD naïve: Clinical history at baseline - Hospitalized tuberculosis, Matched [SNDS]

Not applicable for SNDS data: no event

Table 6.90. bDMARD-Experienced and bDMARD naïve: Baseline healthcare resource utilization during baseline period - Unmatched cohort [SNDS]

	bDMARD-Experienced					bDMARD naïve				
Type of resource use during baseline period[a]	**Bari. Any[c] n = 1982**	**Bari. 4 mg n = 1661**	**Bari. 2 mg n = 317**	**TNFi n = 2374**	**Std. Diff. (Any vs TNFi)**	**Bari. Any n = 1260**	**Bari. 4 mg n = 955**	**Bari. 2 mg n = 305**	**TNFi n = 7828**	**Std. Diff. (Any vs TNFi)**
Physician Office Visits (rheumatologist visits excluded)										
n, patients (%)	1187 (59.9)	971 (58.5)	216 (68.1)	1497 (63.1)	-0.065	796 (63.2)	582 (60.9)	214 (70.2)	4928 (63.0)	0.005
n, events	3308	2653	655	4814		2308	1638	670	15494	
Mean (SD)	1.7 (2.4)	1.6 (2.3)	2.1 (2.7)	2.0 (3.0)	-0.132	1.8 (2.8)	1.7 (2.9)	2.2 (2.5)	2.0 (3.1)	-0.049
Median	1.0	1.0	1.0	1.0		1.0	1.0	1.0	1.0	
Min; Max	[0.0;25.0]	[0.0;25.0]	[0.0;19.0]	[0.0;43.0]		[0.0;41.0]	[0.0;41.0]	[0.0;13.0]	[0.0;85.0]	
Rheumatologist Visits										
n, patients (%)	1253 (63.2)	1057 (63.6)	194 (61.2)	1448 (61.0)	0.046	799 (63.4)	616 (64.5)	183 (60.0)	5071 (64.8)	-0.029
n, events	2850	2342	496	3171		1735	1350	385	11586	
Mean (SD)	1.4 (1.6)	1.4 (1.5)	1.6 (1.8)	1.3 (1.5)	0.066	1.4 (1.5)	1.4 (1.5)	1.3 (1.5)	1.5 (1.5)	-0.069
Median	1.0	1.0	1.0	1.0		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]		[0.0;8.0]	[0.0;8.0]	[0.0;8.0]	[0.0;10.0]	
Other Outpatient Visits										
n, patients (%)	1863 (94.0)	1550 (93.3)	310 (97.8)	2177 (91.7)	0.089	1161 (92.1)	868 (90.9)	293 (96.1)	7134 (91.1)	0.036
n, events	40769	29989	10663	40560		23719	14207	9512	116401	
Mean (SD)	20.6 (34.0)	18.1 (30.3)	33.6 (47.3)	17.1 (28.5)	0.111	18.8 (32.1)	14.9 (24.5)	31.2 (46.7)	14.9 (25.6)	0.136
Median	9.0	8.0	17.0	8.0		7.0	6.0	12.0	6.0	

	bDMARD-Experienced					bDMARD naïve				
Type of resource use during baseline period[a]	**Bari. Any[c] n = 1982**	**Bari. 4 mg n = 1661**	**Bari. 2 mg n = 317**	**TNFi n = 2374**	**Std. Diff. (Any vs TNFi)**	**Bari. Any n = 1260**	**Bari. 4 mg n = 955**	**Bari. 2 mg n = 305**	**TNFi n = 7828**	**Std. Diff. (Any vs TNFi)**
Min; Max	[0.0;322.0]	[0.0;322.0]	[0.0;266.0]	[0.0;280.0]		[0.0;247.0]	[0.0;236.0]	[0.0;247.0]	[0.0;283.0]	
Inpatient Visits[b]										
n, patients (%)	1046 (52.8)	852 (51.3)	192 (60.6)	1112 (46.8)	0.119	547 (43.4)	381 (39.9)	166 (54.4)	3690 (47.1)	-0.075
n, events	3153	2549	594	2921		831	550	281	5353	
Mean (SD)	1.6 (2.2)	1.5 (2.1)	1.9 (2.3)	1.2 (1.9)	0.178	0.7 (1.1)	0.6 (0.9)	0.9 (1.3)	0.7 (1.5)	-0.019
Median	1.0	1.0	1.0	0.0		0.0	0.0	1.0	0.0	
Min; Max	[0.0;14.0]	[0.0;14.0]	[0.0;12.0]	[0.0;16.0]		[0.0;12.0]	[0.0;12.0]	[0.0;12.0]	[0.0;76.0]	
ED Visits	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	
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 = standardized difference; TNFi = tumor necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

[a] Index date excluded

[b] Inpatient visits include number of hospitalisations

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

Table 6.91. bDMARD-Experienced and bDMARD naïve: Baseline healthcare resource utilization during baseline period - Unmatched cohort [SNDS]

bDMARD-experienced and bDMARD naïve are grouped in the table above

Table 6.92. bDMARD-Experienced and bDMARD naïve: Baseline healthcare resource utilization during baseline period - VTE cohort, Matched [SNDS]

	bDMARD-Experienced					bDMARD naïve				
Type of resource use during baseline period[b]	**Bari. Any[d] n = 1600**	**Bari. 4 mg n = 1350**	**Bari. 2 mg n = 248**	**TNFi[a] n = 1600**	**Std. Diff. (Any vs TNFi)**	**Bari. Any n = 1260**	**Bari. 4 mg n = 955**	**Bari. 2 mg n = 305**	**TNFi[a] n = 1260**	**Std. Diff. (Any vs TNFi)**
Physician Office Visits (rheumatologist visits excluded)										
n, patients (%)	968 (60.5)	796 (59.0)	172 (69.4)	989 (61.8)	-0.027	796 (63.2)	582 (60.9)	214 (70.2)	772 (61.3)	0.039
n, events	2707	2170	537	2984		2308	1638	670	2172	
Mean (SD)	1.7 (2.4)	1.6 (2.3)	2.2 (2.8)	1.9 (2.8)	-0.067	1.8 (2.8)	1.7 (2.9)	2.2 (2.5)	1.7 (3.2)	0.036
Median	1.0	1.0	1.0	1.0		1.0	1.0	1.0	1.0	
Min; Max	[0.0;25.0]	[0.0;25.0]	[0.0;19.0]	[0.0;27.0]		[0.0;41.0]	[0.0;41.0]	[0.0;13.0]	[0.0;49.0]	
Rheumatologist Visits										
n, patients (%)	1009 (63.1)	857 (63.5)	150 (60.5)	993 (62.1)	0.021	799 (63.4)	616 (64.5)	183 (60.0)	800 (63.5)	-0.002
n, events	2316	1921	383	2156		1735	1350	385	1796	
Mean (SD)	1.4 (1.6)	1.4 (1.6)	1.5 (1.8)	1.3 (1.5)	0.065	1.4 (1.5)	1.4 (1.5)	1.3 (1.5)	1.4 (1.5)	-0.033
Median	1.0	1.0	1.0	1.0		1.0	1.0	1.0	1.0	
Min; Max	[0.0;11.0]	[0.0;9.0]	[0.0;11.0]	[0.0;8.0]		[0.0;8.0]	[0.0;8.0]	[0.0;8.0]	[0.0;9.0]	

	bDMARD-Experienced					bDMARD naïve				
Type of resource use during baseline period[b]	**Bari. Any[d] n = 1600**	**Bari. 4 mg n = 1350**	**Bari. 2 mg n = 248**	**TNFi[a] n = 1600**	**Std. Diff. (Any vs TNFi)**	**Bari. Any n = 1260**	**Bari. 4 mg n = 955**	**Bari. 2 mg n = 305**	**TNFi[a] n = 1260**	**Std. Diff. (Any vs TNFi)**
Other Outpatient Visits										
n, patients (%)	1489 (93.1)	1246 (92.3)	241 (97.2)	1489 (93.1)	0.000	1161 (92.1)	868 (90.9)	293 (96.1)	1180 (93.7)	-0.059
n, events	30558	22825	7692	30943		23719	14207	9512	22580	
Mean (SD)	19.1 (31.4)	16.9 (28.0)	31.0 (43.8)	19.3 (31.4)	-0.008	18.8 (32.1)	14.9 (24.5)	31.2 (46.7)	17.9 (29.1)	0.030
Median	8.0	8.0	17.0	9.0		7.0	6.0	12.0	8.0	
Min; Max	[0.0;322.0]	[0.0;322.0]	[0.0;266.0]	[0.0;280.0]		[0.0;247.0]	[0.0;236.0]	[0.0;247.0]	[0.0;242.0]	
Inpatient Visits[c]										
n, patients (%)	796 (49.8)	648 (48.0)	148 (59.7)	743 (46.4)	0.066	547 (43.4)	381 (39.9)	166 (54.4)	529 (42.0)	0.029
n, events	2295	1868	427	2096		831	550	281	808	
Mean (SD)	1.4 (2.1)	1.4 (2.0)	1.7 (2.2)	1.3 (2.0)	0.061	0.7 (1.1)	0.6 (0.9)	0.9 (1.3)	0.6 (1.0)	0.018
Median	0.0	0.0	1.0	0.0		0.0	0.0	1.0	0.0	
Min; Max	[0.0;14.0]	[0.0;14.0]	[0.0;8.0]	[0.0;16.0]		[0.0;12.0]	[0.0;12.0]	[0.0;12.0]	[0.0;10.0]	
ED Visits										
n, patients (%)	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	
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 = standardized difference; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

[a] Matching ratio 1:1 is applied

[b] Index date excluded

[c] Inpatient visits include number of hospitalisations

[d] n=3 subjects were dispensed both baricitinib 4mg and 2mg at index date, are included in the overall « Baricitinib Any » group but not in the strata according to the dosage

Table 6.93. bDMARD-Experienced and bDMARD naïve: Baseline healthcare resource utilization during baseline period - VTE cohort, Matched [SNDS]

bDMARD-experienced and bDMARD naïve are grouped in the table above

Table 6.94. bDMARD-Experienced and bDMARD naïve: Baseline healthcare resource utilization during baseline period - MACE cohort, Matched [SNDS]

	bDMARD-Experienced					bDMARD naïve				
Type of resource use during baseline period[b]	**Bari. Any[d] n = 1606**	**Bari. 4 mg n = 1360**	**Bari. 2 mg n = 244**	**TNFi[a] n = 1606**	**Std. Diff. (Any vs TNFi)**	**Bari. Any n = 1257**	**Bari. 4 mg n = 954**	**Bari. 2 mg n = 303**	**TNFi[a] n = 1257**	**Std. Diff. (Any vs TNFi)**
Physician Office Visits (rheumatologist visits excluded)										
n, patients (%)	968 (60.3)	802 (59.0)	166 (68.0)	988 (61.5)	-0.026	793 (63.1)	581 (60.9)	212 (70.0)	761 (60.5)	0.052
n, events	2757	2226	531	2854		2303	1634	669	2078	
Mean (SD)	1.7 (2.4)	1.6 (2.3)	2.2 (2.9)	1.8 (2.6)	-0.024	1.8 (2.9)	1.7 (2.9)	2.2 (2.5)	1.7 (2.5)	0.066
Median	1.0	1.0	1.0	1.0		1.0	1.0	1.0	1.0	
Min; Max	[0.0;25.0]	[0.0;25.0]	[0.0;19.0]	[0.0;26.0]		[0.0;41.0]	[0.0;41.0]	[0.0;13.0]	[0.0;32.0]	
Rheumatologist Visits										
n, patients (%)	1015 (63.2)	860 (63.2)	154 (63.1)	1012 (63.0)	0.004	798 (63.5)	616 (64.6)	182 (60.1)	842 (67.0)	-0.074
n, events	2312	1920	386	2206		1735	1350	385	1905	
Mean (SD)	1.4 (1.6)	1.4 (1.5)	1.6 (1.7)	1.4 (1.5)	0.043	1.4 (1.5)	1.4 (1.5)	1.3 (1.5)	1.5 (1.5)	-0.091
Median	1.0	1.0	1.0	1.0		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]		[0.0;8.0]	[0.0;8.0]	[0.0;8.0]	[0.0;10.0]	
Other Outpatient Visits										
n, patients (%)	1502 (93.5)	1263 (92.9)	238 (97.5)	1481 (92.2)	0.051	1158 (92.1)	867 (90.9)	291 (96.0)	1156 (92.0)	0.006
n, events	32197	23744	8414	29945		23581	14164	9417	23506	

	bDMARD-Experienced					bDMARD naïve				
Type of resource use during baseline period[b]	**Bari. Any[d] n = 1606**	**Bari. 4 mg n = 1360**	**Bari. 2 mg n = 244**	**TNFi[a] n = 1606**	**Std. Diff. (Any vs TNFi)**	**Bari. Any n = 1257**	**Bari. 4 mg n = 954**	**Bari. 2 mg n = 303**	**TNFi[a] n = 1257**	**Std. Diff. (Any vs TNFi)**
Mean (SD)	20.0 (33.2)	17.5 (28.9)	34.5 (48.3)	18.6 (30.9)	0.044	18.8 (32.1)	14.8 (24.5)	31.1 (46.8)	18.7 (33.4)	0.002
Median	9.0	8.0	17.0	8.0		7.0	6.0	12.0	7.0	
Min; Max	[0.0;322.0]	[0.0;322.0]	[0.0;266.0]	[0.0;280.0]		[0.0;247.0]	[0.0;236.0]	[0.0;247.0]	[0.0;242.0]	
Inpatient Visits[c]										
n, patients (%)	801 (49.9)	656 (48.2)	144 (59.0)	727 (45.3)	0.092	544 (43.3)	380 (39.8)	164 (54.1)	583 (46.4)	-0.062
n, events	2278	1862	413	2082		821	548	273	953	
Mean (SD)	1.4 (2.0)	1.4 (2.0)	1.7 (2.2)	1.3 (2.0)	0.060	0.7 (1.0)	0.6 (0.9)	0.9 (1.3)	0.8 (1.8)	-0.070
Median	0.0	0.0	1.0	0.0		0.0	0.0	1.0	0.0	
Min; Max	[0.0;14.0]	[0.0;14.0]	[0.0;12.0]	[0.0;16.0]		[0.0;12.0]	[0.0;12.0]	[0.0;12.0]	[0.0;51.0]	
ED Visits	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	
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 = standardized difference; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

[a] Matching ratio 1:1 is applied

[b] Index date excluded

[c] Inpatient visits include number of hospitalisations

[d] n=3 subjects were dispensed both baricitinib 4mg and 2mg at index date, are included in the overall « Baricitinib Any » group but not in the strata according to the dosage

Table 6.95. bDMARD-Experienced and bDMARD naïve: Baseline healthcare resource utilization during baseline period - MACE cohort, Matched [SNDS]

bDMARD-experienced and bDMARD naïve are grouped in the table above

Table 6.96. bDMARD-Experienced and bDMARD naïve: Baseline healthcare resource utilization during baseline period – Incident Serious Infection Cohort, Matched [SNDS]

	bDMARD-Experienced					bDMARD naïve				
Type of resource use during baseline period[b]	**Bari. Any[d] n = 1643**	**Bari. 4 mg n = 1376**	**Bari. 2 mg n = 264**	**TNFi[a] n = 1643**	**Std. Diff. (Any vs TNFi)**	**Bari. Any n = 1319**	**Bari. 4 mg n = 985**	**Bari. 2 mg n = 334**	**TNFi[a] n = 1319**	**Std. Diff. (Any vs TNFi)**
Physician Office Visits (rheumatologist visits excluded)										
n, patients (%)	983 (59.8)	808 (58.7)	175 (66.3)	1016 (61.8)	-0.041	841 (63.8)	606 (61.5)	235 (70.4)	834 (63.2)	0.011
n, events	2819	2241	578	3168		2468	1720	748	2389	
Mean (SD)	1.7 (2.5)	1.6 (2.3)	2.2 (3.1)	1.9 (2.9)	-0.079	1.9 (2.8)	1.7 (2.9)	2.2 (2.5)	1.8 (3.5)	0.019
Median	1.0	1.0	1.0	1.0		1.0	1.0	1.0	1.0	
Min; Max	[0.0;25.0]	[0.0;25.0]	[0.0;20.0]	[0.0;27.0]		[0.0;41.0]	[0.0;41.0]	[0.0;13.0]	[0.0;85.0]	
Rheumatologist Visits										
n, patients (%)	1019 (62.0)	864 (62.8)	154 (58.3)	1014 (61.7)	0.006	836 (63.4)	638 (64.8)	198 (59.3)	828 (62.8)	0.013
n, events	2303	1916	381	2236		1825	1409	416	1865	
Mean (SD)	1.4 (1.6)	1.4 (1.5)	1.4 (1.8)	1.4 (1.5)	0.026	1.4 (1.5)	1.4 (1.5)	1.2 (1.4)	1.4 (1.5)	-0.020
Median	1.0	1.0	1.0	1.0		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]		[0.0;8.0]	[0.0;8.0]	[0.0;8.0]	[0.0;10.0]	
Other Outpatient Visits										
n, patients (%)	1535 (93.4)	1276 (92.7)	257 (97.3)	1520 (92.5)	0.036	1217 (92.3)	896 (91.0)	321 (96.1)	1236 (93.7)	-0.056
n, events	32247	23047	9085	31653		26249.0	14783	11466	26297	

	bDMARD-Experienced					bDMARD naïve				
Type of resource use during baseline period[b]	**Bari. Any[d] n = 1643**	**Bari. 4 mg n = 1376**	**Bari. 2 mg n = 264**	**TNFi[a] n = 1643**	**Std. Diff. (Any vs TNFi)**	**Bari. Any n = 1319**	**Bari. 4 mg n = 985**	**Bari. 2 mg n = 334**	**TNFi[a] n = 1319**	**Std. Diff. (Any vs TNFi)**
Mean (SD)	19.6 (32.3)	16.7 (27.6)	34.4 (47.7)	19.3 (31.7)	0.011	19.9 (34.5)	15.0 (25.1)	34.3 (50.6)	19.9 (33.2)	-0.001
Median	8.0	8.0	17.0	8.0		7.0	6.0	13.0	8.0	
Min; Max	[0.0;322.0]	[0.0;322.0]	[0.0;257.0]	[0.0;280.0]		[0.0;247.0]	[0.0;245.0]	[0.0;247.0]	[0.0;239.0]	
Inpatient Visits[c]										
n, patients (%)	830 (50.5)	671 (48.8)	157 (59.5)	751 (45.7)	0.096	585 (44.4)	398 (40.4)	187 (56.0)	607 (46.0)	-0.034
n, events	2395	1919	466	2107		884	572	312	940	
Mean (SD)	1.5 (2.1)	1.4 (2.1)	1.8 (2.3)	1.3 (2.0)	0.086	0.7 (1.0)	0.6 (0.9)	0.9 (1.3)	0.7 (1.1)	-0.040
Median	1.0	0.0	1.0	0.0		0.0	0.0	1.0	0.0	
Min; Max	[0.0;14.0]	[0.0;14.0]	[0.0;12.0]	[0.0;11.0]		[0.0;12.0]	[0.0;12.0]	[0.0;12.0]	[0.0;17.0]	
ED Visits	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	
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 = standardized difference; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

Note: Physician office visits do not include rheumatologist visits.

[a] Matching ratio 1:1 is applied

[b] Index date excluded

[c] Inpatient visits include number of hospitalisations

[d] n=3 subjects were dispensed both baricitinib 4mg and 2mg at index date, are included in the overall « Baricitinib Any » group but not in the strata according to the dosage

Table 6.97. bDMARD-Experienced and bDMARD naïve: Baseline healthcare resource utilization during baseline period - Incident Serious Infection Cohort, Matched [SNDS]

bDMARD-experienced and bDMARD naïve are grouped in the table above

Table 6.98. bDMARD-Experienced: Baseline healthcare resource utilization during baseline period - Hospitalized tuberculosis, Matched [SNDS]

Not applicable for SNDS data: no event

Table 6.99. bDMARD naïve: Baseline healthcare resource utilization during baseline period - Hospitalized tuberculosis, Matched [SNDS]

Not applicable for SNDS data: no event

Table 6.100. bDMARD-Experienced: Baseline Prevalence of Outcomes [SNDS]

Prevalence of outcome at baseline in each concerned cohort[a]	Unmatched									
	Baricitinib[b] Any		Baricitinib 4 mg		Baricitinib 2 mg		TNFi		Std. Diff. (Any vs TNFi)	
VTE, N population	1983		1662		317		2378			
VTE, n events (%)	≤ 10		≤ 10		0	(0.0)	≤ 10		-0.036	
MACE, N population	1983		1662		317		2378			
MACE, n events (%)	≤ 10		≤ 10		≤ 10		≤ 10		-0.006	
Serious infection, N population	2067		1718		345		2446			
Serious infection, n events (%)	23	(1.1)	≤ 10		13	(3.8)	16	(0.7)	0.049	
Hospitalized Tuberculosis, N population	2067		1718		345		2446			
Hospitalized Tuberculosis, n events (%)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0.000	

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 = standardized difference; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism, defined based on the case definitions.

[a] Baseline prevalence has been calculated for each distinct cohort for VTE, MACE, serious infection and hospitalized tuberculosis (each outcome is the last exclusion criteria for each concerned cohort).

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

Table 6.101. bDMARD-Naïve: Baseline Prevalence of Outcomes [SNDS]

Prevalence of outcome at baseline in each concerned cohort[a]	Unmatched				
	Baricitinib Any	Baricitinib 4 mg	Baricitinib 2 mg	TNFi	Std. Diff. (Any vs TNFi)
VTE, N population	1261	955	306	7834	
VTE, n events (%)	≤ 10	0 (0.0)	≤ 10	≤ 10	0.001
MACE, N population	1261	955	306	7834	
MACE, n events (%)	≤ 10	≤ 10	≤ 10	29 (0.4)	-0.041
Serious infection, N population	1331	990	341	8069	
Serious infection, n events (%)	≤ 10	≤ 10	≤ 10	48 (0.6)	0.010
Hospitalized Tuberculosis, N population	1331	990	341	8069	
Hospitalized Tuberculosis, n events (%)	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.027

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 = standardized difference; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism, defined based on the case definitions.

[a] Baseline prevalence has been calculated for each distinct cohort for VTE, MACE, serious infection and hospitalized tuberculosis (each outcome is the last exclusion criteria for each concerned cohort).

5.2 CHARACTERISTICS OF PATIENTS UNDER FOLLOW-UP

Table 6.102. bDMARD-Experienced and bDMARD naïve: Duration of follow-up period (in days) - Unmatched cohort [SNDS]

	bDMARD-Experienced					bDMARD naïve				
	Bari. Any [a] n = 1982	Bari. 4 mg n = 1661	Bari. 2 mg n = 317	TNFi n = 2374	Std. Diff. (Any vs TNFi)	Bari. Any n = 1260	Bari. 4 mg n = 955	Bari. 2 mg n = 305	TNFi n = 7828	Std. Diff. (Any vs TNFi)
Duration of follow-up period (in days)					-0.017					-0.07
N (missing)	1982 (0)	1661 (0)	317 (0)	2374 (0)		1260 (0)	955 (0)	305 (0)	7828 (0)	
Mean (SD)	247.8 (199.8)	249.8 (200.7)	236.1 (194.5)	251.2 (209.3)		222.8 (190.3)	228.3 (191.5)	205.5 (185.7)	236.5 (203.2)	
Median	183.0	186.0	172.0	178.0		159.5	168.0	137.0	167.0	
Min; Max	[1.0;831.0]	[1.0;831.0]	[1.0;824.0]	[0.0;851.0]		[0.0;826.0]	[4.0;822.0]	[0.0;826.0]	[0.0;851.0]	
Reason for censoring, n (%)										
Switch	390 (19.7)	329 (19.8)	59 (18.6)	550 (23.2)	-0.085	99 (7.9)	82 (8.6)	17 (5.6)	972 (12.4)	-0.152
Discontinuation	617 (31.1)	509 (30.6)	107 (33.8)	975 (41.1)	-0.208	479 (38.0)	346 (36.2)	133 (43.6)	3714 (47.4)	-0.192
Outcome	14 (0.7)	11 (0.7)	≤ 10	≤ 10	0.051	≤ 10	≤ 10	≤ 10	21 (0.3)	0.064
Death	≤ 10	≤ 10	≤ 10	≤ 10	0.018	≤ 10	≤ 10	≤ 10	≤ 10	0.044
End of study (31/12/2019)	954 (48.1)	809 (48.7)	144 (45.4)	835 (35.2)	0.265	669 (53.1)	520 (54.5)	149 (48.9)	3112 (39.8)	0.270

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor.

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

Table 6.103. bDMARD-Experienced and bDMARD naïve: Duration of follow-up period (in days) - Unmatched cohort [SNDS]

bDMARD-experienced and bDMARD naïve are grouped in the table above

Table 6.104. bDMARD-Experienced and bDMARD naïve: Duration of follow-up period (in days) - VTE cohort, Matched [SNDS]

	bDMARD-Experienced					bDMARD naïve				
	Bari. Any[b] n = 1600	Bari. 4 mg n = 1350	Bari. 2 mg n = 248	TNFi [a] n = 1600	Std. Diff. (Any vs TNFi)	Bari. Any n = 1260	Bari. 4 mg n = 955	Bari. 2 mg n = 305	TNFi [a] n = 1260	Std. Diff. (Any vs TNFi)
Duration of follow-up period (in days)					-0.021					-0.017
N (missing)	1600 (0)	1350 (0)	248 (0)	1600 (0)		1260 (0)	955 (0)	305 (0)	1260 (0)	
Mean (SD)	245.5 (196.7)	247.2 (197.1)	234.8 (194.0)	249.8 (206.9)		222.8 (190.3)	228.3 (191.5)	205.5 (185.7)	226.2 (197.9)	
Median	180.5	182.5	165.5	177.0		159.5	168.0	137.0	157.0	
Min; Max	[1.0;831.0]	[1.0;831.0]	[1.0;824.0]	[0.0;851.0]		[0.0;826.0]	[4.0;822.0]	[0.0;826.0]	[1.0;851.0]	
Reason for censoring, n (%)										
Switch	310 (19.4)	267 (19.8)	43 (17.3)	371 (23.2)	-0.093	99 (7.9)	82 (8.6)	17 (5.6)	158 (12.5)	-0.155
Discontinuation	491 (30.7)	406 (30.1)	84 (33.9)	640 (40.0)	-0.196	479 (38.0)	346 (36.2)	133 (43.6)	614 (48.7)	-0.218
Outcome	11 (0.7)	≤ 10	≤ 10	≤ 10	0.024	≤ 10	≤ 10	≤ 10	≤ 10	0.084
Death	≤ 10	≤ 10	≤ 10	≤ 10	0.021	≤ 10	≤ 10	≤ 10	≤ 10	0.015
End of study (31/12/2019)	781 (48.8)	665 (49.3)	115 (46.4)	576 (36.0)	0.262	669 (53.1)	520 (54.5)	149 (48.9)	483 (38.3)	0.300

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor; VTE = venous thrombotic event.

[a] Matching ratio 1:1 is applied

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

Table 6.105. bDMARD-Experienced and bDMARD naïve: Duration of follow-up period (in days) - VTE cohort, Matched [SNDS]

bDMARD-experienced and bDMARD naïve are grouped in the table above

Table 6.106. bDMARD-Experienced and bDMARD naïve: Duration of follow-up period (in days) - MACE cohort, Matched [SNDS]

	bDMARD-Experienced					bDMARD naïve				
	Bari. Any[b] n = 1606	Bari. 4 mg n = 1360	Bari. 2 mg n = 244	TNFi [a] n = 1606	Std. Diff. (Any vs TNFi)	Bari. Any n = 1257	Bari. 4 mg n = 954	Bari. 2 mg n = 303	TNFi [a] n = 1257	Std. Diff. (Any vs TNFi)
Duration of follow-up period (in days)					-0.022					-0.095
N (missing)	1606 (0)	1360 (0)	244 (0)	1606 (0)		1257 (0)	954 (0)	303 (0)	1257 (0)	
Mean (SD)	244.5 (196.6)	247.0 (198.0)	230.6 (189.2)	248.9 (206.6)		222.2 (189.6)	228.0 (191.1)	203.9 (183.8)	240.9 (202.1)	
Median	181.0	182.0	166.0	178.0		159.0	168.0	137.0	170.0	
Min; Max	[1.0;831.0]	[1.0;831.0]	[1.0;824.0]	[1.0;851.0]		[0.0;826.0]	[4.0;822.0]	[0.0;826.0]	[2.0;851.0]	
Reason for censoring, n (%)										
Switch	311 (19.4)	265 (19.5)	45 (18.4)	362 (22.5)	-0.078	99 (7.9)	82 (8.6)	17 (5.6)	146 (11.6)	-0.126
Discontinuation	507 (31.6)	421 (31.0)	85 (34.8)	647 (40.3)	-0.182	480 (38.2)	347 (36.4)	133 (43.9)	584 (46.5)	-0.168
Outcome	16 (1.0)	11 (0.8)	≤ 10	≤ 10	0.076	≤ 10	≤ 10	≤ 10	≤ 10	0.020
Death	≤ 10	≤ 10	≤ 10	≤ 10	0.000	≤ 10	≤ 10	≤ 10	0 (0.0)	0.080
End of study (31/12/2019)	767 (47.8)	662 (48.7)	105 (43.0)	586 (36.5)	0.23	665 (52.9)	518 (54.3)	147 (48.5)	520 (41.4)	0.233

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor; VTE = venous thrombotic event.

[a] Matching ratio 1:1 is applied

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

Table 6.107. bDMARD-Experienced and bDMARD naïve: Duration of follow-up period (in days) - MACE cohort, Matched [SNDS]

bDMARD-experienced and bDMARD naïve are grouped in the table above

Table 6.108. bDMARD-Experienced and bDMARD naïve: Duration of follow-up period (in days) - Incident Serious Infection Cohort, Matched [SNDS]

	bDMARD-Experienced					bDMARD naïve				
	Bari. Any[b] n = 1643	Bari. 4 mg n = 1376	Bari. 2 mg n = 264	TNFi [a] n = 1643	Std. Diff. (Any vs TNFi)	Bari. Any n = 1319	Bari. 4 mg n = 985	Bari. 2 mg n = 334	TNFi [a] n = 1319	Std. Diff. (Any vs TNFi)
Duration of follow-up period (in days)					-0.046					-0.103
N (missing)	1643 (0)	1376 (0)	264 (0)	1643 (0)		1319 (0)	985 (0)	334 (0)	1319 (0)	
Mean (SD)	243.3 (197.7)	244.3 (196.8)	238.5 (203.4)	252.6 (208.0)		221.9 (188.2)	227.8 (189.6)	204.3 (183.1)	242.3 (208.2)	
Median	178.0	180.5	148.5	183.0		160.0	168.0	136.5	165.0	
Min; Max	[1.0;831.0]	[1.0;831.0]	[1.0;824.0]	[0.0;851.0]		[0.0;826.0]	[4.0;822.0]	[0.0;826.0]	[1.0;851.0]	
Reason for censoring, n (%)										
Switch	328 (20.0)	271 (19.7)	55 (20.8)	380 (23.1)	-0.077	102 (7.7)	82 (8.3)	20 (6.0)	163 (12.4)	-0.154
Discontinuation	513 (31.2)	424 (30.8)	88 (33.3)	633 (38.5)	-0.154	499 (37.8)	352 (35.7)	147 (44.0)	595 (45.1)	-0.148
Outcome	19 (1.2)	12 (0.9)	≤ 10	21 (1.3)	-0.011	17 (1.3)	11 (1.1)	≤ 10	11 (0.8)	0.044
Death	≤ 10	≤ 10	≤ 10	≤ 10	-0.025	≤ 10	≤ 10	≤ 10	≤ 10	0.028
End of study (31/12/2019)	780 (47.5)	668 (48.5)	112 (42.4)	604 (36.8)	0.218	696 (52.8)	538 (54.6)	158 (47.3)	547 (41.5)	0.228

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor; VTE = venous thrombotic event.

[a] Matching ratio 1:1 is applied

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

Table 6.109. bDMARD-Experienced and bDMARD naïve: Duration of follow-up period (in days) - Incident Serious Infection Cohort, Matched [SNDS]

bDMARD-experienced and bDMARD naïve are grouped in the table above

Table 6.110. bDMARD-Experienced: Duration of follow-up period (in days)- Hospitalized tuberculosis, Matched [SNDS]

Not applicable for SNDS data: no event

Table 6.111. bDMARD naïve: Duration of follow-up period (in days)- Hospitalized tuberculosis, Matched [SNDS]

Not applicable for SNDS data: no event

5.3 CHARACTERISTICS OF PATIENTS BY EXPOSURE DURATION

5.3.1 BASELINE CHARACTERISTICS BY EXPOSURE DURATION

Table 6.112. bDMARD-Experienced: Baseline characteristics by exposure duration, Unmatched cohort [SNDS]

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 988	TNFi n = 1210	Std. Diff.	Baricitinib n = 499	TNFi n = 616	Std. Diff.	Baricitinib n = 441	TNFi n = 444	Std. Diff.	Baricitinib n = 54	TNFi n = 104	Std. Diff.
Age [in years]			0.227			0.224			0.214			0.110
N (missing)	988 (0)	1210 (0)		499 (0)	616 (0)		441 (0)	444 (0)		54 (0)	104 (0)	
Mean (SD)	57.8 (13.7)	54.6 (14.3)		58.9 (12.9)	55.8 (14.4)		59.5 (12.0)	56.7 (13.4)		58.0 (11.4)	56.8 (11.3)	
Median	58.0	55.0		60.0	57.0		61.0	57.0		58.5	57.5	
Min; Max	[18.0;90.0]	[18.0;89.0]		[21.0;89.0]	[18.0;91.0]		[20.0;92.0]	[18.0;90.0]		[32.0;77.0]	[26.0;83.0]	
Sex, n (%)			-0.103			-0.095			0.052			-0.022
Male	179 (18.1)	269 (22.2)		95 (19.0)	141 (22.9)		109 (24.7)	100 (22.5)		13 (24.1)	26 (25.0)	
Female	809 (81.9)	941 (77.8)		404 (81.0)	475 (77.1)		332 (75.3)	344 (77.5)		41 (75.9)	78 (75.0)	
Clinical conditions during baseline period, n (%)												
Cancer, excluding NMSC	21 (2.1)	28 (2.3)	-0.013	11 (2.2)	23 (3.7)	-0.090	12 (2.7)	11 (2.5)	0.015	≤ 10	0 (0.0)	0.194
NMSC	0 (0.0)	0 (0.0)	0.000	≤ 10	≤ 10	0.092	0 (0.0)	0 (0.0)	0.000	0 (0.0)	≤ 10	-0.139
Chronic lung disease, excluding cystic fibrosis[c]	136 (13.8)	132 (10.9)	0.087	64 (12.8)	63 (10.2)	0.081	63 (14.3)	47 (10.6)	0.112	≤ 10	≤ 10	-0.046
Cardiovascular conditions												

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 988	TNFi n = 1210	Std. Diff.	Baricitinib n = 499	TNFi n = 616	Std. Diff.	Baricitinib n = 441	TNFi n = 444	Std. Diff.	Baricitinib n = 54	TNFi n = 104	Std. Diff.
Atrial arrhythmia/fibrillation	11 (1.1)	≤ 10	0.093	≤ 10	≤ 10	0.101	≤ 10	≤ 10	-0.047	0 (0.0)	0 (0.0)	0.000
Cardiovascular revascularization	≤ 10	≤ 10	-0.038	≤ 10	≤ 10	-0.049	≤ 10	0 (0.0)	0.117	0 (0.0)	0 (0.0)	0.000
Congestive Heart Failure, hospitalized	≤ 10	≤ 10	0.040	≤ 10	≤ 10	-0.024	≤ 10	≤ 10	0.001	0 (0.0)	0 (0.0)	0.000
Coronary artery disease	25 (2.5)	43 (3.6)	-0.060	22 (4.4)	29 (4.7)	-0.014	23 (5.2)	18 (4.1)	0.055	≤ 10	≤ 10	0.192
Unstable angina	0 (0.0)	0 (0.0)	0.000	0 (0.0)	≤ 10	-0.057	0 (0.0)	≤ 10	-0.067	0 (0.0)	0 (0.0)	0.000
Ventricular arrhythmia	≤ 10	≤ 10	-0.035	≤ 10	≤ 10	-0.006	≤ 10	≤ 10	-0.09	0 (0.0)	0 (0.0)	0.000
Stroke	≤ 10	≤ 10	0.016	≤ 10	≤ 10	0.075	≤ 10	≤ 10	0.001	0 (0.0)	≤ 10	-0.139
Hemorrhagic	≤ 10	0 (0.0)	0.045	≤ 10	≤ 10	0.009	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Ischemic	≤ 10	≤ 10	0.032	≤ 10	≤ 10	0.071	≤ 10	≤ 10	0.000	0 (0.0)	0 (0.0)	0.000
Unknown	≤ 10	≤ 10	-0.014	≤ 10	≤ 10	0.101	≤ 10	≤ 10	0.026	0 (0.0)	≤ 10	-0.139
TIA	≤ 10	≤ 10	0.006	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Diabetes Mellitus[c]	95 (9.6)	124 (10.2)	-0.021	56 (11.2)	65 (10.6)	0.022	56 (12.7)	37 (8.3)	0.143	≤ 10	13 (12.5)	-0.171
Treated insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Treated non insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Dyslipidemia (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 988	TNFi n = 1210	Std. Diff.	Baricitinib n = 499	TNFi n = 616	Std. Diff.	Baricitinib n = 441	TNFi n = 444	Std. Diff.	Baricitinib n = 54	TNFi n = 104	Std. Diff.
Hypertension (not available in SNDS)												
History of hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Current hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Immune disorders	41 (4.1)	40 (3.3)	0.045	13 (2.6)	20 (3.2)	-0.038	17 (3.9)	14 (3.2)	0.038	0 (0.0)	≤ 10	-0.139
AIDS/HIV	0 (0.0)	≤ 10	-0.041	0 (0.0)	0 (0.0)	0.000	0 (0.0)	≤ 10	-0.067	0 (0.0)	0 (0.0)	0.000
Antiphospholipid syndrome	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
SLE	13 (1.3)	≤ 10	0.098	≤ 10	≤ 10	0.009	≤ 10	0 (0.0)	0.117	0 (0.0)	0 (0.0)	0.000
Primary Sjogren Syndrome	29 (2.9)	35 (2.9)	0.003	12 (2.4)	19 (3.1)	-0.042	15 (3.4)	13 (2.9)	0.027	0 (0.0)	≤ 10	-0.139
Liver or pancreatic disorder[c]	29 (2.9)	34 (2.8)	0.008	16 (3.2)	25 (4.1)	-0.046	22 (5.0)	13 (2.9)	0.106	≤ 10	≤ 10	0.081
Obesity (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date)	≤ 10	≤ 10	-0.079	≤ 10	≤ 10	-0.128	0 (0.0)	≤ 10	-0.095	0 (0.0)	0 (0.0)	0.000
RA Severity (CIRAS Index)			-0.107			-0.126			-0.034			0.054
Mean (SD)	6.5 (1.4)	6.6 (1.4)		6.3 (1.2)	6.5 (1.4)		6.4 (1.3)	6.4 (1.3)		6.7 (1.3)	6.6 (1.3)	

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 988	TNFi n = 1210	Std. Diff.	Baricitinib n = 499	TNFi n = 616	Std. Diff.	Baricitinib n = 441	TNFi n = 444	Std. Diff.	Baricitinib n = 54	TNFi n = 104	Std. Diff.
DMARDs, n (%)												
cDMARDs, during baseline period												
n, total (%)	591 (59.8)	713 (58.9)	0.018	322 (64.5)	380 (61.7)	0.059	293 (66.4)	281 (63.3)	0.066	39 (72.2)	75 (72.1)	0.002
Mean (SD)	0.6 (0.5)	0.6 (0.5)	0.010	0.7 (0.6)	0.6 (0.5)	0.081	0.7 (0.6)	0.7 (0.5)	0.077	0.8 (0.6)	0.8 (0.5)	0.084
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	
Min; Max	[0.0;3.0]	[0.0;3.0]		[0.0;3.0]	[0.0;3.0]		[0.0;4.0]	[0.0;2.0]		[0.0;3.0]	[0.0;2.0]	
>1 cDMARD concomitantly	25 (2.5)	30 (2.5)	0.003	14 (2.8)	15 (2.4)	0.023	18 (4.1)	16 (3.6)	0.025	≤ 10	≤ 10	0.108
Hydroxychloroquine	27 (2.7)	38 (3.1)	-0.024	18 (3.6)	18 (2.9)	0.039	20 (4.5)	13 (2.9)	0.085	≤ 10	≤ 10	0.046
Chloroquine	0 (0.0)	≤ 10	-0.041	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	≤ 10	0 (0.0)	0.194
Azathioprin	≤ 10	≤ 10	-0.001	≤ 10	≤ 10	0.009	≤ 10	≤ 10	-0.025	≤ 10	0 (0.0)	0.194
Leflunomide	106 (10.7)	97 (8.0)	0.093	53 (10.6)	49 (8.0)	0.092	46 (10.4)	44 (9.9)	0.017	≤ 10	≤ 10	0.398
Methotrexate	464 (47.0)	570 (47.1)	-0.003	262 (52.5)	313 (50.8)	0.034	234 (53.1)	230 (51.8)	0.025	26 (48.1)	68 (65.4)	-0.353
Mycophenolate mofetil	0 (0.0)	≤ 10	-0.041	0 (0.0)	≤ 10	-0.057	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Sulfasalazin	15 (1.5)	35 (2.9)	-0.094	≤ 10	13 (2.1)	-0.038	12 (2.7)	≤ 10	0.097	≤ 10	≤ 10	0.261
Cyclosporin	0 (0.0)	≤ 10	-0.041	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Penicillamin	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	≤ 10	-0.067	0 (0.0)	0 (0.0)	0.000
bDMARDs, during baseline period												
n, total (%)	988 (100.0)	1210 (100.0)	0.000	499 (100.0)	616 (100.0)	0.000	441 (100.0)	444 (100.0)	0.000	54 (100.0)	104 (100.0)	0.000
Mean (SD)	1.1 (0.3)	1.1 (0.2)	0.221	1.1 (0.4)	1.1 (0.3)	0.233	1.1 (0.3)	1.0 (0.2)	0.261	1.2 (0.4)	1.1 (0.2)	0.484
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 988	TNFi n = 1210	Std. Diff.	Baricitinib n = 499	TNFi n = 616	Std. Diff.	Baricitinib n = 441	TNFi n = 444	Std. Diff.	Baricitinib n = 54	TNFi n = 104	Std. Diff.
Min; Max	[1.0;3.0]	[1.0;3.0]		[1.0;3.0]	[1.0;2.0]		[1.0;3.0]	[1.0;2.0]		[1.0;2.0]	[1.0;2.0]	
cDMARDs, concomitant	508 (51.4)	628 (51.9)	-0.010	289 (57.9)	347 (56.3)	0.032	247 (56.0)	259 (58.3)	-0.047	32 (59.3)	70 (67.3)	-0.168
Adalimumab[b]	129 (13.1)	195 (16.1)	-0.087	57 (11.4)	107 (17.4)	-0.17	59 (13.4)	76 (17.1)	-0.104	≤ 10	30 (28.8)	-0.345
Certolizumab pegol[b]	75 (7.6)	75 (6.2)	0.055	43 (8.6)	40 (6.5)	0.08	31 (7.0)	26 (5.9)	0.048	≤ 10	≤ 10	0.192
Etanercept[b]	200 (20.2)	348 (28.8)	-0.199	92 (18.4)	173 (28.1)	-0.23	64 (14.5)	118 (26.6)	-0.302	≤ 10	25 (24.0)	-0.539
Golimumab[b]	66 (6.7)	79 (6.5)	0.006	33 (6.6)	29 (4.7)	0.083	30 (6.8)	29 (6.5)	0.011	≤ 10	≤ 10	-0.121
Infliximab[b]	48 (4.9)	96 (7.9)	-0.126	24 (4.8)	44 (7.1)	-0.099	18 (4.1)	35 (7.9)	-0.161	≤ 10	≤ 10	-0.239
Rituximab	47 (4.8)	18 (1.5)	0.189	31 (6.2)	15 (2.4)	0.187	33 (7.5)	≤ 10	0.366	11 (20.4)	≤ 10	0.567
Sarilumab	33 (3.3)	18 (1.5)	0.121	14 (2.8)	≤ 10	0.093	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Abatacept	262 (26.5)	247 (20.4)	0.144	148 (29.7)	131 (21.3)	0.194	129 (29.3)	100 (22.5)	0.154	17 (31.5)	12 (11.5)	0.500
Tocilizumab	242 (24.5)	198 (16.4)	0.203	123 (24.6)	104 (16.9)	0.192	127 (28.8)	75 (16.9)	0.287	14 (25.9)	12 (11.5)	0.375
Anakinra	≤ 10	≤ 10	0.028	≤ 10	≤ 10	0.006	≤ 10	≤ 10	-0.03	0 (0.0)	0 (0.0)	0.000
TNFi naïve at baseline	501 (50.7)	428 (35.4)	0.314	268 (53.7)	227 (36.9)	0.344	251 (56.9)	164 (36.9)	0.409	33 (61.1)	24 (23.1)	0.835
≥1 dispensing of bDMARD within 730 days before index date (excluded), n (%)	988 (100.0)	1210 (100.0)	0.000	499 (100.0)	616 (100.0)	0.000	441 (100.0)	444 (100.0)	0.000	54 (100.0)	104 (100.0)	0.000
Other prescription medications during baseline period, n (%)												
Antibiotics	433 (43.8)	512 (42.3)	0.031	215 (43.1)	288 (46.8)	-0.074	195 (44.2)	184 (41.4)	0.056	24 (44.4)	36 (34.6)	0.202

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 988	TNFi n = 1210	Std. Diff.	Baricitinib n = 499	TNFi n = 616	Std. Diff.	Baricitinib n = 441	TNFi n = 444	Std. Diff.	Baricitinib n = 54	TNFi n = 104	Std. Diff.
Antidiabetic agents	97 (9.8)	114 (9.4)	0.013	51 (10.2)	61 (9.9)	0.011	53 (12.0)	37 (8.3)	0.122	≤ 10	14 (13.5)	-0.133
Insulins	42 (4.3)	54 (4.5)	-0.010	21 (4.2)	14 (2.3)	0.110	15 (3.4)	11 (2.5)	0.055	≤ 10	≤ 10	-0.008
Non-insulins	73 (7.4)	87 (7.2)	0.008	42 (8.4)	51 (8.3)	0.005	45 (10.2)	31 (7.0)	0.115	≤ 10	13 (12.5)	-0.171
Cardiovascular												
Antithrombotic agents	131 (13.3)	169 (14.0)	-0.021	83 (16.6)	84 (13.6)	0.084	73 (16.6)	56 (12.6)	0.112	≤ 10	23 (22.1)	-0.189
Anticoagulant	34 (3.4)	47 (3.9)	-0.024	20 (4.0)	19 (3.1)	0.05	14 (3.2)	13 (2.9)	0.014	≤ 10	≤ 10	-0.206
Antiplatelet	105 (10.6)	130 (10.7)	-0.004	67 (13.4)	67 (10.9)	0.078	60 (13.6)	46 (10.4)	0.100	≤ 10	19 (18.3)	-0.147
Antihypertensives	309 (31.3)	377 (31.2)	0.003	180 (36.1)	210 (34.1)	0.042	179 (40.6)	154 (34.7)	0.122	25 (46.3)	38 (36.5)	0.199
Angiotensin converting enzyme inhibitors (ACE)	82 (8.3)	114 (9.4)	-0.040	41 (8.2)	58 (9.4)	-0.042	57 (12.9)	38 (8.6)	0.141	≤ 10	≤ 10	0.249
Angiotensin receptor blockers (ARB)	118 (11.9)	137 (11.3)	0.019	70 (14.0)	99 (16.1)	-0.057	64 (14.5)	70 (15.8)	-0.035	≤ 10	17 (16.3)	-0.213
Beta blocker	126 (12.8)	153 (12.6)	0.003	69 (13.8)	86 (14.0)	-0.004	78 (17.7)	68 (15.3)	0.064	14 (25.9)	16 (15.4)	0.263
Calcium channel blocker	90 (9.1)	116 (9.6)	-0.016	58 (11.6)	64 (10.4)	0.039	54 (12.2)	37 (8.3)	0.129	≤ 10	19 (18.3)	-0.147
Nitrates	≤ 10	≤ 10	-0.014	≤ 10	≤ 10	-0.072	≤ 10	≤ 10	0.073	0 (0.0)	≤ 10	-0.139
Acyclovir	≤ 10	≤ 10	-0.030	0 (0.0)	≤ 10	-0.152	≤ 10	≤ 10	0.001	0 (0.0)	≤ 10	-0.198
Valacyclovir	39 (3.9)	59 (4.9)	-0.045	20 (4.0)	32 (5.2)	-0.057	28 (6.3)	18 (4.1)	0.104	≤ 10	≤ 10	-0.005
Hormonal	135 (13.7)	199 (16.4)	-0.078	72 (14.4)	91 (14.8)	-0.010	56 (12.7)	55 (12.4)	0.009	≤ 10	15 (14.4)	0.062

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 988	TNFi n = 1210	Std. Diff.	Baricitinib n = 499	TNFi n = 616	Std. Diff.	Baricitinib n = 441	TNFi n = 444	Std. Diff.	Baricitinib n = 54	TNFi n = 104	Std. Diff.
HRT	81 (8.2)	105 (8.7)	-0.017	38 (7.6)	43 (7.0)	0.024	37 (8.4)	29 (6.5)	0.071	≤ 10	≤ 10	0.082
Oral Contraceptives	53 (5.4)	97 (8.0)	-0.106	36 (7.2)	40 (6.5)	0.029	18 (4.1)	26 (5.9)	-0.082	≤ 10	≤ 10	-0.086
SERMs	≤ 10	≤ 10	0.032	0 (0.0)	≤ 10	-0.128	≤ 10	≤ 10	0.001	≤ 10	0 (0.0)	0.194
Topic with progestogens and/or estrogens	≤ 10	≤ 10	0.029	≤ 10	≤ 10	-0.069	≤ 10	≤ 10	0.039	0 (0.0)	0 (0.0)	0
Lipid-lowering agents	158 (16.0)	189 (15.6)	0.01	84 (16.8)	92 (14.9)	0.052	87 (19.7)	65 (14.6)	0.135	11 (20.4)	25 (24.0)	-0.088
HMG CoA reductase inhibitors	126 (12.8)	149 (12.3)	0.013	71 (14.2)	81 (13.1)	0.031	68 (15.4)	47 (10.6)	0.144	≤ 10	22 (21.2)	-0.115
Fibrates	16 (1.6)	21 (1.7)	-0.009	≤ 10	≤ 10	0.117	≤ 10	≤ 10	0.001	0 (0.0)	0 (0.0)	0.000
Bile acid sequestrants	≤ 10	≤ 10	0.014	≤ 10	≤ 10	0.013	≤ 10	≤ 10	0.000	0 (0.0)	≤ 10	-0.139
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Other lipid modifying agents	≤ 10	14 (1.2)	-0.035	≤ 10	≤ 10	0.016	≤ 10	≤ 10	0.026	0 (0.0)	0 (0.0)	0.000
Lipid modifying agents, combinations	≤ 10	14 (1.2)	-0.024	≤ 10	≤ 10	-0.018	≤ 10	≤ 10	-0.017	≤ 10	≤ 10	0.108
Rheumatoid arthritis-related												
Aspirin	16 (1.6)	16 (1.3)	0.025	≤ 10	12 (1.9)	-0.079	≤ 10	≤ 10	0.110	0 (0.0)	0 (0.0)	0.000
Cox-2 Inhibitor	59 (6.0)	81 (6.7)	-0.030	29 (5.8)	36 (5.8)	-0.001	25 (5.7)	27 (6.1)	-0.018	≤ 10	≤ 10	-0.339
NSAIDs	362 (36.6)	492 (40.7)	-0.083	172 (34.5)	239 (38.8)	-0.09	148 (33.6)	184 (41.4)	-0.163	17 (31.5)	41 (39.4)	-0.167
Glucocorticosteroid	734 (74.3)	745 (61.6)	0.275	362 (72.5)	383 (62.2)	0.223	295 (66.9)	268 (60.4)	0.136	38 (70.4)	57 (54.8)	0.326

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 988	TNFi n = 1210	Std. Diff.	Baricitinib n = 499	TNFi n = 616	Std. Diff.	Baricitinib n = 441	TNFi n = 444	Std. Diff.	Baricitinib n = 54	TNFi n = 104	Std. Diff.
Vaccines	249 (25.2)	288 (23.8)	0.033	149 (29.9)	178 (28.9)	0.021	117 (26.5)	116 (26.1)	0.009	17 (31.5)	16 (15.4)	0.387
Antineoplastic agents	≤ 10	≤ 10	-0.079	≤ 10	≤ 10	0.045	0 (0.0)	≤ 10	-0.067	0 (0.0)	0 (0.0)	0.000

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; DMARD = disease-modifying antirheumatic drugs; hosp = hospitalized; HRT = hormone replacement therapy; Max = maximum; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Min = minimum; mos = months; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulator; Std. Diff. = standardized difference; TNF = tumor necrosis factor; TNFi = tumor 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] TNF inhibitors.

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

Table 6.113. bDMARD-Naïve: Baseline characteristics by exposure duration, Unmatched cohort[SNDS]

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 698	TNFi n = 4162	Std. Diff.	Baricitinib n = 302	TNFi n = 1927	Std. Diff.	Baricitinib n = 235	TNFi n = 1466	Std. Diff.	Baricitinib n = 25	TNFi n = 273	Std. Diff.
Age [in years]			0.361			0.404			0.259			0.051
N (missing)	698 (0)	4162 (0)		302 (0)	1927 (0)		235 (0)	1466 (0)		25 (0)	273 (0)	
Mean (SD)	59.3 (13.4)	54.3 (14.4)		60.7 (13.1)	55.2 (13.9)		58.7 (12.9)	55.3 (14.0)		57.3 (12.1)	56.7 (13.6)	
Median	60.0	55.0		61.0	56.0		58.0	56.0		61.0	56.0	
Min; Max	[20.0;89.0]	[18.0;94.0]		[19.0;86.0]	[18.0;90.0]		[22.0;86.0]	[18.0;93.0]		[30.0;76.0]	[19.0;84.0]	
Sex, n (%)			-0.186			-0.209			-0.099			-0.225
Male	131 (18.8)	1103 (26.5)		60 (19.9)	555 (28.8)		53 (22.6)	393 (26.8)		≤ 10	81 (29.7)	
Female	567 (81.2)	3059 (73.5)		242 (80.1)	1372 (71.2)		182 (77.4)	1073 (73.2)		20 (80.0)	192 (70.3)	
Clinical conditions during baseline period, n (%)												
Cancer, excluding NMSC	33 (4.7)	119 (2.9)	0.098	11 (3.6)	59 (3.1)	0.032	≤ 10	51 (3.5)	-0.054	0 (0.0)	≤ 10	-0.276
NMSC	≤ 10	≤ 10	0.009	0 (0.0)	≤ 10	-0.072	0 (0.0)	≤ 10	-0.074	0 (0.0)	0 (0.0)	0.000
Chronic lung disease, excluding cystic fibrosis[c]	98 (14.0)	418 (10.0)	0.123	44 (14.6)	222 (11.5)	0.091	27 (11.5)	130 (8.9)	0.087	≤ 10	28 (10.3)	0.171
Cardiovascular conditions												
Atrial arrhythmia/fibrillation	≤ 10	24 (0.6)	0.048	≤ 10	≤ 10	0.055	≤ 10	≤ 10	0.118	0 (0.0)	≤ 10	-0.086
Cardiovascular revascularization	≤ 10	11 (0.3)	0.004	0 (0.0)	≤ 10	-0.065	≤ 10	≤ 10	0.039	0 (0.0)	0 (0.0)	0.000

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 698	TNFi n = 4162	Std. Diff.	Baricitinib n = 302	TNFi n = 1927	Std. Diff.	Baricitinib n = 235	TNFi n = 1466	Std. Diff.	Baricitinib n = 25	TNFi n = 273	Std. Diff.
Congestive Heart Failure, hospitalized	≤ 10	11 (0.3)	-0.027	≤ 10	≤ 10	0.05	≤ 10	≤ 10	0.077	0 (0.0)	0 (0.0)	0
Coronary artery disease	40 (5.7)	138 (3.3)	0.116	16 (5.3)	66 (3.4)	0.092	≤ 10	45 (3.1)	-0.005	≤ 10	≤ 10	0.186
Unstable angina	≤ 10	≤ 10	-0.012	0 (0.0)	≤ 10	-0.056	0 (0.0)	≤ 10	-0.064	0 (0.0)	0 (0.0)	0.000
Ventricular arrhythmia	≤ 10	30 (0.7)	-0.018	≤ 10	≤ 10	0.055	≤ 10	≤ 10	0.102	0 (0.0)	≤ 10	-0.149
Stroke	≤ 10	21 (0.5)	0.027	≤ 10	15 (0.8)	-0.014	≤ 10	≤ 10	0.11	0 (0.0)	≤ 10	-0.086
Hemorrhagic	0 (0.0)	≤ 10	-0.031	0 (0.0)	≤ 10	-0.046	0 (0.0)	≤ 10	-0.037	0 (0.0)	0 (0.0)	0.000
Ischemic	≤ 10	≤ 10	0.019	0 (0.0)	≤ 10	-0.056	≤ 10	≤ 10	0.055	0 (0.0)	0 (0.0)	0.000
Unknown	≤ 10	13 (0.3)	0.039	≤ 10	12 (0.6)	0.005	≤ 10	≤ 10	0.086	0 (0.0)	≤ 10	-0.086
TIA	0 (0.0)	≤ 10	-0.044	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Diabetes Mellitus[c]	65 (9.3)	351 (8.4)	0.031	20 (6.6)	165 (8.6)	-0.073	21 (8.9)	112 (7.6)	0.047	≤ 10	17 (6.2)	0.315
Treated insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Treated non insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Dyslipidemia (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Hypertension (not available in SNDS)												
History of hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 698	TNFi n = 4162	Std. Diff.	Baricitinib n = 302	TNFi n = 1927	Std. Diff.	Baricitinib n = 235	TNFi n = 1466	Std. Diff.	Baricitinib n = 25	TNFi n = 273	Std. Diff.
Current hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Immune disorders	36 (5.2)	118 (2.8)	0.119	≤ 10	49 (2.5)	0.027	≤ 10	31 (2.1)	0.001	≤ 10	≤ 10	0.205
AIDS/HIV	0 (0.0)	≤ 10	-0.054	0 (0.0)	≤ 10	-0.032	0 (0.0)	≤ 10	-0.037	0 (0.0)	≤ 10	-0.086
Antiphospholipid syndrome	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
SLE	≤ 10	30 (0.7)	0.069	≤ 10	≤ 10	0.042	≤ 10	≤ 10	0.003	≤ 10	≤ 10	0.185
Primary Sjogren Syndrome	30 (4.3)	87 (2.1)	0.126	≤ 10	42 (2.2)	0.031	≤ 10	25 (1.7)	0.000	≤ 10	≤ 10	0.129
Liver or pancreatic disorder[c]	18 (2.6)	91 (2.2)	0.026	≤ 10	50 (2.6)	-0.018	≤ 10	34 (2.3)	-0.044	0 (0.0)	≤ 10	-0.122
Obesity (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date)	≤ 10	68 (1.6)	-0.139	≤ 10	30 (1.6)	-0.086	≤ 10	24 (1.6)	-0.120	0 (0.0)	≤ 10	-0.149
RA Severity (CIRAS Index)			-0.201			-0.353			-0.265			-0.262
Mean (SD)	6.5 (1.5)	6.8 (1.6)		6.4 (1.5)	6.9 (1.6)		6.6 (1.5)	7.0 (1.5)		6.5 (1.4)	6.9 (1.6)	
DMARDs, n (%)												
cDMARDs, during baseline period												
n, total (%)	499 (71.5)	2914 (70.0)	0.032	221 (73.2)	1515 (78.6)	-0.128	180 (76.6)	1197 (81.7)	-0.125	18 (72.0)	230 (84.2)	-0.300

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 698	TNFi n = 4162	Std. Diff.	Baricitinib n = 302	TNFi n = 1927	Std. Diff.	Baricitinib n = 235	TNFi n = 1466	Std. Diff.	Baricitinib n = 25	TNFi n = 273	Std. Diff.
Mean (SD)	0.8 (0.6)	0.8 (0.6)	0.086	0.9 (0.7)	0.9 (0.6)	-0.027	0.9 (0.6)	0.9 (0.6)	-0.05	1.0 (0.9)	1.0 (0.5)	0.110
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	
Min; Max	[0.0;3.0]	[0.0;4.0]		[0.0;3.0]	[0.0;4.0]		[0.0;4.0]	[0.0;3.0]		[0.0;3.0]	[0.0;3.0]	
>1 cDMARD concomitantly	58 (8.3)	231 (5.6)	0.109	31 (10.3)	132 (6.9)	0.122	22 (9.4)	122 (8.3)	0.037	≤ 10	32 (11.7)	0.228
Hydroxychloroquine	54 (7.7)	202 (4.9)	0.119	32 (10.6)	102 (5.3)	0.197	19 (8.1)	91 (6.2)	0.073	≤ 10	22 (8.1)	0.445
Chloroquine	0 (0.0)	≤ 10	-0.031	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Azathioprin	≤ 10	11 (0.3)	0.004	≤ 10	≤ 10	-0.014	≤ 10	≤ 10	0.026	0 (0.0)	0 (0.0)	0.000
Leflunomide	121 (17.3)	436 (10.5)	0.199	37 (12.3)	192 (10.0)	0.073	33 (14.0)	153 (10.4)	0.11	≤ 10	33 (12.1)	0.113
Methotrexate	366 (52.4)	2415 (58.0)	-0.113	173 (57.3)	1294 (67.2)	-0.205	141 (60.0)	1009 (68.8)	-0.185	13 (52.0)	195 (71.4)	-0.408
Mycophenolate mofetil	0 (0.0)	≤ 10	-0.022	0 (0.0)	0 (0.0)	0.000	≤ 10	0 (0.0)	0.093	0 (0.0)	0 (0.0)	0.000
Sulfasalazin	38 (5.4)	181 (4.3)	0.051	17 (5.6)	94 (4.9)	0.034	13 (5.5)	90 (6.1)	-0.026	≤ 10	11 (4.0)	0.297
Cyclosporin	≤ 10	0 (0.0)	0.054	0 (0.0)	0 (0.0)	0.000	≤ 10	≤ 10	0.072	0 (0.0)	0 (0.0)	0.000
Penicillamin	0 (0.0)	0 (0.0)	0.000	0 (0.0)	≤ 10	-0.032	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
bDMARDs, during baseline period												
n, total (%)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	
Mean (SD)	0.0 (0.0)	0.0 (0.0)	0.000	0.0 (0.0)	0.0 (0.0)	0.000	0.0 (0.0)	0.0 (0.0)	0.000	0.0 (0.0)	0.0 (0.0)	0.000
Median	0.0	0.0		0.0	0.0		0.0	0.0		0.0	0.0	
Min; Max	[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;0.0]	[0.0;0.0]	
cDMARDs, concomitant	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Adalimumab[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 698	TNFi n = 4162	Std. Diff.	Baricitinib n = 302	TNFi n = 1927	Std. Diff.	Baricitinib n = 235	TNFi n = 1466	Std. Diff.	Baricitinib n = 25	TNFi n = 273	Std. Diff.
Certolizumab pegol[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Etanercept[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Golimumab[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Infliximab[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Rituximab	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Sarilumab	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Abatacept	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Tocilizumab	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Anakinra	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
TNFi naïve at baseline	698 (100.0)	4162 (100.0)	0.000	302 (100.0)	1927 (100.0)	0.000	235 (100.0)	1466 (100.0)	0.000	25 (100.0)	273 (100.0)	0.000
≥1 dispensing of bDMARD within 730 days before index date (excluded), n (%)	250 (35.8)	1318 (31.7)	0.088	107 (35.4)	399 (20.7)	0.332	81 (34.5)	242 (16.5)	0.421	15 (60.0)	47 (17.2)	0.978
Other prescription medications during baseline period, n (%)												
Antibiotics	262 (37.5)	1534 (36.9)	0.014	129 (42.7)	730 (37.9)	0.099	101 (43.0)	524 (35.7)	0.149	≤ 10	72 (26.4)	0.293
Antidiabetic agents	57 (8.2)	325 (7.8)	0.013	22 (7.3)	150 (7.8)	-0.019	20 (8.5)	109 (7.4)	0.040	≤ 10	18 (6.6)	0.403
Insulins	22 (3.2)	121 (2.9)	0.014	≤ 10	54 (2.8)	0.011	≤ 10	34 (2.3)	0.015	≤ 10	≤ 10	0.081
Non-insulins	47 (6.7)	272 (6.5)	0.008	20 (6.6)	128 (6.6)	-0.001	16 (6.8)	91 (6.2)	0.024	≤ 10	15 (5.5)	0.446
Cardiovascular												

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 698	TNFi n = 4162	Std. Diff.	Baricitinib n = 302	TNFi n = 1927	Std. Diff.	Baricitinib n = 235	TNFi n = 1466	Std. Diff.	Baricitinib n = 25	TNFi n = 273	Std. Diff.
Antithrombotic agents	120 (17.2)	586 (14.1)	0.086	51 (16.9)	258 (13.4)	0.098	29 (12.3)	183 (12.5)	-0.004	11 (44.0)	40 (14.7)	0.681
Anticoagulant	42 (6.0)	208 (5.0)	0.045	21 (7.0)	91 (4.7)	0.095	≤ 10	61 (4.2)	-0.04	≤ 10	20 (7.3)	0.025
Antiplatelet	88 (12.6)	410 (9.9)	0.087	37 (12.3)	180 (9.3)	0.094	22 (9.4)	126 (8.6)	0.027	≤ 10	24 (8.8)	0.78
Antihypertensives	233 (33.4)	1136 (27.3)	0.133	106 (35.1)	530 (27.5)	0.164	76 (32.3)	422 (28.8)	0.077	11 (44.0)	66 (24.2)	0.428
Angiotensin converting enzyme inhibitors (ACE)	53 (7.6)	347 (8.3)	-0.028	26 (8.6)	150 (7.8)	0.03	15 (6.4)	108 (7.4)	-0.039	≤ 10	22 (8.1)	0.445
Angiotensin receptor blockers (ARB)	98 (14.0)	438 (10.5)	0.107	45 (14.9)	224 (11.6)	0.097	22 (9.4)	174 (11.9)	-0.082	≤ 10	27 (9.9)	0.068
Beta blocker	114 (16.3)	479 (11.5)	0.140	47 (15.6)	206 (10.7)	0.145	37 (15.7)	169 (11.5)	0.123	≤ 10	30 (11.0)	0.147
Calcium channel blocker	56 (8.0)	300 (7.2)	0.031	33 (10.9)	148 (7.7)	0.112	34 (14.5)	118 (8.0)	0.204	≤ 10	≤ 10	0.424
Nitrates	≤ 10	35 (0.8)	0.031	0 (0.0)	13 (0.7)	-0.117	≤ 10	14 (1.0)	0.031	≤ 10	0 (0.0)	0.289
Acyclovir	≤ 10	23 (0.6)	0.021	≤ 10	11 (0.6)	0.048	0 (0.0)	≤ 10	-0.064	0 (0.0)	≤ 10	-0.122
Valacyclovir	17 (2.4)	113 (2.7)	-0.018	≤ 10	48 (2.5)	0.049	≤ 10	35 (2.4)	0.061	0 (0.0)	11 (4.0)	-0.290
Hormonal	65 (9.3)	608 (14.6)	-0.164	41 (13.6)	282 (14.6)	-0.03	25 (10.6)	207 (14.1)	-0.106	≤ 10	41 (15.0)	-0.088
HRT	41 (5.9)	278 (6.7)	-0.033	25 (8.3)	113 (5.9)	0.094	16 (6.8)	91 (6.2)	0.024	≤ 10	16 (5.9)	-0.086
Oral Contraceptives	23 (3.3)	314 (7.5)	-0.189	14 (4.6)	151 (7.8)	-0.133	≤ 10	114 (7.8)	-0.191	≤ 10	23 (8.4)	-0.016
SERMs	≤ 10	≤ 10	-0.017	≤ 10	11 (0.6)	0.012	≤ 10	≤ 10	0.003	0 (0.0)	0 (0.0)	0.000

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 698	TNFi n = 4162	Std. Diff.	Baricitinib n = 302	TNFi n = 1927	Std. Diff.	Baricitinib n = 235	TNFi n = 1466	Std. Diff.	Baricitinib n = 25	TNFi n = 273	Std. Diff.
Topic with progestogens and/or estrogens	0 (0.0)	28 (0.7)	-0.116	≤ 10	15 (0.8)	-0.060	≤ 10	≤ 10	0.003	0 (0.0)	≤ 10	-0.122
Lipid-lowering agents	114 (16.3)	531 (12.8)	0.102	54 (17.9)	247 (12.8)	0.141	40 (17.0)	203 (13.8)	0.088	≤ 10	31 (11.4)	0.428
HMG CoA reductase inhibitors	94 (13.5)	431 (10.4)	0.096	45 (14.9)	199 (10.3)	0.138	31 (13.2)	166 (11.3)	0.057	≤ 10	23 (8.4)	0.432
Fibrates	≤ 10	40 (1.0)	-0.045	≤ 10	21 (1.1)	-0.046	≤ 10	16 (1.1)	0.082	0 (0.0)	≤ 10	-0.173
Bile acid sequestrants	≤ 10	12 (0.3)	0.024	≤ 10	≤ 10	-0.014	≤ 10	≤ 10	0.026	0 (0.0)	0 (0.0)	0.000
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Other lipid modifying agents	≤ 10	43 (1.0)	-0.018	≤ 10	13 (0.7)	-0.002	≤ 10	12 (0.8)	0.045	0 (0.0)	≤ 10	-0.086
Lipid modifying agents, combinations	11 (1.6)	35 (0.8)	0.067	≤ 10	15 (0.8)	0.125	≤ 10	17 (1.2)	0.076	≤ 10	≤ 10	0.185
Rheumatoid arthritis-related												
Aspirin	≤ 10	47 (1.1)	-0.080	≤ 10	23 (1.2)	-0.055	≤ 10	12 (0.8)	0.045	≤ 10	≤ 10	0.336
Cox-2 Inhibitor	31 (4.4)	248 (6.0)	-0.068	15 (5.0)	121 (6.3)	-0.057	16 (6.8)	94 (6.4)	0.016	≤ 10	24 (8.8)	-0.029
NSAIDs	254 (36.4)	1638 (39.4)	-0.061	115 (38.1)	840 (43.6)	-0.112	85 (36.2)	648 (44.2)	-0.164	≤ 10	104 (38.1)	-0.043
Glucocorticosteroid	504 (72.2)	2669 (64.1)	0.174	235 (77.8)	1365 (70.8)	0.160	174 (74.0)	1032 (70.4)	0.082	17 (68.0)	190 (69.6)	-0.035
Vaccines	223 (31.9)	1541 (37.0)	-0.107	118 (39.1)	857 (44.5)	-0.110	79 (33.6)	684 (46.7)	-0.268	≤ 10	116 (42.5)	-0.400
Antineoplastic agents	≤ 10	≤ 10	0.078	≤ 10	≤ 10	0.036	≤ 10	≤ 10	0.039	≤ 10	0 (0.0)	0.289

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; DMARD = disease-modifying antirheumatic drugs; hosp = hospitalized; HRT = hormone replacement therapy; Max = maximum; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Min = minimum; mos = months; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulator; Std. Diff. = standardized difference; TNF = tumor necrosis factor; TNFi = tumor 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] TNF inhibitors.

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

Table 6.114. bDMARD-Experienced: Baseline characteristics by exposure duration - VTE cohort, Matched [SNDS]

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 809	TNFi[a] n = 812	Std. Diff.	Baricitinib n = 395	TNFi[a] n = 422	Std. Diff.	Baricitinib n = 358	TNFi[a] n = 298	Std. Diff.	Baricitinib n = 38	TNFi[a] n = 68	Std. Diff.
Age [in years]			-0.032			0.017			0.095			-0.422
N (missing)	809 (0)	812 (0)		395 (0)	422 (0)		358 (0)	298 (0)		38 (0)	68 (0)	
Mean (SD)	56.8 (13.8)	57.2 (13.4)		58.0 (12.7)	57.8 (13.9)		59.1 (12.1)	57.9 (13.3)		54.7 (10.9)	59.2 (10.4)	
Median	57.0	58.0		58.0	58.0		60.0	58.0		55.5	60.0	
Min; Max	[18.0;90.0]	[18.0;89.0]		[21.0;87.0]	[18.0;91.0]		[20.0;92.0]	[19.0;90.0]		[32.0;72.0]	[34.0;83.0]	
Sex, n (%)			0.027			-0.014			0.26			0.172
Male	157 (19.4)	149 (18.3)		82 (20.8)	90 (21.3)		97 (27.1)	49 (16.4)		≤ 10	13 (19.1)	
Female	652 (80.6)	663 (81.7)		313 (79.2)	332 (78.7)		261 (72.9)	249 (83.6)		28 (73.7)	55 (80.9)	
Clinical conditions during baseline period, n (%)												
Cancer, excluding NMSC	18 (2.2)	22 (2.7)	-0.031	≤ 10	20 (4.7)	-0.151	≤ 10	≤ 10	0.076	≤ 10	0 (0.0)	0.233
NMSC	0 (0.0)	0 (0.0)	0	≤ 10	0 (0.0)	0.101	0 (0.0)	0 (0.0)	0	0 (0.0)	≤ 10	-0.173
Chronic lung disease, excluding cystic fibrosis[c]	105 (13.0)	95 (11.7)	0.039	49 (12.4)	48 (11.4)	0.032	52 (14.5)	36 (12.1)	0.072	≤ 10	≤ 10	-0.14
Cardiovascular conditions												
Atrial arrhythmia/fibrillation	≤ 10	≤ 10	0.076	≤ 10	≤ 10	0.063	≤ 10	≤ 10	-0.107	0 (0.0)	0 (0.0)	0
Cardiovascular revascularization	≤ 10	≤ 10	-0.05	≤ 10	≤ 10	-0.037	≤ 10	0 (0.0)	0.106	0 (0.0)	0 (0.0)	0

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 809	TNFi[a] n = 812	Std. Diff.	Baricitinib n = 395	TNFi[a] n = 422	Std. Diff.	Baricitinib n = 358	TNFi[a] n = 298	Std. Diff.	Baricitinib n = 38	TNFi[a] n = 68	Std. Diff.
Congestive Heart Failure, hospitalized	≤ 10	≤ 10	0.036	≤ 10	≤ 10	-0.037	≤ 10	≤ 10	0.033	0 (0.0)	0 (0.0)	0
Coronary artery disease	22 (2.7)	26 (3.2)	-0.029	19 (4.8)	23 (5.5)	-0.029	19 (5.3)	11 (3.7)	0.078	≤ 10	≤ 10	0.117
Unstable angina	0 (0.0)	0 (0.0)	0	0 (0.0)	≤ 10	-0.069	0 (0.0)	≤ 10	-0.082	0 (0.0)	0 (0.0)	0
Ventricular arrhythmia	≤ 10	≤ 10	-0.063	≤ 10	≤ 10	-0.026	≤ 10	≤ 10	-0.119	0 (0.0)	0 (0.0)	0
Stroke	≤ 10	≤ 10	0.015	≤ 10	≤ 10	0.077	≤ 10	≤ 10	-0.049	0 (0.0)	≤ 10	-0.173
Hemorrhagic	0 (0.0)	0 (0.0)	0.000	≤ 10	≤ 10	0.003	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Ischemic	≤ 10	0 (0.0)	0.07	≤ 10	≤ 10	0.044	0 (0.0)	≤ 10	-0.082	0 (0.0)	0 (0.0)	0
Unknown	≤ 10	≤ 10	-0.016	≤ 10	≤ 10	0.138	≤ 10	≤ 10	-0.018	0 (0.0)	≤ 10	-0.173
TIA	≤ 10	0 (0.0)	0.05	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Diabetes Mellitus[c]	78 (9.6)	90 (11.1)	-0.047	45 (11.4)	45 (10.7)	0.023	44 (12.3)	25 (8.4)	0.128	≤ 10	≤ 10	-0.130
Treated insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Treated non insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Dyslipidemia (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Hypertension (not available in SNDS)												
History of hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 809	TNFi[a] n = 812	Std. Diff.	Baricitinib n = 395	TNFi[a] n = 422	Std. Diff.	Baricitinib n = 358	TNFi[a] n = 298	Std. Diff.	Baricitinib n = 38	TNFi[a] n = 68	Std. Diff.
Current hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Immune disorders	27 (3.3)	30 (3.7)	-0.019	≤ 10	14 (3.3)	-0.08	14 (3.9)	12 (4.0)	-0.006	0 (0.0)	≤ 10	-0.173
AIDS/HIV	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Antiphospholipid syndrome	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
SLE	≤ 10	≤ 10	0.070	0 (0.0)	≤ 10	-0.069	≤ 10	0 (0.0)	0.106	0 (0.0)	0 (0.0)	0.000
Primary Sjogren Syndrome	18 (2.2)	27 (3.3)	-0.067	≤ 10	13 (3.1)	-0.067	13 (3.6)	12 (4.0)	-0.021	0 (0.0)	≤ 10	-0.173
Liver or pancreatic disorder[c]	25 (3.1)	25 (3.1)	0.001	13 (3.3)	19 (4.5)	-0.063	18 (5.0)	≤ 10	0.164	≤ 10	≤ 10	0.117
Obesity (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date)	≤ 10	≤ 10	0.000	≤ 10	≤ 10	0.003	0 (0.0)	≤ 10	-0.116	0 (0.0)	0 (0.0)	0.000
RA Severity (CIRAS Index)			0.043			-0.025			0.077			0.395
Mean (SD)	6.5 (1.4)	6.5 (1.3)		6.3 (1.2)	6.4 (1.3)		6.4 (1.3)	6.3 (1.2)		6.8 (1.2)	6.4 (1.3)	
DMARDs, n (%)												
cDMARDs, during baseline period												

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 809	TNFi[a] n = 812	Std. Diff.	Baricitinib n = 395	TNFi[a] n = 422	Std. Diff.	Baricitinib n = 358	TNFi[a] n = 298	Std. Diff.	Baricitinib n = 38	TNFi[a] n = 68	Std. Diff.
n, total (%)	495 (61.2)	470 (57.9)	0.067	257 (65.1)	255 (60.4)	0.096	239 (66.8)	190 (63.8)	0.063	29 (76.3)	48 (70.6)	0.13
Mean (SD)	0.6 (0.5)	0.6 (0.5)	0.05	0.7 (0.6)	0.6 (0.5)	0.107	0.7 (0.6)	0.7 (0.6)	0.053	0.9 (0.6)	0.7 (0.5)	0.234
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	
Min; Max	[0.0;3.0]	[0.0;3.0]		[0.0;3.0]	[0.0;2.0]		[0.0;4.0]	[0.0;2.0]		[0.0;3.0]	[0.0;2.0]	
>1 cDMARD concomitantly	19 (2.3)	19 (2.3)	0.001	≤ 10	≤ 10	0.01	14 (3.9)	13 (4.4)	-0.023	≤ 10	≤ 10	0.117
Hydroxychloroquine	21 (2.6)	30 (3.7)	-0.063	14 (3.5)	14 (3.3)	0.013	14 (3.9)	12 (4.0)	-0.006	≤ 10	≤ 10	0.117
Chloroquine	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0
Azathioprin	≤ 10	≤ 10	-0.056	≤ 10	0 (0.0)	0.071	≤ 10	≤ 10	-0.119	0 (0.0)	0 (0.0)	0
Leflunomide	84 (10.4)	78 (9.6)	0.026	42 (10.6)	34 (8.1)	0.089	38 (10.6)	30 (10.1)	0.018	≤ 10	≤ 10	0.518
Methotrexate	397 (49.1)	358 (44.1)	0.100	210 (53.2)	208 (49.3)	0.078	193 (53.9)	152 (51.0)	0.058	19 (50.0)	43 (63.2)	-0.27
Mycophenolate mofetil	0 (0.0)	≤ 10	-0.05	0 (0.0)	≤ 10	-0.069	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0
Sulfasalazin	11 (1.4)	22 (2.7)	-0.096	≤ 10	≤ 10	-0.074	11 (3.1)	≤ 10	0.067	≤ 10	≤ 10	0.308
Cyclosporin	0 (0.0)	≤ 10	-0.05	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0
Penicillamin	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	≤ 10	-0.082	0 (0.0)	0 (0.0)	0
bDMARDs, during baseline period												
n, total (%)	809 (100.0)	812 (100.0)	0.000	395 (100.0)	422 (100.0)	0.000	358 (100.0)	298 (100.0)	0.000	38 (100.0)	68 (100.0)	0.000
Mean (SD)	1.1 (0.3)	1.1 (0.3)	-0.062	1.1 (0.3)	1.1 (0.3)	0.013	1.1 (0.3)	1.1 (0.3)	0.081	1.2 (0.4)	1.1 (0.3)	0.279
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 809	TNFi[a] n = 812	Std. Diff.	Baricitinib n = 395	TNFi[a] n = 422	Std. Diff.	Baricitinib n = 358	TNFi[a] n = 298	Std. Diff.	Baricitinib n = 38	TNFi[a] n = 68	Std. Diff.
Min; Max	[1.0;3.0]	[1.0;3.0]		[1.0;3.0]	[1.0;2.0]		[1.0;3.0]	[1.0;2.0]		[1.0;2.0]	[1.0;2.0]	
cDMARDs, concomitant	439 (54.3)	403 (49.6)	0.093	236 (59.7)	228 (54.0)	0.116	210 (58.7)	173 (58.1)	0.012	24 (63.2)	43 (63.2)	-0.002
Adalimumab[b]	108 (13.3)	115 (14.2)	-0.024	52 (13.2)	64 (15.2)	-0.057	51 (14.2)	41 (13.8)	0.014	≤ 10	20 (29.4)	-0.26
Certolizumab pegol[b]	55 (6.8)	57 (7.0)	-0.009	35 (8.9)	29 (6.9)	0.074	24 (6.7)	20 (6.7)	0.000	≤ 10	≤ 10	0.042
Etanercept[b]	187 (23.1)	186 (22.9)	0.005	84 (21.3)	90 (21.3)	-0.002	59 (16.5)	59 (19.8)	-0.086	≤ 10	13 (19.1)	-0.433
Golimumab[b]	53 (6.6)	56 (6.9)	-0.014	22 (5.6)	22 (5.2)	0.016	25 (7.0)	21 (7.0)	-0.003	≤ 10	≤ 10	-0.084
Infliximab[b]	42 (5.2)	43 (5.3)	-0.005	21 (5.3)	22 (5.2)	0.005	15 (4.2)	17 (5.7)	-0.07	≤ 10	≤ 10	0.04
Rituximab	25 (3.1)	18 (2.2)	0.054	13 (3.3)	15 (3.6)	-0.015	15 (4.2)	≤ 10	0.23	≤ 10	≤ 10	0.234
Sarilumab	16 (2.0)	14 (1.7)	0.019	≤ 10	≤ 10	0.045	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0
Abatacept	193 (23.9)	211 (26.0)	-0.049	112 (28.4)	113 (26.8)	0.035	112 (31.3)	85 (28.5)	0.06	14 (36.8)	≤ 10	0.523
Tocilizumab	180 (22.2)	180 (22.2)	0.002	82 (20.8)	94 (22.3)	-0.037	88 (24.6)	71 (23.8)	0.018	≤ 10	≤ 10	0.166
Anakinra	≤ 10	≤ 10	0.063	≤ 10	≤ 10	-0.033	≤ 10	≤ 10	-0.057	0 (0.0)	0 (0.0)	0
TNFi naïve at baseline	382 (47.2)	366 (45.1)	0.043	194 (49.1)	197 (46.7)	0.049	193 (53.9)	144 (48.3)	0.112	21 (55.3)	20 (29.4)	0.542
≥ 1 dispensing of bDMARD within 730 days before index date (excluded), n (%)	809 (100.0)	812 (100.0)	0.000	395 (100.0)	422 (100.0)	0.000	358 (100.0)	298 (100.0)	0.000	38 (100.0)	68 (100.0)	0.000

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 809	TNFi[a] n = 812	Std. Diff.	Baricitinib n = 395	TNFi[a] n = 422	Std. Diff.	Baricitinib n = 358	TNFi[a] n = 298	Std. Diff.	Baricitinib n = 38	TNFi[a] n = 68	Std. Diff.
Other prescription medications during baseline period, n (%)												
Antibiotics	354 (43.8)	346 (42.6)	0.023	158 (40.0)	207 (49.1)	-0.183	157 (43.9)	118 (39.6)	0.086	18 (47.4)	24 (35.3)	0.247
Antidiabetic agents	81 (10.0)	81 (10.0)	0.001	39 (9.9)	44 (10.4)	-0.018	44 (12.3)	24 (8.1)	0.141	≤ 10	≤ 10	0.042
Insulins	34 (4.2)	41 (5.0)	-0.04	16 (4.1)	≤ 10	0.127	11 (3.1)	≤ 10	0.067	≤ 10	≤ 10	0.211
Non-insulins	59 (7.3)	61 (7.5)	-0.008	32 (8.1)	39 (9.2)	-0.041	37 (10.3)	22 (7.4)	0.104	≤ 10	≤ 10	-0.039
Cardiovascular												
Antithrombotic agents	108 (13.3)	119 (14.7)	-0.038	65 (16.5)	57 (13.5)	0.083	60 (16.8)	42 (14.1)	0.074	≤ 10	16 (23.5)	-0.196
Anticoagulant	29 (3.6)	33 (4.1)	-0.025	17 (4.3)	13 (3.1)	0.065	14 (3.9)	12 (4.0)	-0.006	≤ 10	≤ 10	-0.162
Antiplatelet	86 (10.6)	91 (11.2)	-0.019	50 (12.7)	46 (10.9)	0.055	47 (13.1)	32 (10.7)	0.074	≤ 10	13 (19.1)	-0.163
Antihypertensives	240 (29.7)	285 (35.1)	-0.116	139 (35.2)	153 (36.3)	-0.022	144 (40.2)	110 (36.9)	0.068	15 (39.5)	28 (41.2)	-0.035
Angiotensin converting enzyme inhibitors (ACE)	67 (8.3)	84 (10.3)	-0.071	32 (8.1)	43 (10.2)	-0.073	47 (13.1)	26 (8.7)	0.142	≤ 10	≤ 10	0.17
Angiotensin receptor blockers (ARB)	88 (10.9)	108 (13.3)	-0.074	49 (12.4)	75 (17.8)	-0.15	54 (15.1)	54 (18.1)	-0.082	≤ 10	13 (19.1)	-0.333

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 809	TNFi[a] n = 812	Std. Diff.	Baricitinib n = 395	TNFi[a] n = 422	Std. Diff.	Baricitinib n = 358	TNFi[a] n = 298	Std. Diff.	Baricitinib n = 38	TNFi[a] n = 68	Std. Diff.
Beta blocker	96 (11.9)	117 (14.4)	-0.075	55 (13.9)	62 (14.7)	-0.022	62 (17.3)	49 (16.4)	0.023	≤ 10	12 (17.6)	0.211
Calcium channel blocker	65 (8.0)	87 (10.7)	-0.092	44 (11.1)	44 (10.4)	0.023	44 (12.3)	26 (8.7)	0.117	≤ 10	14 (20.6)	-0.469
Nitrates	≤ 10	≤ 10	-0.057	≤ 10	≤ 10	-0.145	≤ 10	≤ 10	0.113	0 (0.0)	≤ 10	-0.173
Acyclovir	≤ 10	≤ 10	-0.029	0 (0.0)	≤ 10	-0.17	0 (0.0)	≤ 10	-0.082	0 (0.0)	≤ 10	-0.173
Valacyclovir	32 (4.0)	37 (4.6)	-0.03	15 (3.8)	24 (5.7)	-0.089	22 (6.1)	≤ 10	0.131	≤ 10	≤ 10	-0.019
Hormonal	114 (14.1)	122 (15.0)	-0.027	60 (15.2)	57 (13.5)	0.048	47 (13.1)	35 (11.7)	0.042	≤ 10	≤ 10	0.299
HRT	65 (8.0)	73 (9.0)	-0.034	29 (7.3)	34 (8.1)	-0.027	30 (8.4)	18 (6.0)	0.091	≤ 10	≤ 10	0.25
Oral Contraceptives	48 (5.9)	51 (6.3)	-0.015	33 (8.4)	20 (4.7)	0.147	16 (4.5)	17 (5.7)	-0.056	≤ 10	≤ 10	0.145
SERMs	≤ 10	≤ 10	0.029	0 (0.0)	≤ 10	-0.12	≤ 10	≤ 10	0.033	≤ 10	0 (0.0)	0.233
Topic with progestogens and/or estrogens	≤ 10	0 (0.0)	0.086	≤ 10	≤ 10	0.003	≤ 10	0 (0.0)	0.106	0 (0.0)	0 (0.0)	0
Lipid-lowering agents	131 (16.2)	136 (16.7)	-0.015	60 (15.2)	71 (16.8)	-0.045	70 (19.6)	49 (16.4)	0.081	≤ 10	18 (26.5)	-0.128
HMG CoA reductase inhibitors	107 (13.2)	107 (13.2)	0.001	51 (12.9)	63 (14.9)	-0.058	56 (15.6)	37 (12.4)	0.093	≤ 10	16 (23.5)	-0.06
Fibrates	13 (1.6)	15 (1.8)	-0.019	≤ 10	≤ 10	0.105	≤ 10	≤ 10	-0.004	0 (0.0)	0 (0.0)	0

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 809	TNFi[a] n = 812	Std. Diff.	Baricitinib n = 395	TNFi[a] n = 422	Std. Diff.	Baricitinib n = 358	TNFi[a] n = 298	Std. Diff.	Baricitinib n = 38	TNFi[a] n = 68	Std. Diff.
Bile acid sequestrants	≤ 10	≤ 10	-0.019	≤ 10	≤ 10	0.003	≤ 10	≤ 10	-0.01	0 (0.0)	0 (0.0)	0
Nicotinic acid and derivatives	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)	0
Other lipid modifying agents	≤ 10	11 (1.4)	-0.06	≤ 10	≤ 10	0.044	≤ 10	≤ 10	0.019	0 (0.0)	0 (0.0)	0
Lipid modifying agents, combinations	≤ 10	≤ 10	-0.036	≤ 10	≤ 10	-0.043	≤ 10	≤ 10	-0.072	0 (0.0)	≤ 10	-0.246
Rheumatoid arthritis-related												
Aspirin	14 (1.7)	≤ 10	0.053	≤ 10	≤ 10	-0.033	≤ 10	≤ 10	0.048	0 (0.0)	0 (0.0)	0
Cox-2 Inhibitor	49 (6.1)	47 (5.8)	0.011	24 (6.1)	20 (4.7)	0.059	19 (5.3)	19 (6.4)	-0.046	≤ 10	≤ 10	-0.316
NSAIDs	303 (37.5)	338 (41.6)	-0.085	143 (36.2)	149 (35.3)	0.019	117 (32.7)	115 (38.6)	-0.124	16 (42.1)	31 (45.6)	-0.07
Glucocorticosteroid	573 (70.8)	564 (69.5)	0.03	272 (68.9)	299 (70.9)	-0.043	228 (63.7)	191 (64.1)	-0.009	23 (60.5)	36 (52.9)	0.154
Vaccines	205 (25.3)	176 (21.7)	0.087	119 (30.1)	118 (28.0)	0.048	106 (29.6)	76 (25.5)	0.092	≤ 10	≤ 10	0.291
Antineoplastic agents	≤ 10	≤ 10	-0.083	≤ 10	≤ 10	0.003	0 (0.0)	≤ 10	-0.082	0 (0.0)	0 (0.0)	0

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs;
Concom. cDMARDs = concomitant cDMARDs; DMARD = disease-modifying antirheumatic drugs; hosp = hospitalized; HRT = hormone replacement therapy; Max = maximum;
MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Min = minimum;
mos = months; N = number of patients in the specified category; NMSC = non-melanoma skin cancer;
RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulator; Std. Diff. = standardized difference; TNF = tumor necrosis factor; TNFi = tumor 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] TNF inhibitors.

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

Table 6.115. bDMARD-Naïve: Baseline characteristics by exposure duration - VTE cohort, Matched [SNDS]

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 698	TNFi[a] n = 693	Std. Diff.	Baricitinib n = 302	TNFi[a] n = 314	Std. Diff.	Baricitinib n = 235	TNFi[a] n = 210	Std. Diff.	Baricitinib n = 25	TNFi[a] n = 43	Std. Diff.
Age [in years]			0.018			0.071			0.029			-0.36
N (missing)	698 (0)	693 (0)		302 (0)	314 (0)		235 (0)	210 (0)		25 (0)	43 (0)	
Mean (SD)	59.3 (13.4)	59.1 (13.0)		60.7 (13.1)	59.8 (13.0)		58.7 (12.9)	58.4 (13.6)		57.3 (12.1)	61.8 (12.7)	
Median	60.0	60.0		61.0	60.0		58.0	58.0		61.0	63.0	
Min; Max	[20.0;89.0]	[23.0;92.0]		[19.0;86.0]	[18.0;90.0]		[22.0;86.0]	[27.0;89.0]		[30.0;76.0]	[22.0;84.0]	
Sex, n (%)			-0.106			-0.029			0.016			0.162
Male	131 (18.8)	160 (23.1)		60 (19.9)	66 (21.0)		53 (22.6)	46 (21.9)		≤ 10	≤ 10	
Female	567 (81.2)	533 (76.9)		242 (80.1)	248 (79.0)		182 (77.4)	164 (78.1)		20 (80.0)	37 (86.0)	
Clinical conditions during baseline period, n (%)												
Cancer, excluding NMSC	33 (4.7)	23 (3.3)	0.072	11 (3.6)	14 (4.5)	-0.041	≤ 10	≤ 10	-0.019	0 (0.0)	≤ 10	-0.312
NMSC	≤ 10	≤ 10	0.000	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Chronic lung disease, excluding cystic fibrosis[c]	98 (14.0)	89 (12.8)	0.035	44 (14.6)	53 (16.9)	-0.064	27 (11.5)	18 (8.6)	0.097	≤ 10	≤ 10	0.057
Cardiovascular conditions												
Atrial arrhythmia/fibrillation	≤ 10	≤ 10	0.014	≤ 10	≤ 10	0.004	≤ 10	≤ 10	0.118	0 (0.0)	0 (0.0)	0
Cardiovascular revascularization	≤ 10	≤ 10	0.031	0 (0.0)	≤ 10	-0.113	≤ 10	≤ 10	-0.008	0 (0.0)	0 (0.0)	0

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 698	TNFi[a] n = 693	Std. Diff.	Baricitinib n = 302	TNFi[a] n = 314	Std. Diff.	Baricitinib n = 235	TNFi[a] n = 210	Std. Diff.	Baricitinib n = 25	TNFi[a] n = 43	Std. Diff.
Congestive Heart Failure, hospitalized	≤ 10	≤ 10	-0.031	≤ 10	≤ 10	0.003	≤ 10	≤ 10	-0.054	0 (0.0)	0 (0.0)	0
Coronary artery disease	40 (5.7)	24 (3.5)	0.108	16 (5.3)	16 (5.1)	0.009	≤ 10	11 (5.2)	-0.114	≤ 10	≤ 10	0.259
Unstable angina	≤ 10	0 (0.0)	0.054	0 (0.0)	0 (0.0)	0	0 (0.0)	≤ 10	-0.098	0 (0.0)	0 (0.0)	0
Ventricular arrhythmia	≤ 10	≤ 10	-0.019	≤ 10	≤ 10	0.04	≤ 10	≤ 10	-0.015	0 (0.0)	≤ 10	-0.218
Stroke	≤ 10	≤ 10	0.038	≤ 10	≤ 10	-0.111	≤ 10	≤ 10	0.118	0 (0.0)	0 (0.0)	0
Hemorrhagic	0 (0.0)	≤ 10	-0.054	0 (0.0)	≤ 10	-0.08	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Ischemic	≤ 10	≤ 10	0	0 (0.0)	≤ 10	-0.08	≤ 10	0 (0.0)	0.093	0 (0.0)	0 (0.0)	0
Unknown	≤ 10	0 (0.0)	0.107	≤ 10	≤ 10	-0.063	≤ 10	≤ 10	0.086	0 (0.0)	0 (0.0)	0
TIA	0 (0.0)	≤ 10	-0.054	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Diabetes Mellitus[c]	65 (9.3)	68 (9.8)	-0.017	20 (6.6)	25 (8.0)	-0.052	21 (8.9)	20 (9.5)	-0.02	≤ 10	≤ 10	0.286
Treated insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Treated non insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Dyslipidemia (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Hypertension (not available in SNDS)												
History of hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 698	TNFi[a] n = 693	Std. Diff.	Baricitinib n = 302	TNFi[a] n = 314	Std. Diff.	Baricitinib n = 235	TNFi[a] n = 210	Std. Diff.	Baricitinib n = 25	TNFi[a] n = 43	Std. Diff.
Current hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Immune disorders	36 (5.2)	31 (4.5)	0.032	≤ 10	11 (3.5)	-0.03	≤ 10	≤ 10	-0.047	≤ 10	≤ 10	0.259
AIDS/HIV	0 (0.0)	≤ 10	-0.054	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Antiphospholipid syndrome	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
SLE	≤ 10	≤ 10	0.124	≤ 10	≤ 10	0.003	≤ 10	≤ 10	-0.105	≤ 10	≤ 10	0.096
Primary Sjogren Syndrome	30 (4.3)	28 (4.0)	0.013	≤ 10	≤ 10	-0.032	≤ 10	≤ 10	0.022	≤ 10	0 (0.0)	0.289
Liver or pancreatic disorder[c]	18 (2.6)	19 (2.7)	-0.01	≤ 10	≤ 10	-0.015	≤ 10	≤ 10	-0.129	0 (0.0)	0 (0.0)	0
Obesity (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date)	≤ 10	≤ 10	-0.025	≤ 10	≤ 10	0.003	≤ 10	≤ 10	-0.008	0 (0.0)	0 (0.0)	0
RA Severity (CIRAS Index)			0.021			-0.106			-0.087			-0.149
Mean (SD)	6.5 (1.5)	6.4 (1.6)		6.4 (1.5)	6.5 (1.5)		6.6 (1.5)	6.8 (1.6)		6.5 (1.4)	6.7 (1.5)	
DMARDs, n (%)												
cDMARDs, during baseline period												
n, total (%)	499 (71.5)	477 (68.8)		221 (73.2)	250 (79.6)	-0.152	180 (76.6)	172 (81.9)	-0.131	18 (72.0)	34 (79.1)	-0.165

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 698	TNFi[a] n = 693	Std. Diff.	Baricitinib n = 302	TNFi[a] n = 314	Std. Diff.	Baricitinib n = 235	TNFi[a] n = 210	Std. Diff.	Baricitinib n = 25	TNFi[a] n = 43	Std. Diff.
Mean (SD)	0.8 (0.6)	0.8 (0.6)		0.9 (0.7)	0.9 (0.6)	-0.04	0.9 (0.6)	1.0 (0.6)	-0.145	1.0 (0.9)	1.0 (0.7)	0.076
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	
Min; Max	[0.0;3.0]	[0.0;4.0]		[0.0;3.0]	[0.0;3.0]		[0.0;4.0]	[0.0;3.0]		[0.0;3.0]	[0.0;3.0]	
>1 cDMARD concomitantly	58 (8.3)	43 (6.2)		31 (10.3)	19 (6.1)	0.154	22 (9.4)	22 (10.5)	-0.037	≤ 10	≤ 10	0.231
Hydroxychloroquine	54 (7.7)	52 (7.5)		32 (10.6)	21 (6.7)	0.139	19 (8.1)	26 (12.4)	-0.142	≤ 10	≤ 10	0.193
Chloroquine	0 (0.0)	≤ 10		0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Azathioprin	≤ 10	≤ 10		≤ 10	≤ 10	-0.044	≤ 10	≤ 10	-0.008	0 (0.0)	0 (0.0)	0
Leflunomide	121 (17.3)	89 (12.8)		37 (12.3)	27 (8.6)	0.12	33 (14.0)	32 (15.2)	-0.034	≤ 10	≤ 10	0.203
Methotrexate	366 (52.4)	367 (53.0)		173 (57.3)	214 (68.2)	-0.226	141 (60.0)	131 (62.4)	-0.049	13 (52.0)	29 (67.4)	-0.319
Mycophenolate mofetil	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0.000	≤ 10	0 (0.0)	0.093	0 (0.0)	0 (0.0)	0
Sulfasalazin	38 (5.4)	38 (5.5)		17 (5.6)	14 (4.5)	0.054	13 (5.5)	16 (7.6)	-0.084	≤ 10	≤ 10	0.268
Cyclosporin	≤ 10	0 (0.0)		0 (0.0)	0 (0.0)	0.000	≤ 10	0 (0.0)	0.093	0 (0.0)	0 (0.0)	0
Penicillamin	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
bDMARDs, during baseline period												
n, total (%)	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Mean (SD)	0.0 (0.0)	0.0 (0.0)	0.000	0.0 (0.0)	0.0 (0.0)	0.000	0.0 (0.0)	0.0 (0.0)	0.000	0.0 (0.0)	0.0 (0.0)	0.000
Median	0.0	0.0		0.0	0.0		0.0	0.0		0.0	0.0	
Min; Max	[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;0.0]	[0.0;0.0]	
cDMARDs, concomitant	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Adalimumab[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 698	TNFi[a] n = 693	Std. Diff.	Baricitinib n = 302	TNFi[a] n = 314	Std. Diff.	Baricitinib n = 235	TNFi[a] n = 210	Std. Diff.	Baricitinib n = 25	TNFi[a] n = 43	Std. Diff.
Certolizumab pegol[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Etanercept[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Golimumab[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Infliximab[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Rituximab	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Sarilumab	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Abatacept	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Tocilizumab	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Anakinra	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
TNFi naïve at baseline	698 (100.0)	693 (100.0)		302 (100.0)	314 (100.0)		235 (100.0)	210 (100.0)		25 (100.0)	43 (100.0)	0.000
≥1 dispensing of bDMARD within 730 days before index date (excluded), n (%)	250 (35.8)	245 (35.4)	0.010	107 (35.4)	76 (24.2)	0.247	81 (34.5)	38 (18.1)	0.379	15 (60.0)	≤ 10	0.803
Other prescription medications during baseline period, n (%)												
Antibiotics	262 (37.5)	271 (39.1)		129 (42.7)	112 (35.7)	0.145	101 (43.0)	63 (30.0)	0.272	≤ 10	≤ 10	0.366
Antidiabetic agents	57 (8.2)	62 (8.9)		22 (7.3)	20 (6.4)	0.036	20 (8.5)	19 (9.0)	-0.019	≤ 10	≤ 10	0.388
Insulins	22 (3.2)	28 (4.0)		≤ 10	≤ 10	0.093	≤ 10	≤ 10	0.081	≤ 10	≤ 10	-0.032
Non-insulins	47 (6.7)	50 (7.2)		20 (6.6)	19 (6.1)	0.024	16 (6.8)	18 (8.6)	-0.066	≤ 10	≤ 10	0.48
Cardiovascular												

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 698	TNFi[a] n = 693	Std. Diff.	Baricitinib n = 302	TNFi[a] n = 314	Std. Diff.	Baricitinib n = 235	TNFi[a] n = 210	Std. Diff.	Baricitinib n = 25	TNFi[a] n = 43	Std. Diff.
Antithrombotic agents	120 (17.2)	112 (16.2)		51 (16.9)	47 (15.0)	0.053	29 (12.3)	28 (13.3)	-0.03	11 (44.0)	≤ 10	0.702
Anticoagulant	42 (6.0)	38 (5.5)		21 (7.0)	18 (5.7)	0.05	≤ 10	12 (5.7)	-0.111	≤ 10	≤ 10	0.138
Antiplatelet	88 (12.6)	79 (11.4)		37 (12.3)	30 (9.6)	0.087	22 (9.4)	17 (8.1)	0.045	≤ 10	≤ 10	0.762
Antihypertensives	233 (33.4)	242 (34.9)		106 (35.1)	98 (31.2)	0.083	76 (32.3)	67 (31.9)	0.009	11 (44.0)	≤ 10	0.45
Angiotensin converting enzyme inhibitors (ACE)	53 (7.6)	72 (10.4)		26 (8.6)	30 (9.6)	-0.033	15 (6.4)	19 (9.0)	-0.1	≤ 10	≤ 10	0.677
Angiotensin receptor blockers (ARB)	98 (14.0)	96 (13.9)		45 (14.9)	37 (11.8)	0.092	22 (9.4)	26 (12.4)	-0.097	≤ 10	≤ 10	0.012
Beta blocker	114 (16.3)	94 (13.6)		47 (15.6)	42 (13.4)	0.062	37 (15.7)	28 (13.3)	0.068	≤ 10	≤ 10	0.127
Calcium channel blocker	56 (8.0)	71 (10.2)		33 (10.9)	31 (9.9)	0.035	34 (14.5)	22 (10.5)	0.121	≤ 10	≤ 10	0.203
Nitrates	≤ 10	≤ 10		0 (0.0)	≤ 10	-0.161	≤ 10	≤ 10	0.031	≤ 10	0 (0.0)	0.289
Acyclovir	≤ 10	≤ 10		≤ 10	≤ 10	0.084	0 (0.0)	0 (0.0)	0	0 (0.0)	≤ 10	-0.218
Valacyclovir	17 (2.4)	19 (2.7)		≤ 10	≤ 10	0.026	≤ 10	≤ 10	-0.069	0 (0.0)	≤ 10	-0.387
Hormonal	65 (9.3)	82 (11.8)		41 (13.6)	43 (13.7)	-0.003	25 (10.6)	22 (10.5)	0.005	≤ 10	≤ 10	0.012
HRT	41 (5.9)	54 (7.8)		25 (8.3)	24 (7.6)	0.024	16 (6.8)	13 (6.2)	0.025	≤ 10	≤ 10	-0.131
Oral Contraceptives	23 (3.3)	27 (3.9)		14 (4.6)	15 (4.8)	-0.007	≤ 10	≤ 10	-0.046	≤ 10	≤ 10	0.138
SERMs	≤ 10	≤ 10		≤ 10	≤ 10	0.003	≤ 10	0 (0.0)	0.093	0 (0.0)	0 (0.0)	0

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 698	TNFi[a] n = 693	Std. Diff.	Baricitinib n = 302	TNFi[a] n = 314	Std. Diff.	Baricitinib n = 235	TNFi[a] n = 210	Std. Diff.	Baricitinib n = 25	TNFi[a] n = 43	Std. Diff.
Topic with progestogens and/or estrogens	0 (0.0)	≤ 10		≤ 10	≤ 10	-0.044	≤ 10	0 (0.0)	0.093	0 (0.0)	0 (0.0)	0
Lipid-lowering agents	114 (16.3)	99 (14.3)		54 (17.9)	49 (15.6)	0.061	40 (17.0)	30 (14.3)	0.075	≤ 10	≤ 10	0.576
HMG CoA reductase inhibitors	94 (13.5)	81 (11.7)		45 (14.9)	36 (11.5)	0.102	31 (13.2)	20 (9.5)	0.116	≤ 10	≤ 10	0.575
Fibrates	≤ 10	≤ 10		≤ 10	≤ 10	-0.132	≤ 10	≤ 10	0.016	0 (0.0)	0 (0.0)	0
Bile acid sequestrants	≤ 10	≤ 10		≤ 10	0 (0.0)	0.082	≤ 10	≤ 10	-0.064	0 (0.0)	0 (0.0)	0
Nicotinic acid and derivatives	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)	0
Other lipid modifying agents	≤ 10	≤ 10		≤ 10	≤ 10	-0.063	≤ 10	≤ 10	-0.013	0 (0.0)	≤ 10	-0.218
Lipid modifying agents, combinations	11 (1.6)	≤ 10		≤ 10	≤ 10	0.079	≤ 10	≤ 10	-0.017	≤ 10	0 (0.0)	0.289
Rheumatoid arthritis-related												
Aspirin	≤ 10	≤ 10		≤ 10	≤ 10	-0.063	≤ 10	0 (0.0)	0.161	≤ 10	≤ 10	0.259
Cox-2 Inhibitor	31 (4.4)	43 (6.2)		15 (5.0)	19 (6.1)	-0.048	16 (6.8)	13 (6.2)	0.025	≤ 10	≤ 10	0.138
NSAIDs	254 (36.4)	273 (39.4)		115 (38.1)	117 (37.3)	0.017	85 (36.2)	87 (41.4)	-0.108	≤ 10	15 (34.9)	0.023
Glucocorticosteroid	504 (72.2)	511 (73.7)		235 (77.8)	251 (79.9)	-0.052	174 (74.0)	160 (76.2)	-0.05	17 (68.0)	35 (81.4)	-0.312
Vaccines	223 (31.9)	224 (32.3)		118 (39.1)	135 (43.0)	-0.08	79 (33.6)	81 (38.6)	-0.103	≤ 10	14 (32.6)	-0.191
Antineoplastic agents	≤ 10	≤ 10		≤ 10	≤ 10	0.002	≤ 10	0 (0.0)	0.093	≤ 10	0 (0.0)	0.289

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs;
Concom. cDMARDs = concomitant cDMARDs; DMARD = disease-modifying antirheumatic drugs; hosp = hospitalized; HRT = hormone replacement therapy; Max = maximum; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Min = minimum;
mos = months; N = number of patients in the specified category; NMSC = non-melanoma skin cancer;
RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulator; Std. Diff. = standardized difference; TNF = tumor necrosis factor; TNFi = tumor 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] TNF inhibitors.

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

Table 6.116. bDMARD-Experienced: Baseline characteristics by exposure duration - MACE cohort, Matched [SNDS]

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 812	TNFi[a] n = 813	Std. Diff.	Baricitinib n = 406	TNFi[a] n = 432	Std. Diff.	Baricitinib n = 348	TNFi[a] n = 287	Std. Diff.	Baricitinib n = 40	TNFi[a] n = 74	Std. Diff.
Age [in years]			-0.023			0.073			0.037			-0.183
N (missing)	812 (0)	813 (0)		406 (0)	432 (0)		348 (0)	287 (0)		40 (0)	74 (0)	
Mean (SD)	56.9 (13.8)	57.2 (13.6)		58.3 (13.1)	57.3 (14.0)		59.4 (11.8)	59.0 (12.5)		56.3 (11.6)	58.4 (11.4)	
Median	57.0	58.0		59.0	58.5		60.5	59.0		56.5	59.0	
Min; Max	[18.0;90.0]	[18.0;89.0]		[21.0;88.0]	[18.0;91.0]		[20.0;86.0]	[24.0;90.0]		[32.0;76.0]	[26.0;83.0]	
Sex, n (%)			0.059			0.061			0.139			-0.046
Male	153 (18.8)	135 (16.6)		87 (21.4)	82 (19.0)		88 (25.3)	56 (19.5)		≤ 10	20 (27.0)	
Female	659 (81.2)	678 (83.4)		319 (78.6)	350 (81.0)		260 (74.7)	231 (80.5)		30 (75.0)	54 (73.0)	
Clinical conditions during baseline period, n (%)												
Cancer, excluding NMSC	19 (2.3)	24 (3.0)	-0.038	≤ 10	19 (4.4)	-0.122	12 (3.4)	≤ 10	0.038	≤ 10	0 (0.0)	0.227
NMSC	0 (0.0)	0 (0.0)	0	≤ 10	≤ 10	0.097	0 (0.0)	0 (0.0)	0	0 (0.0)	≤ 10	-0.166
Chronic lung disease, excluding cystic fibrosis[c]	112 (13.8)	96 (11.8)	0.059	47 (11.6)	46 (10.6)	0.03	54 (15.5)	29 (10.1)	0.163	≤ 10	≤ 10	-0.07
Cardiovascular conditions												
Atrial arrhythmia/fibrillation	≤ 10	≤ 10	0.075	≤ 10	≤ 10	0.076	0 (0.0)	≤ 10	-0.119	0 (0.0)	0 (0.0)	0
Cardiovascular revascularization	0 (0.0)	≤ 10	-0.07	0 (0.0)	≤ 10	-0.068	≤ 10	0 (0.0)	0.076	0 (0.0)	0 (0.0)	0

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 812	TNFi[a] n = 813	Std. Diff.	Baricitinib n = 406	TNFi[a] n = 432	Std. Diff.	Baricitinib n = 348	TNFi[a] n = 287	Std. Diff.	Baricitinib n = 40	TNFi[a] n = 74	Std. Diff.
Congestive Heart Failure, hospitalized	≤ 10	≤ 10	0.017	0 (0.0)	≤ 10	-0.096	≤ 10	0 (0.0)	0.076	0 (0.0)	0 (0.0)	0
Coronary artery disease	20 (2.5)	33 (4.1)	-0.09	16 (3.9)	19 (4.4)	-0.023	17 (4.9)	15 (5.2)	-0.016	≤ 10	≤ 10	-0.013
Unstable angina	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	0 (0.0)	≤ 10	-0.084	0 (0.0)	0 (0.0)	0
Ventricular arrhythmia	≤ 10	≤ 10	-0.07	≤ 10	≤ 10	-0.066	0 (0.0)	≤ 10	-0.119	0 (0.0)	0 (0.0)	0
Stroke	≤ 10	≤ 10	0	≤ 10	≤ 10	0.097	≤ 10	≤ 10	-0.019	0 (0.0)	≤ 10	-0.166
Hemorrhagic	≤ 10	0 (0.0)	0.05	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Ischemic	≤ 10	0 (0.0)	0.05	≤ 10	≤ 10	0.003	0 (0.0)	≤ 10	-0.084	0 (0.0)	0 (0.0)	0
Unknown	≤ 10	≤ 10	-0.035	≤ 10	0 (0.0)	0.141	≤ 10	≤ 10	0.019	0 (0.0)	≤ 10	-0.166
TIA	≤ 10	0 (0.0)	0.05	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Diabetes Mellitus[c]	82 (10.1)	87 (10.7)	-0.02	45 (11.1)	45 (10.4)	0.022	44 (12.6)	26 (9.1)	0.115	≤ 10	≤ 10	-0.109
Treated insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Treated non insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Dyslipidemia (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Hypertension (not available in SNDS)												
History of hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 812	TNFi[a] n = 813	Std. Diff.	Baricitinib n = 406	TNFi[a] n = 432	Std. Diff.	Baricitinib n = 348	TNFi[a] n = 287	Std. Diff.	Baricitinib n = 40	TNFi[a] n = 74	Std. Diff.
Current hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Immune disorders	27 (3.3)	27 (3.3)	0	≤ 10	17 (3.9)	-0.116	13 (3.7)	14 (4.9)	-0.056	0 (0.0)	0 (0.0)	0
AIDS/HIV	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	0 (0.0)	≤ 10	-0.084	0 (0.0)	0 (0.0)	0
Antiphospholipid syndrome	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
SLE	≤ 10	≤ 10	0.083	≤ 10	≤ 10	0.003	≤ 10	0 (0.0)	0.132	0 (0.0)	0 (0.0)	0
Primary Sjogren Syndrome	20 (2.5)	26 (3.2)	-0.044	≤ 10	16 (3.7)	-0.122	11 (3.2)	13 (4.5)	-0.071	0 (0.0)	0 (0.0)	0
Liver or pancreatic disorder[c]	27 (3.3)	25 (3.1)	0.014	13 (3.2)	16 (3.7)	-0.028	12 (3.4)	≤ 10	0.083	≤ 10	≤ 10	0.219
Obesity (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date)	≤ 10	≤ 10	-0.022	≤ 10	≤ 10	-0.109	0 (0.0)	≤ 10	-0.084	0 (0.0)	0 (0.0)	0
RA Severity (CIRAS Index)			0.026			-0.014			0.072			0.297
Mean (SD)	6.5 (1.4)	6.5 (1.4)		6.4 (1.2)	6.4 (1.3)		6.4 (1.2)	6.3 (1.2)		6.8 (1.3)	6.4 (1.2)	
DMARDs, n (%)												
cDMARDs, during baseline period												
n, total (%)	496 (61.1)	467 (57.4)	0.074	264 (65.0)	267 (61.8)	0.067	229 (65.8)	185 (64.5)	0.028	29 (72.5)	54 (73.0)	-0.011

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 812	TNFi[a] n = 813	Std. Diff.	Baricitinib n = 406	TNFi[a] n = 432	Std. Diff.	Baricitinib n = 348	TNFi[a] n = 287	Std. Diff.	Baricitinib n = 40	TNFi[a] n = 74	Std. Diff.
Mean (SD)	0.6 (0.5)	0.6 (0.6)	0.049	0.7 (0.5)	0.6 (0.5)	0.059	0.7 (0.6)	0.7 (0.5)	0.046	0.8 (0.5)	0.8 (0.5)	0.036
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	
Min; Max	[0.0;3.0]	[0.0;3.0]		[0.0;3.0]	[0.0;3.0]		[0.0;4.0]	[0.0;2.0]		[0.0;2.0]	[0.0;2.0]	
>1 cDMARD concomitantly	18 (2.2)	22 (2.7)	-0.032	≤ 10	≤ 10	0.026	13 (3.7)	≤ 10	0.053	≤ 10	≤ 10	-0.013
Hydroxychloroquine	20 (2.5)	33 (4.1)	-0.09	12 (3.0)	15 (3.5)	-0.029	12 (3.4)	≤ 10	0.018	≤ 10	≤ 10	-0.013
Chloroquine	0 (0.0)	≤ 10	-0.05	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Azathioprin	≤ 10	≤ 10	0	≤ 10	≤ 10	0.003	≤ 10	≤ 10	-0.011	≤ 10	0 (0.0)	0.227
Leflunomide	76 (9.4)	85 (10.5)	-0.037	37 (9.1)	42 (9.7)	-0.021	34 (9.8)	36 (12.5)	-0.088	≤ 10	≤ 10	0.25
Methotrexate	406 (50.0)	353 (43.4)	0.132	222 (54.7)	211 (48.8)	0.117	188 (54.0)	143 (49.8)	0.084	21 (52.5)	49 (66.2)	-0.282
Mycophenolate mofetil	0 (0.0)	≤ 10	-0.05	0 (0.0)	≤ 10	-0.068	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Sulfasalazin	12 (1.5)	19 (2.3)	-0.063	≤ 10	≤ 10	-0.105	≤ 10	≤ 10	0.086	≤ 10	≤ 10	0.302
Cyclosporin	0 (0.0)	≤ 10	-0.05	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Penicillamin	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	0 (0.0)	≤ 10	-0.084	0 (0.0)	0 (0.0)	0
bDMARDs, during baseline period												
n, total (%)	812 (100.0)	813 (100.0)	0	406 (100.0)	432 (100.0)	0	348 (100.0)	287 (100.0)	0	40 (100.0)	74 (100.0)	0
Mean (SD)	1.1 (0.3)	1.1 (0.3)	-0.059	1.1 (0.3)	1.1 (0.3)	0.027	1.1 (0.3)	1.1 (0.3)	-0.025	1.2 (0.4)	1.1 (0.3)	0.281
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	
Min; Max	[1.0;2.0]	[1.0;3.0]		[1.0;3.0]	[1.0;2.0]		[1.0;3.0]	[1.0;2.0]		[1.0;2.0]	[1.0;2.0]	
cDMARDs, concomitant	427 (52.6)	416 (51.2)	0.028	243 (59.9)	242 (56.0)	0.078	200 (57.5)	166 (57.8)	-0.008	25 (62.5)	52 (70.3)	-0.165
Adalimumab[b]	107 (13.2)	113 (13.9)	-0.021	50 (12.3)	68 (15.7)	-0.099	55 (15.8)	39 (13.6)	0.063	≤ 10	19 (25.7)	-0.268

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 812	TNFi[a] n = 813	Std. Diff.	Baricitinib n = 406	TNFi[a] n = 432	Std. Diff.	Baricitinib n = 348	TNFi[a] n = 287	Std. Diff.	Baricitinib n = 40	TNFi[a] n = 74	Std. Diff.
Certolizumab pegol[b]	57 (7.0)	62 (7.6)	-0.023	36 (8.9)	30 (6.9)	0.071	22 (6.3)	16 (5.6)	0.032	≤ 10	≤ 10	0.237
Etanercept[b]	184 (22.7)	177 (21.8)	0.021	82 (20.2)	99 (22.9)	-0.066	55 (15.8)	59 (20.6)	-0.124	≤ 10	15 (20.3)	-0.29
Golimumab[b]	51 (6.3)	54 (6.6)	-0.015	23 (5.7)	18 (4.2)	0.069	25 (7.2)	20 (7.0)	0.008	≤ 10	≤ 10	-0.157
Infliximab[b]	42 (5.2)	44 (5.4)	-0.011	25 (6.2)	17 (3.9)	0.102	12 (3.4)	14 (4.9)	-0.072	≤ 10	≤ 10	-0.126
Rituximab	28 (3.4)	18 (2.2)	0.075	17 (4.2)	14 (3.2)	0.05	13 (3.7)	≤ 10	0.208	≤ 10	≤ 10	0.31
Sarilumab	14 (1.7)	14 (1.7)	0	11 (2.7)	≤ 10	0.041	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Abatacept	199 (24.5)	219 (26.9)	-0.056	113 (27.8)	115 (26.6)	0.027	104 (29.9)	85 (29.6)	0.006	11 (27.5)	≤ 10	0.352
Tocilizumab	178 (21.9)	176 (21.6)	0.007	85 (20.9)	96 (22.2)	-0.031	83 (23.9)	70 (24.4)	-0.013	≤ 10	11 (14.9)	0.197
Anakinra	≤ 10	≤ 10	0.042	≤ 10	≤ 10	-0.014	≤ 10	≤ 10	-0.059	0 (0.0)	0 (0.0)	0
TNFi naïve at baseline	389 (47.9)	373 (45.9)	0.041	203 (50.0)	202 (46.8)	0.065	186 (53.4)	143 (49.8)	0.073	21 (52.5)	21 (28.4)	0.507
≥1 dispensing of bDMARD within 730 days before index date (excluded), n (%)	812 (100.0)	813 (100.0)	0.000	406 (100.0)	432 (100.0)	0.000	348 (100.0)	287 (100.0)	0.000	40 (100.0)	74 (100.0)	0.000
Other prescription medications during baseline period, n (%)												
Antibiotics	350 (43.1)	359 (44.2)	-0.021	167 (41.1)	206 (47.7)	-0.132	151 (43.4)	110 (38.3)	0.103	21 (52.5)	20 (27.0)	0.539
Antidiabetic agents	82 (10.1)	79 (9.7)	0.013	41 (10.1)	43 (10.0)	0.005	40 (11.5)	26 (9.1)	0.08	≤ 10	11 (14.9)	0.004
Insulins	39 (4.8)	37 (4.6)	0.012	17 (4.2)	≤ 10	0.121	12 (3.4)	≤ 10	0.06	≤ 10	≤ 10	0.12
Non-insulins	58 (7.1)	63 (7.7)	-0.023	33 (8.1)	36 (8.3)	-0.008	34 (9.8)	24 (8.4)	0.049	≤ 10	11 (14.9)	-0.069
Cardiovascular												

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 812	TNFi[a] n = 813	Std. Diff.	Baricitinib n = 406	TNFi[a] n = 432	Std. Diff.	Baricitinib n = 348	TNFi[a] n = 287	Std. Diff.	Baricitinib n = 40	TNFi[a] n = 74	Std. Diff.
Antithrombotic agents	102 (12.6)	128 (15.7)	-0.091	67 (16.5)	56 (13.0)	0.1	53 (15.2)	41 (14.3)	0.027	≤ 10	18 (24.3)	-0.309
Anticoagulant	24 (3.0)	35 (4.3)	-0.072	19 (4.7)	11 (2.5)	0.115	≤ 10	≤ 10	-0.015	≤ 10	≤ 10	-0.087
Antiplatelet	83 (10.2)	100 (12.3)	-0.066	51 (12.6)	47 (10.9)	0.052	44 (12.6)	33 (11.5)	0.035	≤ 10	17 (23.0)	-0.355
Antihypertensives	242 (29.8)	281 (34.6)	-0.102	142 (35.0)	152 (35.2)	-0.004	139 (39.9)	107 (37.3)	0.055	16 (40.0)	29 (39.2)	0.017
Angiotensin converting enzyme inhibitors (ACE)	64 (7.9)	76 (9.3)	-0.052	32 (7.9)	40 (9.3)	-0.049	48 (13.8)	24 (8.4)	0.174	≤ 10	≤ 10	0.267
Angiotensin receptor blockers (ARB)	96 (11.8)	107 (13.2)	-0.041	51 (12.6)	74 (17.1)	-0.129	52 (14.9)	54 (18.8)	-0.104	≤ 10	14 (18.9)	-0.256
Beta blocker	97 (11.9)	118 (14.5)	-0.076	50 (12.3)	66 (15.3)	-0.086	58 (16.7)	51 (17.8)	-0.029	≤ 10	12 (16.2)	0.16
Calcium channel blocker	68 (8.4)	82 (10.1)	-0.059	46 (11.3)	44 (10.2)	0.037	41 (11.8)	20 (7.0)	0.166	≤ 10	16 (21.6)	-0.409
Nitrates	≤ 10	≤ 10	-0.053	≤ 10	≤ 10	-0.143	≤ 10	≤ 10	0.027	0 (0.0)	≤ 10	-0.166
Acyclovir	≤ 10	≤ 10	-0.045	0 (0.0)	≤ 10	-0.137	≤ 10	≤ 10	-0.011	0 (0.0)	0 (0.0)	0
Valacyclovir	32 (3.9)	35 (4.3)	-0.018	17 (4.2)	21 (4.9)	-0.032	22 (6.3)	13 (4.5)	0.079	≤ 10	≤ 10	-0.013
Hormonal	108 (13.3)	131 (16.1)	-0.08	62 (15.3)	63 (14.6)	0.019	42 (12.1)	29 (10.1)	0.063	≤ 10	≤ 10	0.174
HRT	61 (7.5)	80 (9.8)	-0.083	30 (7.4)	29 (6.7)	0.026	26 (7.5)	17 (5.9)	0.062	≤ 10	≤ 10	0.196
Oral Contraceptives	45 (5.5)	52 (6.4)	-0.036	33 (8.1)	26 (6.0)	0.082	15 (4.3)	12 (4.2)	0.006	≤ 10	≤ 10	0.029
SERMs	≤ 10	≤ 10	0.029	0 (0.0)	≤ 10	-0.137	≤ 10	≤ 10	0.033	≤ 10	0 (0.0)	0.227

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 812	TNFi[a] n = 813	Std. Diff.	Baricitinib n = 406	TNFi[a] n = 432	Std. Diff.	Baricitinib n = 348	TNFi[a] n = 287	Std. Diff.	Baricitinib n = 40	TNFi[a] n = 74	Std. Diff.
Topic with progestogens and/or estrogens	≤ 10	≤ 10	0.05	≤ 10	≤ 10	-0.089	≤ 10	0 (0.0)	0.108	0 (0.0)	0 (0.0)	0
Lipid-lowering agents	122 (15.0)	143 (17.6)	-0.07	65 (16.0)	69 (16.0)	0.001	68 (19.5)	52 (18.1)	0.036	≤ 10	20 (27.0)	-0.166
HMG CoA reductase inhibitors	101 (12.4)	115 (14.1)	-0.05	56 (13.8)	60 (13.9)	-0.003	51 (14.7)	39 (13.6)	0.031	≤ 10	18 (24.3)	-0.104
Fibrates	11 (1.4)	15 (1.8)	-0.039	≤ 10	≤ 10	0.062	≤ 10	≤ 10	-0.006	0 (0.0)	0 (0.0)	0
Bile acid sequestrants	≤ 10	≤ 10	0.022	≤ 10	≤ 10	0.004	≤ 10	≤ 10	-0.011	0 (0.0)	0 (0.0)	0
Nicotinic acid and derivatives	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)	0
Other lipid modifying agents	≤ 10	11 (1.4)	-0.075	≤ 10	≤ 10	0.004	≤ 10	≤ 10	0.019	0 (0.0)	0 (0.0)	0
Lipid modifying agents, combinations	≤ 10	≤ 10	-0.023	≤ 10	≤ 10	-0.043	≤ 10	≤ 10	-0.006	0 (0.0)	≤ 10	-0.236
Rheumatoid arthritis-related												
Aspirin	14 (1.7)	≤ 10	0.041	≤ 10	≤ 10	-0.05	≤ 10	≤ 10	0.079	0 (0.0)	0 (0.0)	0
Cox-2 Inhibitor	50 (6.2)	51 (6.3)	-0.005	23 (5.7)	23 (5.3)	0.015	19 (5.5)	17 (5.9)	-0.02	≤ 10	≤ 10	-0.297
NSAIDs	305 (37.6)	331 (40.7)	-0.065	149 (36.7)	163 (37.7)	-0.021	121 (34.8)	117 (40.8)	-0.124	15 (37.5)	27 (36.5)	0.021
Glucocorticosteroid	577 (71.1)	557 (68.5)	0.056	282 (69.5)	288 (66.7)	0.06	221 (63.5)	193 (67.2)	-0.079	25 (62.5)	44 (59.5)	0.062
Vaccines	211 (26.0)	181 (22.3)	0.087	124 (30.5)	120 (27.8)	0.061	99 (28.4)	72 (25.1)	0.076	12 (30.0)	≤ 10	0.448
Antineoplastic agents	≤ 10	≤ 10	-0.105	≤ 10	≤ 10	0.044	0 (0.0)	≤ 10	-0.084	0 (0.0)	0 (0.0)	0

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs;
Concom. cDMARDs = concomitant cDMARDs; DMARD = disease-modifying antirheumatic drugs; hosp = hospitalized; HRT = hormone replacement therapy; Max = maximum; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Min = minimum;
mos = months; N = number of patients in the specified category; NMSC = non-melanoma skin cancer;
RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulator; Std. Diff. = standardized difference; TNF = tumor necrosis factor; TNFi = tumor 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] TNF inhibitors.

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

Table 6.117. bDMARD-Naïve: Baseline Characteristics by Exposure Duration, MACE Cohort Matched [SNDS]

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 697	TNFi[a] n = 656	Std. Diff.	Baricitinib n = 301	TNFi[a] n = 305	Std. Diff.	Baricitinib n = 236	TNFi[a] n = 249	Std. Diff.	Baricitinib n = 23	TNFi[a] n = 47	Std. Diff.
Age [in years]			0.016			0.054			-0.02			-0.06
N (missing)	697 (0)	656 (0)		301 (0)	305 (0)		236 (0)	249 (0)		23 (0)	47 (0)	
Mean (SD)	59.3 (13.5)	59.1 (12.9)		60.5 (13.1)	59.8 (13.8)		58.8 (12.8)	59.1 (13.4)		56.3 (11.9)	57.0 (12.7)	
Median	60.0	60.0		61.0	61.0		59.0	60.0		60.0	57.0	
Min; Max	[20.0;89.0]	[19.0;92.0]		[19.0;86.0]	[22.0;90.0]		[22.0;86.0]	[20.0;93.0]		[30.0;74.0]	[27.0;81.0]	
Sex, n (%)			0.009			-0.058			0.089			-0.099
Male	132 (18.9)	122 (18.6)		60 (19.9)	68 (22.3)		53 (22.5)	47 (18.9)		≤ 10	≤ 10	
Female	565 (81.1)	534 (81.4)		241 (80.1)	237 (77.7)		183 (77.5)	202 (81.1)		19 (82.6)	37 (78.7)	
Clinical conditions during baseline period, n (%)												
Cancer, excluding NMSC	32 (4.6)	24 (3.7)	0.047	11 (3.7)	11 (3.6)	0.003	≤ 10	13 (5.2)	-0.139	0 (0.0)	≤ 10	-0.209
NMSC	≤ 10	≤ 10	-0.003	0 (0.0)	0 (0.0)	0	0 (0.0)	≤ 10	-0.09	0 (0.0)	0 (0.0)	0
Chronic lung disease, excluding cystic fibrosis[c]	98 (14.1)	77 (11.7)	0.069	42 (14.0)	51 (16.7)	-0.077	27 (11.4)	21 (8.4)	0.101	≤ 10	≤ 10	-0.099
Cardiovascular conditions												
Atrial arrhythmia/fibrillation	≤ 10	≤ 10	0.044	≤ 10	≤ 10	0.002	≤ 10	≤ 10	0.127	0 (0.0)	0 (0.0)	0
Cardiovascular revascularization	≤ 10	≤ 10	-0.002	0 (0.0)	≤ 10	-0.081	≤ 10	0 (0.0)	0.092	0 (0.0)	0 (0.0)	0

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 697	TNFi[a] n = 656	Std. Diff.	Baricitinib n = 301	TNFi[a] n = 305	Std. Diff.	Baricitinib n = 236	TNFi[a] n = 249	Std. Diff.	Baricitinib n = 23	TNFi[a] n = 47	Std. Diff.
Congestive Heart Failure, hospitalized	≤ 10	≤ 10	-0.057	≤ 10	≤ 10	-0.035	≤ 10	≤ 10	0.057	0 (0.0)	0 (0.0)	0
Coronary artery disease	39 (5.6)	30 (4.6)	0.047	17 (5.6)	19 (6.2)	-0.025	≤ 10	≤ 10	-0.012	≤ 10	≤ 10	0.005
Unstable angina	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)	0
Ventricular arrhythmia	≤ 10	≤ 10	0.034	≤ 10	≤ 10	-0.035	≤ 10	≤ 10	0.08	0 (0.0)	≤ 10	-0.209
Stroke	≤ 10	≤ 10	0.041	≤ 10	≤ 10	-0.092	≤ 10	0 (0.0)	0.186	0 (0.0)	≤ 10	-0.209
Hemorrhagic	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)	0
Ischemic	≤ 10	0 (0.0)	0.054	0 (0.0)	≤ 10	-0.081	≤ 10	0 (0.0)	0.092	0 (0.0)	0 (0.0)	0
Unknown	≤ 10	≤ 10	0.021	≤ 10	≤ 10	-0.066	≤ 10	0 (0.0)	0.161	0 (0.0)	≤ 10	-0.209
TIA	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)	0
Diabetes Mellitus[c]	64 (9.2)	60 (9.1)	0.001	21 (7.0)	26 (8.5)	-0.058	20 (8.5)	20 (8.0)	0.016	≤ 10	≤ 10	0.267
Treated insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Treated non insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Dyslipidemia (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Hypertension (not available in SNDS)												
History of hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 697	TNFi[a] n = 656	Std. Diff.	Baricitinib n = 301	TNFi[a] n = 305	Std. Diff.	Baricitinib n = 236	TNFi[a] n = 249	Std. Diff.	Baricitinib n = 23	TNFi[a] n = 47	Std. Diff.
Current hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Immune disorders	35 (5.0)	25 (3.8)	0.059	≤ 10	≤ 10	-0.017	≤ 10	≤ 10	-0.09	≤ 10	≤ 10	0.007
AIDS/HIV	0 (0.0)	≤ 10	-0.055	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Antiphospholipid syndrome	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
SLE	≤ 10	≤ 10	0.033	≤ 10	≤ 10	0.048	≤ 10	≤ 10	-0.118	≤ 10	≤ 10	0.126
Primary Sjogren Syndrome	29 (4.2)	18 (2.7)	0.078	≤ 10	≤ 10	-0.037	≤ 10	≤ 10	-0.023	≤ 10	≤ 10	-0.09
Liver or pancreatic disorder[c]	17 (2.4)	14 (2.1)	0.02	≤ 10	≤ 10	-0.039	≤ 10	11 (4.4)	-0.159	0 (0.0)	≤ 10	-0.209
Obesity (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date)	≤ 10	≤ 10	-0.048	≤ 10	≤ 10	-0.066	≤ 10	≤ 10	-0.087	0 (0.0)	0 (0.0)	0
RA Severity (CIRAS Index)			-0.008			-0.198			-0.054			-0.321
Mean (SD)	6.5 (1.5)	6.5 (1.5)		6.4 (1.5)	6.7 (1.6)		6.6 (1.5)	6.7 (1.6)		6.6 (1.4)	7.1 (1.5)	
DMARDs, n (%)												
cDMARDs, during baseline period												
n, total (%)	498 (71.4)	456 (69.5)	0.043	221 (73.4)	249 (81.6)	-0.198	179 (75.8)	203 (81.5)	-0.139	18 (78.3)	38 (80.9)	-0.064

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 697	TNFi[a] n = 656	Std. Diff.	Baricitinib n = 301	TNFi[a] n = 305	Std. Diff.	Baricitinib n = 236	TNFi[a] n = 249	Std. Diff.	Baricitinib n = 23	TNFi[a] n = 47	Std. Diff.
Mean (SD)	0.8 (0.6)	0.8 (0.6)	0.05	0.9 (0.7)	0.9 (0.6)	-0.116	0.9 (0.6)	1.0 (0.6)	-0.172	1.1 (0.9)	1.0 (0.7)	0.163
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	
Min; Max	[0.0;3.0]	[0.0;3.0]		[0.0;3.0]	[0.0;3.0]		[0.0;4.0]	[0.0;3.0]		[0.0;3.0]	[0.0;3.0]	
>1 cDMARD concomitantly	58 (8.3)	43 (6.6)	0.067	32 (10.6)	21 (6.9)	0.133	21 (8.9)	27 (10.8)	-0.065	≤ 10	≤ 10	0.12
Hydroxychloroquine	54 (7.7)	41 (6.3)	0.059	33 (11.0)	22 (7.2)	0.131	18 (7.6)	24 (9.6)	-0.072	≤ 10	≤ 10	0.28
Chloroquine	0 (0.0)	≤ 10	-0.055	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Azathioprin	≤ 10	≤ 10	-0.003	≤ 10	≤ 10	-0.046	≤ 10	0 (0.0)	0.092	0 (0.0)	0 (0.0)	0
Leflunomide	119 (17.1)	100 (15.2)	0.05	38 (12.6)	43 (14.1)	-0.043	32 (13.6)	36 (14.5)	-0.026	≤ 10	≤ 10	0.068
Methotrexate	366 (52.5)	352 (53.7)	-0.023	173 (57.5)	195 (63.9)	-0.133	141 (59.7)	167 (67.1)	-0.153	13 (56.5)	31 (66.0)	-0.195
Mycophenolate mofetil	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	≤ 10	0 (0.0)	0.092	0 (0.0)	0 (0.0)	0
Sulfasalazin	39 (5.6)	30 (4.6)	0.047	16 (5.3)	25 (8.2)	-0.115	13 (5.5)	19 (7.6)	-0.086	≤ 10	≤ 10	0.317
Cyclosporin	≤ 10	0 (0.0)	0.054	0 (0.0)	0 (0.0)	0	≤ 10	0 (0.0)	0.092	0 (0.0)	0 (0.0)	0
Penicillamin	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)	0
bDMARDs, during baseline period												
n, total (%)	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Mean (SD)	0.0 (0.0)	0.0 (0.0)	0.000	0.0 (0.0)	0.0 (0.0)	0.000	0.0 (0.0)	0.0 (0.0)	0.000	0.0 (0.0)	0.0 (0.0)	0.000
Median	0.0	0.0		0.0	0.0		0.0	0.0		0.0	0.0	
Min; Max	[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;0.0]	[0.0;0.0]	
cDMARDs, concomitant	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Adalimumab[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 697	TNFi[a] n = 656	Std. Diff.	Baricitinib n = 301	TNFi[a] n = 305	Std. Diff.	Baricitinib n = 236	TNFi[a] n = 249	Std. Diff.	Baricitinib n = 23	TNFi[a] n = 47	Std. Diff.
Certolizumab pegol[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Etanercept[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Golimumab[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Infliximab[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Rituximab	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Sarilumab	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Abatacept	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Tocilizumab	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Anakinra	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
TNFi naïve at baseline	697 (100.0)	656 (100.0)	0.000	301 (100.0)	305 (100.0)	0.000	236 (100.0)	249 (100.0)	0.000	23 (100.0)	47 (100.0)	0.000
≥1 dispensing of bDMARD within 730 days before index date (excluded), n (%)	248 (35.6)	190 (29.0)	0.142	106 (35.2)	67 (22.0)	0.296	83 (35.2)	43 (17.3)	0.416	14 (60.9)	≤ 10	1.151
Other prescription medications during baseline period, n (%)												
Antibiotics	263 (37.7)	271 (41.3)	-0.073	127 (42.2)	114 (37.4)	0.099	102 (43.2)	88 (35.3)	0.162	≤ 10	13 (27.7)	0.335
Antidiabetic agents	56 (8.0)	52 (7.9)	0.004	23 (7.6)	26 (8.5)	-0.032	20 (8.5)	20 (8.0)	0.016	≤ 10	≤ 10	0.267
Insulins	22 (3.2)	23 (3.5)	-0.02	≤ 10	11 (3.6)	-0.016	≤ 10	≤ 10	0.072	≤ 10	≤ 10	0.005
Non-insulins	46 (6.6)	44 (6.7)	-0.004	20 (6.6)	23 (7.5)	-0.035	17 (7.2)	18 (7.2)	-0.001	≤ 10	≤ 10	0.433
Cardiovascular												

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 697	TNFi[a] n = 656	Std. Diff.	Baricitinib n = 301	TNFi[a] n = 305	Std. Diff.	Baricitinib n = 236	TNFi[a] n = 249	Std. Diff.	Baricitinib n = 23	TNFi[a] n = 47	Std. Diff.
Antithrombotic agents	117 (16.8)	110 (16.8)	0.001	51 (16.9)	49 (16.1)	0.024	31 (13.1)	33 (13.3)	-0.004	≤ 10	≤ 10	0.508
Anticoagulant	41 (5.9)	32 (4.9)	0.045	21 (7.0)	14 (4.6)	0.102	≤ 10	11 (4.4)	-0.053	≤ 10	≤ 10	0.088
Antiplatelet	86 (12.3)	83 (12.7)	-0.01	37 (12.3)	37 (12.1)	0.005	24 (10.2)	23 (9.2)	0.032	≤ 10	≤ 10	0.602
Antihypertensives	234 (33.6)	214 (32.6)	0.02	103 (34.2)	102 (33.4)	0.016	77 (32.6)	74 (29.7)	0.063	≤ 10	13 (27.7)	0.245
Angiotensin converting enzyme inhibitors (ACE)	53 (7.6)	64 (9.8)	-0.077	27 (9.0)	23 (7.5)	0.052	16 (6.8)	22 (8.8)	-0.077	≤ 10	≤ 10	0.538
Angiotensin receptor blockers (ARB)	99 (14.2)	81 (12.3)	0.055	42 (14.0)	37 (12.1)	0.054	21 (8.9)	35 (14.1)	-0.162	≤ 10	≤ 10	-0.053
Beta blocker	114 (16.4)	96 (14.6)	0.048	45 (15.0)	53 (17.4)	-0.066	38 (16.1)	33 (13.3)	0.081	≤ 10	≤ 10	0.075
Calcium channel blocker	55 (7.9)	61 (9.3)	-0.05	33 (11.0)	33 (10.8)	0.005	36 (15.3)	15 (6.0)	0.303	≤ 10	≤ 10	0.007
Nitrates	≤ 10	≤ 10	0.044	0 (0.0)	≤ 10	-0.163	≤ 10	≤ 10	-0.058	≤ 10	0 (0.0)	0.302
Acyclovir	≤ 10	≤ 10	-0.005	≤ 10	≤ 10	0.083	0 (0.0)	≤ 10	-0.09	0 (0.0)	≤ 10	-0.209
Valacyclovir	17 (2.4)	17 (2.6)	-0.01	≤ 10	11 (3.6)	-0.016	≤ 10	≤ 10	0.033	0 (0.0)	≤ 10	-0.431
Hormonal	64 (9.2)	70 (10.7)	-0.05	41 (13.6)	34 (11.1)	0.075	26 (11.0)	32 (12.9)	-0.057	≤ 10	≤ 10	-0.167
HRT	40 (5.7)	42 (6.4)	-0.028	25 (8.3)	20 (6.6)	0.067	17 (7.2)	13 (5.2)	0.082	≤ 10	≤ 10	-0.17
Oral Contraceptives	23 (3.3)	25 (3.8)	-0.028	14 (4.7)	15 (4.9)	-0.013	≤ 10	16 (6.4)	-0.141	≤ 10	≤ 10	-0.066
SERMs	≤ 10	≤ 10	-0.057	≤ 10	0 (0.0)	0.116	≤ 10	≤ 10	-0.087	0 (0.0)	0 (0.0)	0

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 697	TNFi[a] n = 656	Std. Diff.	Baricitinib n = 301	TNFi[a] n = 305	Std. Diff.	Baricitinib n = 236	TNFi[a] n = 249	Std. Diff.	Baricitinib n = 23	TNFi[a] n = 47	Std. Diff.
Topic with progestogens and/or estrogens	0 (0.0)	≤ 10	-0.078	≤ 10	≤ 10	0.001	≤ 10	≤ 10	0.004	0 (0.0)	0 (0.0)	0
Lipid-lowering agents	111 (15.9)	97 (14.8)	0.032	56 (18.6)	47 (15.4)	0.085	41 (17.4)	40 (16.1)	0.035	≤ 10	≤ 10	0.178
HMG CoA reductase inhibitors	92 (13.2)	87 (13.3)	-0.002	47 (15.6)	33 (10.8)	0.142	32 (13.6)	33 (13.3)	0.009	≤ 10	≤ 10	0.13
Fibrates	≤ 10	≤ 10	0.021	≤ 10	≤ 10	-0.092	≤ 10	≤ 10	0.11	0 (0.0)	0 (0.0)	0
Bile acid sequestrants	≤ 10	≤ 10	0.021	≤ 10	≤ 10	0.001	≤ 10	≤ 10	-0.049	0 (0.0)	0 (0.0)	0
Nicotinic acid and derivatives	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)	0
Other lipid modifying agents	≤ 10	≤ 10	0.05	≤ 10	≤ 10	0.001	≤ 10	≤ 10	0.046	0 (0.0)	0 (0.0)	0
Lipid modifying agents, combinations	12 (1.7)	≤ 10	0.087	≤ 10	≤ 10	0.002	≤ 10	≤ 10	0.08	≤ 10	≤ 10	0.126
Rheumatoid arthritis-related												
Aspirin	≤ 10	≤ 10	-0.059	≤ 10	≤ 10	-0.035	≤ 10	≤ 10	0.006	≤ 10	0 (0.0)	0.436
Cox-2 Inhibitor	31 (4.4)	30 (4.6)	-0.006	15 (5.0)	18 (5.9)	-0.041	16 (6.8)	11 (4.4)	0.103	≤ 10	≤ 10	0.007
NSAIDs	252 (36.2)	223 (34.0)	0.045	115 (38.2)	115 (37.7)	0.01	85 (36.0)	102 (41.0)	-0.102	≤ 10	17 (36.2)	0.061
Glucocorticosteroid	503 (72.2)	476 (72.6)	-0.009	232 (77.1)	258 (84.6)	-0.192	176 (74.6)	186 (74.7)	-0.003	16 (69.6)	34 (72.3)	-0.061
Vaccines	221 (31.7)	215 (32.8)	-0.023	119 (39.5)	111 (36.4)	0.065	80 (33.9)	98 (39.4)	-0.114	≤ 10	16 (34.0)	-0.174
Antineoplastic agents	≤ 10	≤ 10	0.058	≤ 10	0 (0.0)	0.082	≤ 10	≤ 10	0.057	0 (0.0)	0 (0.0)	0

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs;
Concom. cDMARDs = concomitant cDMARDs; DMARD = disease-modifying antirheumatic drugs; hosp = hospitalized; HRT = hormone replacement therapy; Max = maximum; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Min = minimum;
mos = months; N = number of patients in the specified category; NMSC = non-melanoma skin cancer;
RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulator; Std. Diff. = standardized difference; TNF = tumor necrosis factor; TNFi = tumor 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] TNF inhibitors.

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

Table 6.118. bDMARD-Experienced: Baseline characteristics by exposure duration - Incident Serious Infection cohort ,Matched [SNDS]

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 843	TNFi[a] n = 820	Std. Diff.	Baricitinib n = 398	TNFi[a] n = 444	Std. Diff.	Baricitinib n = 359	TNFi[a] n = 308	Std. Diff.	Baricitinib n = 43	TNFi[a] n = 71	Std. Diff.
Age [in years]			-0.027			-0.001			0.04			-0.195
N (missing)	843 (0)	820 (0)		398 (0)	444 (0)		359 (0)	308 (0)		43 (0)	71 (0)	
Mean (SD)	57.2 (14.0)	57.6 (13.5)		57.7 (12.8)	57.8 (13.9)		59.6 (12.1)	59.1 (13.4)		56.7 (11.6)	58.9 (10.9)	
Median	58.0	58.0		58.0	58.0		60.0	59.0		57.0	59.0	
Min; Max	[18.0;98.0]	[18.0;89.0]		[21.0;87.0]	[19.0;91.0]		[20.0;92.0]	[18.0;90.0]		[32.0;77.0]	[34.0;83.0]	
Sex, n (%)			0.059			0.035			0.08			0.086
Male	162 (19.2)	139 (17.0)		79 (19.8)	82 (18.5)		89 (24.8)	66 (21.4)		≤ 10	14 (19.7)	
Female	681 (80.8)	681 (83.0)		319 (80.2)	362 (81.5)		270 (75.2)	242 (78.6)		33 (76.7)	57 (80.3)	
Clinical conditions during baseline period, n (%)												
Cancer, excluding NMSC	16 (1.9)	21 (2.6)	-0.045	≤ 10	18 (4.1)	-0.119	≤ 10	≤ 10	-0.026	≤ 10	0 (0.0)	0.218
NMSC	0 (0.0)	0 (0.0)	0	≤ 10	≤ 10	0.076	0 (0.0)	0 (0.0)	0	0 (0.0)	≤ 10	-0.169
Chronic lung disease, excluding cystic fibrosis[c]	112 (13.3)	100 (12.2)	0.033	52 (13.1)	52 (11.7)	0.041	54 (15.0)	35 (11.4)	0.109	≤ 10	≤ 10	0.14
Cardiovascular conditions												
Atrial arrhythmia/fibrillation	≤ 10	11 (1.3)	-0.014	≤ 10	≤ 10	0.013	≤ 10	≤ 10	-0.086	0 (0.0)	0 (0.0)	0
Cardiovascular revascularization	≤ 10	≤ 10	-0.067	≤ 10	≤ 10	-0.034	≤ 10	0 (0.0)	0.075	0 (0.0)	0 (0.0)	0

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 843	TNFi[a] n = 820	Std. Diff.	Baricitinib n = 398	TNFi[a] n = 444	Std. Diff.	Baricitinib n = 359	TNFi[a] n = 308	Std. Diff.	Baricitinib n = 43	TNFi[a] n = 71	Std. Diff.
Congestive Heart Failure, hospitalized	≤ 10	≤ 10	0.054	≤ 10	≤ 10	0.008	≤ 10	≤ 10	-0.008	0 (0.0)	0 (0.0)	0
Coronary artery disease	30 (3.6)	35 (4.3)	-0.037	11 (2.8)	24 (5.4)	-0.134	22 (6.1)	16 (5.2)	0.04	≤ 10	≤ 10	-0.031
Unstable angina	0 (0.0)	≤ 10	-0.049	0 (0.0)	≤ 10	-0.067	0 (0.0)	≤ 10	-0.081	0 (0.0)	0 (0.0)	0
Ventricular arrhythmia	≤ 10	≤ 10	0.042	≤ 10	≤ 10	-0.048	≤ 10	≤ 10	-0.116	0 (0.0)	0 (0.0)	0
Stroke	≤ 10	≤ 10	-0.003	≤ 10	≤ 10	0.056	≤ 10	≤ 10	-0.017	0 (0.0)	≤ 10	-0.169
Hemorrhagic	≤ 10	0 (0.0)	0.049	≤ 10	≤ 10	0.005	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Ischemic	≤ 10	≤ 10	-0.002	≤ 10	≤ 10	0.076	≤ 10	≤ 10	-0.008	0 (0.0)	0 (0.0)	0
Unknown	≤ 10	≤ 10	-0.017	≤ 10	≤ 10	0.088	≤ 10	≤ 10	0.014	0 (0.0)	≤ 10	-0.169
TIA	≤ 10	≤ 10	-0.03	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Diabetes Mellitus[c]	77 (9.1)	81 (9.9)	-0.025	41 (10.3)	48 (10.8)	-0.017	45 (12.5)	29 (9.4)	0.1	≤ 10	≤ 10	-0.288
Treated insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Treated non insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Dyslipidemia (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Hypertension (not available in SNDS)												
History of hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 843	TNFi[a] n = 820	Std. Diff.	Baricitinib n = 398	TNFi[a] n = 444	Std. Diff.	Baricitinib n = 359	TNFi[a] n = 308	Std. Diff.	Baricitinib n = 43	TNFi[a] n = 71	Std. Diff.
Current hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Immune disorders	30 (3.6)	32 (3.9)	-0.018	≤ 10	19 (4.3)	-0.098	11 (3.1)	13 (4.2)	-0.062	0 (0.0)	≤ 10	-0.169
AIDS/HIV	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	0 (0.0)	≤ 10	-0.081	0 (0.0)	0 (0.0)	0
Antiphospholipid syndrome	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
SLE	12 (1.4)	≤ 10	0.113	≤ 10	≤ 10	0.046	≤ 10	0 (0.0)	0.106	0 (0.0)	0 (0.0)	0
Primary Sjogren Syndrome	19 (2.3)	30 (3.7)	-0.083	≤ 10	18 (4.1)	-0.119	≤ 10	12 (3.9)	-0.079	0 (0.0)	≤ 10	-0.169
Liver or pancreatic disorder[c]	27 (3.2)	23 (2.8)	0.023	13 (3.3)	21 (4.7)	-0.075	14 (3.9)	≤ 10	0.074	≤ 10	≤ 10	-0.107
Obesity (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date)	≤ 10	≤ 10	-0.042	≤ 10	≤ 10	-0.086	0 (0.0)	≤ 10	-0.114	0 (0.0)	0 (0.0)	0
RA Severity (CIRAS Index)			0.011			0.001			0.055			0.194
Mean (SD)	6.5 (1.4)	6.5 (1.3)		6.4 (1.2)	6.4 (1.3)		6.4 (1.2)	6.3 (1.3)		6.7 (1.3)	6.4 (1.3)	
DMARDs, n (%)												
cDMARDs, during baseline period												
n, total (%)	513 (60.9)	477 (58.2)	0.055	257 (64.6)	275 (61.9)	0.055	246 (68.5)	192 (62.3)	0.13	31 (72.1)	52 (73.2)	-0.026

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 843	TNFi[a] n = 820	Std. Diff.	Baricitinib n = 398	TNFi[a] n = 444	Std. Diff.	Baricitinib n = 359	TNFi[a] n = 308	Std. Diff.	Baricitinib n = 43	TNFi[a] n = 71	Std. Diff.
Mean (SD)	0.6 (0.5)	0.6 (0.5)	0.044	0.7 (0.6)	0.6 (0.5)	0.077	0.7 (0.5)	0.7 (0.6)	0.113	0.8 (0.6)	0.8 (0.5)	0.055
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	
Min; Max	[0.0;3.0]	[0.0;3.0]		[0.0;3.0]	[0.0;2.0]		[0.0;4.0]	[0.0;2.0]		[0.0;3.0]	[0.0;2.0]	
>1 cDMARD concomitantly	20 (2.4)	15 (1.8)	0.038	≤ 10	≤ 10	0.049	12 (3.3)	12 (3.9)	-0.03	≤ 10	≤ 10	-0.031
Hydroxychloroquine	23 (2.7)	30 (3.7)	-0.053	≤ 10	15 (3.4)	-0.051	14 (3.9)	11 (3.6)	0.017	≤ 10	≤ 10	-0.031
Chloroquine	0 (0.0)	≤ 10	-0.049	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	≤ 10	0 (0.0)	0.218
Azathioprin	≤ 10	≤ 10	0.021	≤ 10	0 (0.0)	0.071	≤ 10	≤ 10	-0.048	≤ 10	0 (0.0)	0.218
Leflunomide	80 (9.5)	82 (10.0)	-0.017	40 (10.1)	42 (9.5)	0.02	30 (8.4)	40 (13.0)	-0.15	≤ 10	≤ 10	0.283
Methotrexate	417 (49.5)	368 (44.9)	0.092	213 (53.5)	219 (49.3)	0.084	203 (56.5)	145 (47.1)	0.19	23 (53.5)	47 (66.2)	-0.262
Mycophenolate mofetil	0 (0.0)	≤ 10	-0.049	0 (0.0)	≤ 10	-0.067	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Sulfasalazin	12 (1.4)	17 (2.1)	-0.05	≤ 10	≤ 10	0.014	11 (3.1)	≤ 10	0.121	≤ 10	≤ 10	0.19
Cyclosporin	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)	0
Penicillamin	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	0 (0.0)	≤ 10	-0.081	0 (0.0)	0 (0.0)	0
bDMARDs, during baseline period												
n, total (%)	843 (100.0)	820 (100.0)	0	398 (100.0)	444 (100.0)	0	359 (100.0)	308 (100.0)	0	43 (100.0)	71 (100.0)	0
Mean (SD)	1.1 (0.3)	1.1 (0.3)	-0.056	1.1 (0.3)	1.1 (0.3)	-0.065	1.1 (0.2)	1.1 (0.2)	-0.004	1.1 (0.3)	1.1 (0.3)	0.082
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	
Min; Max	[1.0;2.0]	[1.0;3.0]		[1.0;3.0]	[1.0;2.0]		[1.0;2.0]	[1.0;2.0]		[1.0;2.0]	[1.0;2.0]	
cDMARDs, concomitant	456 (54.1)	420 (51.2)	0.058	236 (59.3)	249 (56.1)	0.065	214 (59.6)	175 (56.8)	0.057	27 (62.8)	50 (70.4)	-0.162
Adalimumab[b]	117 (13.9)	112 (13.7)	0.006	42 (10.6)	61 (13.7)	-0.098	51 (14.2)	48 (15.6)	-0.039	≤ 10	20 (28.2)	-0.354

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 843	TNFi[a] n = 820	Std. Diff.	Baricitinib n = 398	TNFi[a] n = 444	Std. Diff.	Baricitinib n = 359	TNFi[a] n = 308	Std. Diff.	Baricitinib n = 43	TNFi[a] n = 71	Std. Diff.
Certolizumab pegol[b]	62 (7.4)	62 (7.6)	-0.008	29 (7.3)	35 (7.9)	-0.023	22 (6.1)	22 (7.1)	-0.041	≤ 10	≤ 10	-0.102
Etanercept[b]	183 (21.7)	178 (21.7)	0	82 (20.6)	97 (21.8)	-0.03	59 (16.4)	67 (21.8)	-0.136	≤ 10	17 (23.9)	-0.573
Golimumab[b]	52 (6.2)	59 (7.2)	-0.041	25 (6.3)	22 (5.0)	0.058	26 (7.2)	20 (6.5)	0.03	≤ 10	≤ 10	-0.055
Infliximab[b]	44 (5.2)	43 (5.2)	-0.001	23 (5.8)	20 (4.5)	0.058	14 (3.9)	14 (4.5)	-0.032	≤ 10	≤ 10	-0.17
Rituximab	24 (2.8)	18 (2.2)	0.042	≤ 10	14 (3.2)	-0.039	15 (4.2)	≤ 10	0.232	≤ 10	≤ 10	0.521
Sarilumab	23 (2.7)	16 (2.0)	0.051	≤ 10	≤ 10	0.016	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Abatacept	212 (25.1)	224 (27.3)	-0.049	108 (27.1)	127 (28.6)	-0.033	111 (30.9)	80 (26.0)	0.11	15 (34.9)	≤ 10	0.499
Tocilizumab	182 (21.6)	177 (21.6)	0	98 (24.6)	97 (21.8)	0.066	83 (23.1)	71 (23.1)	0.002	≤ 10	11 (15.5)	0.141
Anakinra	≤ 10	≤ 10	0.029	≤ 10	≤ 10	-0.039	≤ 10	≤ 10	-0.116	0 (0.0)	0 (0.0)	0
TNFi naïve at baseline	404 (47.9)	376 (45.9)	0.042	203 (51.0)	213 (48.0)	0.061	195 (54.3)	141 (45.8)	0.171	29 (67.4)	21 (29.6)	0.819
≥1 dispensing of bDMARD within 730 days before index date (excluded), n (%)	843 (100.0)	820 (100.0)	0.000	398 (100.0)	444 (100.0)	0.000	359 (100.0)	308 (100.0)	0.000	43 (100.0)	71 (100.0)	0.000
Other prescription medications during baseline period, n (%)												
Antibiotics	368 (43.7)	363 (44.3)	-0.012	160 (40.2)	208 (46.8)	-0.134	165 (46.0)	126 (40.9)	0.102	20 (46.5)	23 (32.4)	0.292
Antidiabetic agents	80 (9.5)	74 (9.0)	0.016	37 (9.3)	46 (10.4)	-0.036	43 (12.0)	29 (9.4)	0.083	≤ 10	≤ 10	-0.192
Insulins	33 (3.9)	34 (4.1)	-0.012	15 (3.8)	≤ 10	0.089	15 (4.2)	≤ 10	0.068	≤ 10	≤ 10	-0.107
Non-insulins	60 (7.1)	56 (6.8)	0.011	31 (7.8)	39 (8.8)	-0.036	35 (9.7)	26 (8.4)	0.046	≤ 10	≤ 10	-0.288
Cardiovascular												

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 843	TNFi[a] n = 820	Std. Diff.	Baricitinib n = 398	TNFi[a] n = 444	Std. Diff.	Baricitinib n = 359	TNFi[a] n = 308	Std. Diff.	Baricitinib n = 43	TNFi[a] n = 71	Std. Diff.
Antithrombotic agents	132 (15.7)	146 (17.8)	-0.058	73 (18.3)	74 (16.7)	0.044	74 (20.6)	58 (18.8)	0.045	≤ 10	19 (26.8)	-0.257
Anticoagulant	55 (6.5)	56 (6.8)	-0.012	29 (7.3)	31 (7.0)	0.012	27 (7.5)	25 (8.1)	-0.022	≤ 10	≤ 10	0.055
Antiplatelet	90 (10.7)	104 (12.7)	-0.063	49 (12.3)	47 (10.6)	0.054	51 (14.2)	37 (12.0)	0.065	≤ 10	17 (23.9)	-0.401
Antihypertensives	265 (31.4)	281 (34.3)	-0.06	136 (34.2)	166 (37.4)	-0.067	151 (42.1)	129 (41.9)	0.004	18 (41.9)	30 (42.3)	-0.008
Angiotensin converting enzyme inhibitors (ACE)	75 (8.9)	78 (9.5)	-0.021	31 (7.8)	49 (11.0)	-0.111	52 (14.5)	30 (9.7)	0.146	≤ 10	≤ 10	0.283
Angiotensin receptor blockers (ARB)	98 (11.6)	106 (12.9)	-0.04	57 (14.3)	77 (17.3)	-0.083	54 (15.0)	56 (18.2)	-0.084	≤ 10	15 (21.1)	-0.416
Beta blocker	116 (13.8)	118 (14.4)	-0.018	53 (13.3)	72 (16.2)	-0.082	67 (18.7)	66 (21.4)	-0.069	≤ 10	11 (15.5)	0.141
Calcium channel blocker	72 (8.5)	89 (10.9)	-0.078	39 (9.8)	50 (11.3)	-0.048	40 (11.1)	30 (9.7)	0.046	≤ 10	15 (21.1)	-0.334
Nitrates	≤ 10	≤ 10	-0.015	≤ 10	≤ 10	-0.168	≤ 10	≤ 10	0.052	0 (0.0)	0 (0.0)	0
Acyclovir	≤ 10	≤ 10	-0.047	0 (0.0)	≤ 10	-0.179	≤ 10	≤ 10	-0.008	0 (0.0)	≤ 10	-0.169
Valacyclovir	34 (4.0)	39 (4.8)	-0.035	16 (4.0)	22 (5.0)	-0.045	22 (6.1)	13 (4.2)	0.086	≤ 10	≤ 10	-0.031
Hormonal	116 (13.8)	127 (15.5)	-0.049	63 (15.8)	61 (13.7)	0.059	43 (12.0)	38 (12.3)	-0.011	≤ 10	≤ 10	0.123
HRT	65 (7.7)	75 (9.1)	-0.052	30 (7.5)	30 (6.8)	0.03	26 (7.2)	24 (7.8)	-0.021	≤ 10	≤ 10	0.106
Oral Contraceptives	49 (5.8)	56 (6.8)	-0.042	34 (8.5)	26 (5.9)	0.104	14 (3.9)	15 (4.9)	-0.047	≤ 10	≤ 10	-0.003
SERMs	≤ 10	≤ 10	0.027	0 (0.0)	≤ 10	-0.135	≤ 10	≤ 10	0.035	≤ 10	0 (0.0)	0.218

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 843	TNFi[a] n = 820	Std. Diff.	Baricitinib n = 398	TNFi[a] n = 444	Std. Diff.	Baricitinib n = 359	TNFi[a] n = 308	Std. Diff.	Baricitinib n = 43	TNFi[a] n = 71	Std. Diff.
Topic with progestogens and/or estrogens	≤ 10	≤ 10	0.048	≤ 10	≤ 10	-0.034	≤ 10	0 (0.0)	0.106	0 (0.0)	0 (0.0)	0
Lipid-lowering agents	138 (16.4)	145 (17.7)	-0.035	59 (14.8)	78 (17.6)	-0.075	69 (19.2)	54 (17.5)	0.044	≤ 10	21 (29.6)	-0.32
HMG CoA reductase inhibitors	112 (13.3)	119 (14.5)	-0.036	50 (12.6)	68 (15.3)	-0.08	52 (14.5)	40 (13.0)	0.044	≤ 10	19 (26.8)	-0.322
Fibrates	15 (1.8)	15 (1.8)	-0.004	≤ 10	≤ 10	0.065	≤ 10	≤ 10	0.015	0 (0.0)	0 (0.0)	0
Bile acid sequestrants	≤ 10	≤ 10	0.065	≤ 10	≤ 10	0.005	0 (0.0)	≤ 10	-0.081	0 (0.0)	0 (0.0)	0
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0.00	0 (0.0)	0 (0.0)	0.00	0 (0.0)	0 (0.0)	0
Other lipid modifying agents	≤ 10	12 (1.5)	-0.073	≤ 10	≤ 10	0.009	≤ 10	≤ 10	-0.045	0 (0.0)	0 (0.0)	0
Lipid modifying agents, combinations	≤ 10	11 (1.3)	-0.037	≤ 10	≤ 10	-0.039	≤ 10	≤ 10	0.004	≤ 10	≤ 10	-0.031
Rheumatoid arthritis-related												
Aspirin	14 (1.7)	≤ 10	0.048	≤ 10	≤ 10	-0.068	≤ 10	≤ 10	0.052	0 (0.0)	0 (0.0)	0
Cox-2 Inhibitor	50 (5.9)	49 (6.0)	-0.002	22 (5.5)	24 (5.4)	0.005	17 (4.7)	17 (5.5)	-0.036	≤ 10	≤ 10	-0.319
NSAIDs	308 (36.5)	304 (37.1)	-0.011	136 (34.2)	163 (36.7)	-0.053	117 (32.6)	121 (39.3)	-0.14	13 (30.2)	24 (33.8)	-0.077
Glucocorticosteroid	610 (72.4)	567 (69.1)	0.071	277 (69.6)	304 (68.5)	0.024	230 (64.1)	207 (67.2)	-0.066	27 (62.8)	45 (63.4)	-0.012
Vaccines	221 (26.2)	201 (24.5)	0.039	123 (30.9)	127 (28.6)	0.05	104 (29.0)	81 (26.3)	0.06	14 (32.6)	≤ 10	0.448
Antineoplastic agents	≤ 10	≤ 10	-0.095	≤ 10	0 (0.0)	0.071	0 (0.0)	≤ 10	-0.081	0 (0.0)	0 (0.0)	0

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs;
Concom. cDMARDs = concomitant cDMARDs; DMARD = disease-modifying antirheumatic drugs; hosp = hospitalized; HRT = hormone replacement therapy; Max = maximum; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Min = minimum;
mos = months; N = number of patients in the specified category; NMSC = non-melanoma skin cancer;
RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulator; Std. Diff. = standardized difference; TNF = tumor necrosis factor; TNFi = tumor 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] TNF inhibitors.

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

Table 6.119. bDMARD- Naïve: Baseline characteristics by exposure duration - Incident Serious Infection cohort, Matched [SNDS]

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 732	TNFi[a] n = 705	Std. Diff.	Baricitinib n = 316	TNFi[a] n = 301	Std. Diff.	Baricitinib n = 246	TNFi[a] n = 263	Std. Diff.	Baricitinib n = 25	TNFi[a] n = 50	Std. Diff.
Age [in years]			0.062			-0.008			-0.041			-0.12
N (missing)	732 (0)	705 (0)		316 (0)	301 (0)		246 (0)	263 (0)		25 (0)	50 (0)	
Mean (SD)	60.1 (13.8)	59.2 (13.1)		61.1 (13.1)	61.2 (12.8)		59.3 (13.0)	59.9 (13.8)		57.8 (12.7)	59.3 (12.4)	
Median	60.0	61.0		62.0	62.0		59.0	61.0		61.0	58.5	
Min; Max	[20.0;91.0]	[22.0;94.0]		[19.0;86.0]	[18.0;89.0]		[22.0;86.0]	[22.0;86.0]		[30.0;79.0]	[22.0;81.0]	
Sex, n (%)			0.032			-0.049			0.054			0
Male	142 (19.4)	128 (18.2)		63 (19.9)	66 (21.9)		55 (22.4)	53 (20.2)		≤ 10	≤ 10	
Female	590 (80.6)	577 (81.8)		253 (80.1)	235 (78.1)		191 (77.6)	210 (79.8)		20 (80.0)	40 (80.0)	
Clinical conditions during baseline period, n (%)												
Cancer, excluding NMSC	36 (4.9)	26 (3.7)	0.061	15 (4.7)	≤ 10	0.072	≤ 10	14 (5.3)	-0.125	0 (0.0)	≤ 10	-0.357
NMSC	≤ 10	≤ 10	-0.002	0 (0.0)	≤ 10	-0.082	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Chronic lung disease, excluding cystic fibrosis[c]	105 (14.3)	106 (15.0)	-0.02	45 (14.2)	49 (16.3)	-0.057	31 (12.6)	31 (11.8)	0.025	≤ 10	≤ 10	-0.053
Cardiovascular conditions												
Atrial arrhythmia/fibrillation	23 (3.1)	14 (2.0)	0.073	≤ 10	≤ 10	-0.008	≤ 10	≤ 10	-0.053	0 (0.0)	0 (0.0)	0
Cardiovascular revascularization	≤ 10	≤ 10	0.029	0 (0.0)	≤ 10	-0.082	≤ 10	≤ 10	-0.047	0 (0.0)	0 (0.0)	0

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 732	TNFi[a] n = 705	Std. Diff.	Baricitinib n = 316	TNFi[a] n = 301	Std. Diff.	Baricitinib n = 246	TNFi[a] n = 263	Std. Diff.	Baricitinib n = 25	TNFi[a] n = 50	Std. Diff.
Congestive Heart Failure, hospitalized	≤ 10	≤ 10	-0.002	≤ 10	≤ 10	-0.036	≤ 10	≤ 10	0.006	0 (0.0)	0 (0.0)	0
Coronary artery disease	43 (5.9)	28 (4.0)	0.088	19 (6.0)	11 (3.7)	0.11	≤ 10	12 (4.6)	-0.116	≤ 10	≤ 10	0.078
Unstable angina	≤ 10	≤ 10	-0.032	0 (0.0)	0 (0.0)	0	0 (0.0)	≤ 10	-0.124	0 (0.0)	0 (0.0)	0
Ventricular arrhythmia	≤ 10	11 (1.6)	-0.054	≤ 10	≤ 10	-0.141	≤ 10	≤ 10	0.046	0 (0.0)	0 (0.0)	0
Stroke	≤ 10	≤ 10	0.027	≤ 10	≤ 10	-0.071	≤ 10	≤ 10	0.152	0 (0.0)	0 (0.0)	0
Hemorrhagic	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)	0
Ischemic	≤ 10	≤ 10	0.022	0 (0.0)	0 (0.0)	0	≤ 10	≤ 10	0.056	0 (0.0)	0 (0.0)	0
Unknown	≤ 10	≤ 10	0.05	≤ 10	≤ 10	-0.071	≤ 10	≤ 10	0.094	0 (0.0)	0 (0.0)	0
TIA	≤ 10	≤ 10	-0.001	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Diabetes Mellitus[c]	77 (10.5)	70 (9.9)	0.02	24 (7.6)	31 (10.3)	-0.095	19 (7.7)	23 (8.7)	-0.037	≤ 10	≤ 10	0.426
Treated insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Treated non insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Dyslipidemia (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Hypertension (not available in SNDS)												
History of hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 732	TNFi[a] n = 705	Std. Diff.	Baricitinib n = 316	TNFi[a] n = 301	Std. Diff.	Baricitinib n = 246	TNFi[a] n = 263	Std. Diff.	Baricitinib n = 25	TNFi[a] n = 50	Std. Diff.
Current hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Immune disorders	39 (5.3)	28 (4.0)	0.064	≤ 10	11 (3.7)	-0.046	≤ 10	≤ 10	-0.03	≤ 10	≤ 10	0.278
AIDS/HIV	0 (0.0)	≤ 10	-0.053	0 (0.0)	0 (0.0)	0	0 (0.0)	≤ 10	-0.087	0 (0.0)	0 (0.0)	0
Antiphospholipid syndrome	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
SLE	≤ 10	≤ 10	0.035	≤ 10	≤ 10	-0.041	≤ 10	≤ 10	-0.084	≤ 10	≤ 10	0.117
Primary Sjogren Syndrome	33 (4.5)	22 (3.1)	0.073	≤ 10	≤ 10	-0.008	≤ 10	≤ 10	0.036	≤ 10	0 (0.0)	0.289
Liver or pancreatic disorder[c]	19 (2.6)	26 (3.7)	-0.063	≤ 10	≤ 10	0.016	≤ 10	≤ 10	-0.047	0 (0.0)	≤ 10	-0.202
Obesity (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date)	≤ 10	≤ 10	-0.026	≤ 10	≤ 10	-0.041	≤ 10	≤ 10	-0.047	0 (0.0)	≤ 10	-0.202
RA Severity (CIRAS Index)			-0.048			-0.015			0.008			-0.143
Mean (SD)	6.4 (1.5)	6.5 (1.5)		6.4 (1.5)	6.4 (1.4)		6.6 (1.5)	6.6 (1.5)		6.4 (1.4)	6.7 (1.5)	
DMARDs, n (%)												
cDMARDs, during baseline period												
n, total (%)	518 (70.8)	508 (72.1)	-0.029	228 (72.2)	244 (81.1)	-0.212	184 (74.8)	212 (80.6)	-0.14	18 (72.0)	39 (78.0)	-0.139

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 732	TNFi[a] n = 705	Std. Diff.	Baricitinib n = 316	TNFi[a] n = 301	Std. Diff.	Baricitinib n = 246	TNFi[a] n = 263	Std. Diff.	Baricitinib n = 25	TNFi[a] n = 50	Std. Diff.
Mean (SD)	0.8 (0.7)	0.8 (0.6)	-0.001	0.8 (0.7)	1.0 (0.7)	-0.206	0.9 (0.6)	0.9 (0.6)	-0.132	1.0 (0.9)	0.9 (0.6)	0.204
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	
Min; Max	[0.0;3.0]	[0.0;4.0]		[0.0;3.0]	[0.0;4.0]		[0.0;4.0]	[0.0;3.0]		[0.0;3.0]	[0.0;3.0]	
>1 cDMARD concomitantly	61 (8.3)	54 (7.7)	0.025	31 (9.8)	31 (10.3)	-0.016	20 (8.1)	29 (11.0)	-0.099	≤ 10	≤ 10	0.104
Hydroxychloroquine	56 (7.7)	51 (7.2)	0.016	33 (10.4)	26 (8.6)	0.062	18 (7.3)	24 (9.1)	-0.066	≤ 10	≤ 10	0.379
Chloroquine	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)	0
Azathioprin	≤ 10	≤ 10	0.022	≤ 10	0 (0.0)	0.08	≤ 10	0 (0.0)	0.09	0 (0.0)	0 (0.0)	0
Leflunomide	127 (17.3)	119 (16.9)	0.013	39 (12.3)	50 (16.6)	-0.122	33 (13.4)	35 (13.3)	0.003	≤ 10	≤ 10	0.116
Methotrexate	379 (51.8)	383 (54.3)	-0.051	177 (56.0)	194 (64.5)	-0.173	144 (58.5)	174 (66.2)	-0.158	13 (52.0)	32 (64.0)	-0.245
Mycophenolate mofetil	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	≤ 10	0 (0.0)	0.09	0 (0.0)	0 (0.0)	0
Sulfasalazin	39 (5.3)	28 (4.0)	0.064	17 (5.4)	26 (8.6)	-0.128	13 (5.3)	14 (5.3)	-0.002	≤ 10	≤ 10	0.4
Cyclosporin	≤ 10	0 (0.0)	0.052	0 (0.0)	0 (0.0)	0	≤ 10	0 (0.0)	0.09	0 (0.0)	0 (0.0)	0
Penicillamin	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)	0
bDMARDs, during baseline period												
n, total (%)	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Mean (SD)	0.0 (0.0)	0.0 (0.0)	0.000	0.0 (0.0)	0.0 (0.0)	0.000	0.0 (0.0)	0.0 (0.0)	0.000	0.0 (0.0)	0.0 (0.0)	0.000
Median	0.0	0.0		0.0	0.0		0.0	0.0		0.0	0.0	
Min; Max	[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;0.0]	[0.0;0.0]	
cDMARDs, concomitant	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Adalimumab[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 732	TNFi[a] n = 705	Std. Diff.	Baricitinib n = 316	TNFi[a] n = 301	Std. Diff.	Baricitinib n = 246	TNFi[a] n = 263	Std. Diff.	Baricitinib n = 25	TNFi[a] n = 50	Std. Diff.
Certolizumab pegol[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Etanercept[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Golimumab[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Infliximab[b]	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Rituximab	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Sarilumab	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Abatacept	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Tocilizumab	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Anakinra	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
TNFi naïve at baseline	732 (100.0)	705 (100.0)	0.000	316 (100.0)	301 (100.0)	0.000	246 (100.0)	263 (100.0)	0.000	25 (100.0)	50 (100.0)	0.000
≥ 1 dispensing of bDMARD within 730 days before index date (excluded), n (%)	271 (37.0)	216 (30.6)	0.135	113 (35.8)	68 (22.6)	0.293	85 (34.6)	45 (17.1)	0.407	16 (64.0)	11 (22.0)	0.937
Other prescription medications during baseline period, n (%)												
Antibiotics	284 (38.8)	290 (41.1)	-0.048	135 (42.7)	129 (42.9)	-0.003	105 (42.7)	90 (34.2)	0.175	≤ 10	21 (42.0)	-0.041
Antidiabetic agents	69 (9.4)	69 (9.8)	-0.012	26 (8.2)	29 (9.6)	-0.049	18 (7.3)	22 (8.4)	-0.039	≤ 10	≤ 10	0.351
Insulins	25 (3.4)	24 (3.4)	0.001	12 (3.8)	≤ 10	0.026	≤ 10	≤ 10	-0.014	≤ 10	≤ 10	0
Non-insulins	58 (7.9)	58 (8.2)	-0.011	24 (7.6)	27 (9.0)	-0.05	14 (5.7)	18 (6.8)	-0.048	≤ 10	≤ 10	0.351
Cardiovascular												

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 732	TNFi[a] n = 705	Std. Diff.	Baricitinib n = 316	TNFi[a] n = 301	Std. Diff.	Baricitinib n = 246	TNFi[a] n = 263	Std. Diff.	Baricitinib n = 25	TNFi[a] n = 50	Std. Diff.
Antithrombotic agents	156 (21.3)	134 (19.0)	0.058	66 (20.9)	61 (20.3)	0.015	40 (16.3)	50 (19.0)	-0.072	12 (48.0)	≤ 10	0.73
Anticoagulant	80 (10.9)	63 (8.9)	0.067	35 (11.1)	30 (10.0)	0.036	19 (7.7)	24 (9.1)	-0.051	≤ 10	≤ 10	0.134
Antiplatelet	94 (12.8)	77 (10.9)	0.059	39 (12.3)	33 (11.0)	0.043	21 (8.5)	26 (9.9)	-0.047	≤ 10	≤ 10	0.739
Antihypertensives	262 (35.8)	238 (33.8)	0.043	115 (36.4)	132 (43.9)	-0.153	86 (35.0)	102 (38.8)	-0.079	11 (44.0)	19 (38.0)	0.122
Angiotensin converting enzyme inhibitors (ACE)	60 (8.2)	72 (10.2)	-0.07	29 (9.2)	37 (12.3)	-0.101	19 (7.7)	23 (8.7)	-0.037	≤ 10	≤ 10	0.447
Angiotensin receptor blockers (ARB)	112 (15.3)	90 (12.8)	0.073	49 (15.5)	55 (18.3)	-0.074	23 (9.3)	50 (19.0)	-0.28	≤ 10	≤ 10	0
Beta blocker	133 (18.2)	107 (15.2)	0.08	54 (17.1)	50 (16.6)	0.013	42 (17.1)	44 (16.7)	0.009	≤ 10	≤ 10	-0.22
Calcium channel blocker	62 (8.5)	64 (9.1)	-0.022	36 (11.4)	37 (12.3)	-0.028	38 (15.4)	31 (11.8)	0.107	≤ 10	≤ 10	0.134
Nitrates	≤ 10	≤ 10	0.07	0 (0.0)	≤ 10	-0.116	≤ 10	≤ 10	0.007	≤ 10	0 (0.0)	0.289
Acyclovir	≤ 10	≤ 10	-0.003	≤ 10	≤ 10	0.105	0 (0.0)	≤ 10	-0.124	0 (0.0)	≤ 10	-0.202
Valacyclovir	17 (2.3)	26 (3.7)	-0.08	≤ 10	≤ 10	0.051	≤ 10	≤ 10	0.034	0 (0.0)	≤ 10	-0.417
Hormonal	66 (9.0)	80 (11.3)	-0.077	41 (13.0)	29 (9.6)	0.106	26 (10.6)	23 (8.7)	0.062	≤ 10	≤ 10	0
HRT	41 (5.6)	46 (6.5)	-0.039	25 (7.9)	19 (6.3)	0.062	17 (6.9)	14 (5.3)	0.066	≤ 10	≤ 10	0
Oral Contraceptives	24 (3.3)	31 (4.4)	-0.058	14 (4.4)	≤ 10	0.057	≤ 10	≤ 10	-0.03	≤ 10	≤ 10	0
SERMs	≤ 10	≤ 10	-0.032	≤ 10	0 (0.0)	0.113	≤ 10	0 (0.0)	0.09	0 (0.0)	0 (0.0)	0

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 732	TNFi[a] n = 705	Std. Diff.	Baricitinib n = 316	TNFi[a] n = 301	Std. Diff.	Baricitinib n = 246	TNFi[a] n = 263	Std. Diff.	Baricitinib n = 25	TNFi[a] n = 50	Std. Diff.
Topic with progestogens and/or estrogens	0 (0.0)	≤ 10	-0.093	≤ 10	0 (0.0)	0.08	≤ 10	0 (0.0)	0.09	0 (0.0)	0 (0.0)	0
Lipid-lowering agents	122 (16.7)	103 (14.6)	0.057	62 (19.6)	59 (19.6)	0.001	43 (17.5)	46 (17.5)	0	≤ 10	≤ 10	0.349
HMG CoA reductase inhibitors	100 (13.7)	86 (12.2)	0.044	53 (16.8)	45 (15.0)	0.05	32 (13.0)	41 (15.6)	-0.074	≤ 10	≤ 10	0.316
Fibrates	≤ 10	≤ 10	-0.003	≤ 10	≤ 10	-0.16	≤ 10	≤ 10	0.098	0 (0.0)	≤ 10	-0.202
Bile acid sequestrants	≤ 10	≤ 10	0.022	≤ 10	≤ 10	-0.003	≤ 10	≤ 10	0.056	0 (0.0)	0 (0.0)	0
Nicotinic acid and derivatives	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)	0
Other lipid modifying agents	≤ 10	12 (1.7)	-0.065	≤ 10	≤ 10	-0.005	≤ 10	≤ 10	0.094	0 (0.0)	0 (0.0)	0
Lipid modifying agents, combinations	11 (1.5)	≤ 10	0.046	≤ 10	≤ 10	0.04	≤ 10	≤ 10	0.109	≤ 10	0 (0.0)	0.289
Rheumatoid arthritis-related												
Aspirin	≤ 10	≤ 10	-0.083	≤ 10	≤ 10	-0.071	≤ 10	≤ 10	0.007	≤ 10	0 (0.0)	0.417
Cox-2 Inhibitor	31 (4.2)	48 (6.8)	-0.113	15 (4.7)	11 (3.7)	0.055	16 (6.5)	20 (7.6)	-0.043	≤ 10	≤ 10	0.169
NSAIDs	262 (35.8)	242 (34.3)	0.031	117 (37.0)	115 (38.2)	-0.024	91 (37.0)	111 (42.2)	-0.107	≤ 10	17 (34.0)	-0.043
Glucocorticosteroid	536 (73.2)	510 (72.3)	0.02	247 (78.2)	234 (77.7)	0.01	181 (73.6)	204 (77.6)	-0.093	17 (68.0)	42 (84.0)	-0.381
Vaccines	234 (32.0)	240 (34.0)	-0.044	124 (39.2)	129 (42.9)	-0.074	87 (35.4)	106 (40.3)	-0.102	≤ 10	18 (36.0)	-0.264
Antineoplastic agents	≤ 10	≤ 10	0.035	≤ 10	0 (0.0)	0.08	≤ 10	0 (0.0)	0.09	≤ 10	0 (0.0)	0.289

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs;
Concom. cDMARDs = concomitant cDMARDs; DMARD = disease-modifying antirheumatic drugs; hosp = hospitalized; HRT = hormone replacement therapy; Max = maximum; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Min = minimum;
mos = months; N = number of patients in the specified category; NMSC = non-melanoma skin cancer;
RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulator; Std. Diff. = standardized difference; TNF = tumor necrosis factor; TNFi = tumor 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] TNF inhibitors.

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

Table 6.120. bDMARD-Experienced: Baseline characteristics by exposure duration - Hospitalized Tuberculosis cohort, Matched [SNDS]

Not applicable for SNDS data: no event

Table 6.121. bDMARD-Naïve: Baseline Characteristics by Exposure Duration - Hospitalized Tuberculosis cohort, Matched [SNDS]

Not applicable for SNDS data: no event

5.3.2 BASELINE HEALTHCARE RESOURCE UTILIZATION BY EXPOSURE DURATION

Table 6.122. bDMARD-Experienced: Baseline healthcare resource utilization by exposure duration, Unmatched cohort [SNDS]

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 988	TNFi n = 1210	Std. Diff.	Baricitinib n = 499	TNFi n = 616	Std. Diff.	Baricitinib n = 441	TNFi n = 444	Std. Diff.	Baricitinib n = 54	TNFi n = 104	Std. Diff.
Physician Office Visits (rheumatologist visits excluded)												
n, patients (%)	566 (57.3)	761 (62.9)	-0.115	315 (63.1)	410 (66.6)	-0.072	269 (61.0)	253 (57.0)	0.082	37 (68.5)	73 (70.2)	-0.036
n, events	1495	2351		871	1426		828	763		114	274	
Mean (SD)	1.5 (2.1)	1.9 (2.7)	-0.177	1.7 (2.6)	2.3 (3.8)	-0.177	1.9 (2.7)	1.7 (2.5)	0.060	2.1 (2.7)	2.6 (3.0)	-0.182
Median	1.0	1.0		1.0	1.0		1.0	1.0		2.0	2.0	
Min; Max	[0.0;16.0]	[0.0;27.0]		[0.0;25.0]	[0.0;43.0]		[0.0;19.0]	[0.0;19.0]		[0.0;16.0]	[0.0;17.0]	
Rheumatologist Visits												
n, patients (%)	614 (62.1)	730 (60.3)	0.037	316 (63.3)	367 (59.6)	0.077	282 (63.9)	275 (61.9)	0.042	41 (75.9)	76 (73.1)	0.065
n, events	1402	1600		709	819		637	579		102	173	
Mean (SD)	1.4 (1.6)	1.3 (1.5)	0.063	1.4 (1.6)	1.3 (1.5)	0.059	1.4 (1.6)	1.3 (1.5)	0.091	1.9 (1.6)	1.7 (1.7)	0.140
Median	1.0	1.0		1.0	1.0		1.0	1.0		2.0	1.5	
Min; Max	[0.0;11.0]	[0.0;10.0]		[0.0;8.0]	[0.0;8.0]		[0.0;9.0]	[0.0;13.0]		[0.0;6.0]	[0.0;10.0]	
Other Outpatient Visits												
n, patients (%)	930 (94.1)	1110 (91.7)	0.094	468 (93.8)	571 (92.7)	0.044	416 (94.3)	402 (90.5)	0.144	49 (90.7)	94 (90.4)	0.012
n, events	19431	20661		10438	10374		10007	7709		893	1816	
Mean (SD)	19.7 (33.7)	17.1 (28.1)	0.084	20.9 (32.4)	16.8 (28.3)	0.134	22.7 (37.4)	17.4 (28.7)	0.16	16.5 (24.2)	17.5 (33.1)	-0.032

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 988	TNFi n = 1210	Std. Diff.	Baricitinib n = 499	TNFi n = 616	Std. Diff.	Baricitinib n = 441	TNFi n = 444	Std. Diff.	Baricitinib n = 54	TNFi n = 104	Std. Diff.
Median	8.0	8.0		10.0	7.0		9.0	8.0		6.0	8.0	
Min; Max	[0.0;322.0]	[0.0;255.0]		[0.0;266.0]	[0.0;275.0]		[0.0;257.0]	[0.0;242.0]		[0.0;125.0]	[0.0;280.0]	
Inpatient Visits[a]												
n, patients (%)	516 (52.2)	556 (46.0)	0.126	258 (51.7)	313 (50.8)	0.018	242 (54.9)	204 (45.9)	0.179	30 (55.6)	39 (37.5)	0.368
n, events	1565	1474		762	793		747	553		79	101	
Mean (SD)	1.6 (2.2)	1.2 (1.9)	0.179	1.5 (2.1)	1.3 (1.8)	0.121	1.7 (2.2)	1.2 (1.9)	0.217	1.5 (1.9)	1.0 (1.6)	0.275
Median	1.0	0.0		1.0	1.0		1.0	0.0		1.0	0.0	
Min; Max	[0.0;14.0]	[0.0;16.0]		[0.0;11.0]	[0.0;9.0]		[0.0;10.0]	[0.0;9.0]		[0.0;7.0]	[0.0;7.0]	
ED Visits	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
n, patients												
n, events												
Mean (SD)												
Median												
Min; Max												

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; mos = months; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

[a] Inpatient visits include number of hospitalisations

Table 6.123. bDMARD-Naïve: Baseline healthcare resource utilization by exposure duration, Unmatched cohort [SNDS]

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 698	TNFi n = 4162	Std. Diff.	Baricitinib n = 302	TNFi n = 1927	Std. Diff.	Baricitinib n = 235	TNFi n = 1466	Std. Diff.	Baricitinib n = 25	TNFi n = 273	Std. Diff.
Physician Office Visits (rheumatologist visits excluded)												
n, patients (%)	425 (60.9)	2574 (61.8)	-0.020	192 (63.6)	1211 (62.8)	0.015	159 (67.7)	945 (64.5)	0.068	20 (80.0)	198 (72.5)	0.176
n, events	1218	8229		529	3737		516	2803		45	725	
Mean (SD)	1.7 (2.8)	2.0 (3.3)	-0.075	1.8 (2.6)	1.9 (2.9)	-0.068	2.2 (3.3)	1.9 (2.7)	0.095	1.8 (1.6)	2.7 (3.3)	-0.328
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	2.0	
Min; Max	[0.0;41.0]	[0.0;85.0]		[0.0;24.0]	[0.0;49.0]		[0.0;31.0]	[0.0;25.0]		[0.0;6.0]	[0.0;22.0]	
Rheumatologist Visits												
n, patients (%)	431 (61.7)	2540 (61.0)	0.015	195 (64.6)	1294 (67.2)	-0.055	156 (66.4)	1027 (70.1)	-0.079	17 (68.0)	210 (76.9)	-0.201
n, events	919	5631		416	3020		363	2431		37	504	
Mean (SD)	1.3 (1.4)	1.4 (1.5)	-0.025	1.4 (1.5)	1.6 (1.5)	-0.125	1.5 (1.5)	1.7 (1.6)	-0.074	1.5 (1.2)	1.8 (1.5)	-0.263
Median	1.0	1.0		1.0	1.0		1.0	1.0		2.0	2.0	
Min; Max	[0.0;8.0]	[0.0;10.0]		[0.0;8.0]	[0.0;10.0]		[0.0;7.0]	[0.0;10.0]		[0.0;4.0]	[0.0;7.0]	
Other Outpatient Visits												
n, patients (%)	640 (91.7)	3750 (90.1)	0.055	283 (93.7)	1764 (91.5)	0.083	216 (91.9)	1370 (93.5)	-0.059	22 (88.0)	250 (91.6)	-0.118
n, events	13527	61986		5778	28601		4033	21978		381	3836	
Mean (SD)	19.4 (33.3)	14.9 (27.2)	0.148	19.1 (32.3)	14.8 (23.8)	0.151	17.2 (28.3)	15.0 (24.0)	0.083	15.2 (30.0)	14.1 (22.0)	0.045
Median	7.0	6.0		7.0	7.0		6.0	7.0		8.0	6.0	
Min; Max	[0.0;226.0]	[0.0;283.0]		[0.0;247.0]	[0.0;230.0]		[0.0;186.0]	[0.0;242.0]		[0.0;152.0]	[0.0;223.0]	

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 698	TNFi n = 4162	Std. Diff.	Baricitinib n = 302	TNFi n = 1927	Std. Diff.	Baricitinib n = 235	TNFi n = 1466	Std. Diff.	Baricitinib n = 25	TNFi n = 273	Std. Diff.
Inpatient Visits[a]												
n, patients (%)	300 (43.0)	1885 (45.3)	-0.047	137 (45.4)	953 (49.5)	-0.082	99 (42.1)	719 (49.0)	-0.139	11 (44.0)	133 (48.7)	-0.095
n, events	460	2729		196	1407		159	1036		16	181	
Mean (SD)	0.7 (1.1)	0.7 (1.3)	0.003	0.6 (1.0)	0.7 (1.9)	-0.052	0.7 (1.1)	0.7 (1.7)	0.021	0.6 (0.9)	0.7 (0.9)	-0.025
Median	0.0	0.0		0.0	0.0		0.0	0.0		0.0	0.0	
Min; Max	[0.0;12.0]	[0.0;51.0]		[0.0;12.0]	[0.0;76.0]		[0.0;7.0]	[0.0;56.0]		[0.0;3.0]	[0.0;6.0]	
ED Visits	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
n, patients												
n, events												
Mean (SD)												
Median												
Min; Max												

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; mos = months; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

[a] Inpatient visits include number of hospitalisations

Table 6.124. bDMARD-Experienced: Baseline healthcare resource utilization by exposure duration - VTE Cohort, matched [SNDS]

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 809	TNFi[a] n = 812	Std. Diff.	Baricitinib n = 395	TNFi[a] n = 422	Std. Diff.	Baricitinib n = 358	TNFi[a] n = 298	Std. Diff.	Baricitinib n = 38	TNFi[a] n = 68	Std. Diff.
Physician Office Visits (rheumatologist visits excluded)												
n, patients (%)	463 (57.2)	504 (62.1)	-0.099	256 (64.8)	274 (64.9)	-0.003	224 (62.6)	166 (55.7)	0.14	25 (65.8)	45 (66.2)	-0.008
n, events	1216	1427		725	927		687	474		79	156	
Mean (SD)	1.5 (2.1)	1.8 (2.5)	-0.11	1.8 (2.7)	2.2 (3.4)	-0.118	1.9 (2.7)	1.6 (2.3)	0.129	2.1 (2.9)	2.3 (3.1)	-0.072
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	
Min; Max	[0.0;16.0]	[0.0;27.0]		[0.0;25.0]	[0.0;27.0]		[0.0;19.0]	[0.0;15.0]		[0.0;16.0]	[0.0;17.0]	
Rheumatologist Visits												
n, patients (%)	501 (61.9)	508 (62.6)	-0.013	252 (63.8)	250 (59.2)	0.094	229 (64.0)	186 (62.4)	0.032	27 (71.1)	49 (72.1)	-0.022
n, events	1152	1123		573	558		523	376		68	99	
Mean (SD)	1.4 (1.6)	1.4 (1.5)	0.026	1.5 (1.6)	1.3 (1.5)	0.084	1.5 (1.7)	1.3 (1.3)	0.134	1.8 (1.5)	1.5 (1.3)	0.236
Median	1.0	1.0		1.0	1.0		1.0	1.0		2.0	1.0	
Min; Max	[0.0;11.0]	[0.0;8.0]		[0.0;8.0]	[0.0;8.0]		[0.0;9.0]	[0.0;6.0]		[0.0;5.0]	[0.0;6.0]	
Other Outpatient Visits												
n, patients (%)	754 (93.2)	757 (93.2)	-0.001	367 (92.9)	399 (94.5)	-0.068	334 (93.3)	273 (91.6)	0.064	34 (89.5)	60 (88.2)	0.039
n, events	14554	16152		7736	8055		7658	5496		610	1240	
Mean (SD)	18.0 (31.1)	19.9 (31.8)	-0.061	19.6 (30.0)	19.1 (31.9)	0.016	21.4 (33.9)	18.4 (28.2)	0.095	16.1 (26.0)	18.2 (36.4)	-0.069
Median	8.0	9.0		10.0	8.0		9.0	9.0		4.0	8.0	
Min; Max	[0.0;322.0]	[0.0;255.0]		[0.0;266.0]	[0.0;275.0]		[0.0;201.0]	[0.0;186.0]		[0.0;125.0]	[0.0;280.0]	

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 809	TNFi[a] n = 812	Std. Diff.	Baricitinib n = 395	TNFi[a] n = 422	Std. Diff.	Baricitinib n = 358	TNFi[a] n = 298	Std. Diff.	Baricitinib n = 38	TNFi[a] n = 68	Std. Diff.
Inpatient Visits[b]												
n, patients (%)	402 (49.7)	368 (45.3)	0.088	192 (48.6)	217 (51.4)	-0.056	186 (52.0)	136 (45.6)	0.127	16 (42.1)	22 (32.4)	0.203
n, events	1166	1058		528	585		559	398		42	55	
Mean (SD)	1.4 (2.1)	1.3 (2.1)	0.067	1.3 (2.0)	1.4 (1.9)	-0.026	1.6 (2.2)	1.3 (2.0)	0.107	1.1 (1.8)	0.8 (1.6)	0.173
Median	0.0	0.0		0.0	1.0		1.0	0.0		0.0	0.0	
Min; Max	[0.0;14.0]	[0.0;16.0]		[0.0;9.0]	[0.0;8.0]		[0.0;10.0]	[0.0;9.0]		[0.0;7.0]	[0.0;7.0]	
ED Visits	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
n, patients												
n, events												
Mean (SD)												
Median												
Min; Max												

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; mos = months; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

[a] Matching ratio 1:1 is applied

[b] Inpatient visits include number of hospitalisations

Table 6.125. bDMARD-Naïve: Baseline healthcare resource utilization by exposure duration - VTE cohort, matched [SNDS]

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 698	TNFi[a] n = 693	Std. Diff.	Baricitinib n = 302	TNFi[a] n = 314	Std. Diff.	Baricitinib n = 235	TNFi[a] n = 210	Std. Diff.	Baricitinib n = 25	TNFi[a] n = 43	Std. Diff.
Physician Office Visits (rheumatologist visits excluded)												
n, patients (%)	425 (60.9)	422 (60.9)	0	192 (63.6)	184 (58.6)	0.102	159 (67.7)	136 (64.8)	0.061	20 (80.0)	30 (69.8)	0.238
n, events	1218	1223		529	508		516	341		45	100	
Mean (SD)	1.7 (2.8)	1.8 (3.4)	-0.006	1.8 (2.6)	1.6 (3.3)	0.045	2.2 (3.3)	1.6 (2.3)	0.203	1.8 (1.6)	2.3 (3.2)	-0.207
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	
Min; Max	[0.0;41.0]	[0.0;47.0]		[0.0;24.0]	[0.0;49.0]		[0.0;31.0]	[0.0;22.0]		[0.0;6.0]	[0.0;19.0]	
Rheumatologist Visits												
n, patients (%)	431 (61.7)	414 (59.7)	0.041	195 (64.6)	203 (64.6)	-0.002	156 (66.4)	149 (71.0)	-0.099	17 (68.0)	34 (79.1)	-0.253
n, events	919	886		416	472		363	343		37	95	
Mean (SD)	1.3 (1.4)	1.3 (1.5)	0.026	1.4 (1.5)	1.5 (1.5)	-0.083	1.5 (1.5)	1.6 (1.5)	-0.06	1.5 (1.2)	2.2 (1.9)	-0.45
Median	1.0	1.0		1.0	1.0		1.0	1.0		2.0	2.0	
Min; Max	[0.0;8.0]	[0.0;9.0]		[0.0;8.0]	[0.0;7.0]		[0.0;7.0]	[0.0;6.0]		[0.0;4.0]	[0.0;7.0]	
Other Outpatient Visits												
n, patients (%)	640 (91.7)	636 (91.8)	-0.003	283 (93.7)	300 (95.5)	-0.081	216 (91.9)	202 (96.2)	-0.182	22 (88.0)	42 (97.7)	-0.382
n, events	13527	12786		5778	5124		4033	3734		381	936	
Mean (SD)	19.4 (33.3)	18.5 (32.0)	0.029	19.1 (32.3)	16.3 (21.1)	0.103	17.2 (28.3)	17.8 (27.1)	-0.022	15.2 (30.0)	21.8 (38.4)	-0.19

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 698	TNFi[a] n = 693	Std. Diff.	Baricitinib n = 302	TNFi[a] n = 314	Std. Diff.	Baricitinib n = 235	TNFi[a] n = 210	Std. Diff.	Baricitinib n = 25	TNFi[a] n = 43	Std. Diff.
Median	7.0	7.0		7.0	8.0		6.0	8.5		8.0	12.0	
Min; Max	[0.0;226.0]	[0.0;237.0]		[0.0;247.0]	[0.0;185.0]		[0.0;186.0]	[0.0;242.0]		[0.0;152.0]	[0.0;223.0]	
Inpatient Visits[b]												
n, patients (%)	300 (43.0)	282 (40.7)	0.046	137 (45.4)	126 (40.1)	0.106	99 (42.1)	100 (47.6)	-0.111	11 (44.0)	21 (48.8)	-0.097
n, events	460	441		196	198		159	139		16	30	
Mean (SD)	0.7 (1.1)	0.6 (1.0)	0.022	0.6 (1.0)	0.6 (1.0)	0.018	0.7 (1.1)	0.7 (0.9)	0.015	0.6 (0.9)	0.7 (1.1)	-0.059
Median	0.0	0.0		0.0	0.0		0.0	0.0		0.0	0.0	
Min; Max	[0.0;12.0]	[0.0;10.0]		[0.0;12.0]	[0.0;9.0]		[0.0;7.0]	[0.0;5.0]		[0.0;3.0]	[0.0;6.0]	
ED Visits	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
n, patients												
n, events												
Mean (SD)												
Median												
Min; Max												

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; mos = months; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

[a] Matching ratio 1:1 is applied

[b] Inpatient visits include number of hospitalisations

Table 6.126. bDMARD-Experienced: Baseline healthcare resource utilization by exposure duration - MACE cohort, Matched [SNDS]

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 812	TNFi[a] n = 813	Std. Diff.	Baricitinib n = 406	TNFi[a] n = 432	Std. Diff.	Baricitinib n = 348	TNFi[a] n = 287	Std. Diff.	Baricitinib n = 40	TNFi[a] n = 74	Std. Diff.
Physician Office Visits (rheumatologist visits excluded)												
n, patients (%)	468 (57.6)	509 (62.6)	-0.102	259 (63.8)	278 (64.4)	-0.012	214 (61.5)	154 (53.7)	0.159	27 (67.5)	47 (63.5)	0.084
n, events	1256	1433		750	842		674	412		77	167	
Mean (SD)	1.5 (2.1)	1.8 (2.4)	-0.096	1.8 (2.7)	1.9 (3.1)	-0.035	1.9 (2.8)	1.4 (2.1)	0.205	1.9 (2.8)	2.3 (3.1)	-0.113
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	
Min; Max	[0.0;16.0]	[0.0;17.0]		[0.0;25.0]	[0.0;26.0]		[0.0;19.0]	[0.0;12.0]		[0.0;16.0]	[0.0;17.0]	
Rheumatologist Visits												
n, patients (%)	506 (62.3)	506 (62.2)	0.002	252 (62.1)	266 (61.6)	0.010	229 (65.8)	185 (64.5)	0.028	28 (70.0)	55 (74.3)	-0.097
n, events	1147	1119		576	590		520	384		69	113	
Mean (SD)	1.4 (1.5)	1.4 (1.5)	0.024	1.4 (1.6)	1.4 (1.5)	0.034	1.5 (1.6)	1.3 (1.5)	0.100	1.7 (1.5)	1.5 (1.3)	0.138
Median	1.0	1.0		1.0	1.0		1.0	1.0		2.0	1.0	
Min; Max	[0.0;8.0]	[0.0;8.0]		[0.0;8.0]	[0.0;8.0]		[0.0;9.0]	[0.0;13.0]		[0.0;5.0]	[0.0;6.0]	
Other Outpatient Visits												
n, patients (%)	760 (93.6)	753 (92.6)	0.039	380 (93.6)	402 (93.1)	0.022	327 (94.0)	260 (90.6)	0.127	35 (87.5)	66 (89.2)	-0.053
n, events	15682.0	15586		8402.0	7038		7523.0	5867.0		590	1454	
Mean (SD)	19.3 (33.2)	19.2 (31.7)	0.004	20.7 (30.9)	16.3 (25.2)	0.156	21.6 (36.2)	20.4 (34.0)	0.034	14.8 (25.3)	19.6 (38.3)	-0.151
Median	8.0	8.0		10.0	7.0		9.0	10.0		4.0	8.5	
Min; Max	[0.0;322.0]	[0.0;255.0]		[0.0;266.0]	[0.0;238.0]		[0.0;242.0]	[0.0;242.0]		[0.0;125.0]	[0.0;280.0]	

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 812	TNFi[a] n = 813	Std. Diff.	Baricitinib n = 406	TNFi[a] n = 432	Std. Diff.	Baricitinib n = 348	TNFi[a] n = 287	Std. Diff.	Baricitinib n = 40	TNFi[a] n = 74	Std. Diff.
Inpatient Visits[b]												
n, patients (%)	407 (50.1)	370 (45.5)	0.092	199 (49.0)	210 (48.6)	0.008	176 (50.6)	125 (43.6)	0.141	19 (47.5)	22 (29.7)	0.371
n, events	1193	1072		527	571		502	371		56	68	
Mean (SD)	1.5 (2.1)	1.3 (2.1)	0.072	1.3 (1.9)	1.3 (1.9)	-0.013	1.4 (2.1)	1.3 (2.0)	0.073	1.4 (2.1)	0.9 (1.7)	0.251
Median	1.0	0.0		0.0	0.0		1.0	0.0		0.0	0.0	
Min; Max	[0.0;14.0]	[0.0;16.0]		[0.0;8.0]	[0.0;8.0]		[0.0;8.0]	[0.0;7.0]		[0.0;7.0]	[0.0;7.0]	
ED Visits	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
n, patients												
n, events												
Mean (SD)												
Median												
Min; Max												

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; mos = months; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

[a] Matching ratio 1:1 is applied

[b] Inpatient visits include number of hospitalisations

Table 6.127. bDMARD-Naïve: Baseline healthcare resource utilization by exposure duration - MACE cohort, Matched [SNDS]

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 697	TNFi[a] n = 656	Std. Diff.	Baricitinib n = 301	TNFi[a] n = 305	Std. Diff.	Baricitinib n = 236	TNFi[a] n = 249	Std. Diff.	Baricitinib n = 23	TNFi[a] n = 47	Std. Diff.
Physician Office Visits (rheumatologist visits excluded)												
n, patients (%)	423 (60.7)	399 (60.8)	-0.003	192 (63.8)	186 (61.0)	0.058	160 (67.8)	144 (57.8)	0.207	18 (78.3)	32 (68.1)	0.231
n, events	1211	1066		537	532		516	367		39	113	
Mean (SD)	1.7 (2.8)	1.6 (2.5)	0.042	1.8 (2.6)	1.7 (2.9)	0.015	2.2 (3.2)	1.5 (2.1)	0.26	1.7 (1.5)	2.4 (2.5)	-0.345
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	2.0	
Min; Max	[0.0;41.0]	[0.0;29.0]		[0.0;24.0]	[0.0;32.0]		[0.0;31.0]	[0.0;11.0]		[0.0;6.0]	[0.0;11.0]	
Rheumatologist Visits												
n, patients (%)	430 (61.7)	417 (63.6)	-0.039	196 (65.1)	217 (71.1)	-0.13	156 (66.1)	175 (70.3)	-0.09	16 (69.6)	33 (70.2)	-0.014
n, events	917	951		417	508		366	368		35	78	
Mean (SD)	1.3 (1.4)	1.4 (1.5)	-0.091	1.4 (1.5)	1.7 (1.6)	-0.182	1.6 (1.5)	1.5 (1.5)	0.049	1.5 (1.2)	1.7 (1.6)	-0.098
Median	1.0	1.0		1.0	1.0		1.0	1.0		2.0	2.0	
Min; Max	[0.0;8.0]	[0.0;7.0]		[0.0;8.0]	[0.0;9.0]		[0.0;7.0]	[0.0;10.0]		[0.0;4.0]	[0.0;7.0]	
Other Outpatient Visits												
n, patients (%)	639 (91.7)	601 (91.6)	0.002	282 (93.7)	281 (92.1)	0.061	216 (91.5)	233 (93.6)	-0.078	21 (91.3)	41 (87.2)	0.132
n, events	13313	12615		5838	5615		4052	4338		378	938	
Mean (SD)	19.1 (33.1)	19.2 (35.7)	-0.004	19.4 (32.9)	18.4 (29.3)	0.032	17.2 (28.2)	17.4 (31.8)	-0.008	16.4 (31.0)	20.0 (35.4)	-0.106
Median	7.0	7.0		7.0	8.0		6.0	7.0		8.0	7.0	
Min; Max	[0.0;226.0]	[0.0;239.0]		[0.0;247.0]	[0.0;186.0]		[0.0;186.0]	[0.0;242.0]		[0.0;152.0]	[0.0;223.0]	

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 697	TNFi[a] n = 656	Std. Diff.	Baricitinib n = 301	TNFi[a] n = 305	Std. Diff.	Baricitinib n = 236	TNFi[a] n = 249	Std. Diff.	Baricitinib n = 23	TNFi[a] n = 47	Std. Diff.
Inpatient Visits[b]												
n, patients (%)	298 (42.8)	294 (44.8)	-0.042	137 (45.5)	147 (48.2)	-0.054	99 (41.9)	114 (45.8)	-0.077	≤ 10	28 (59.6)	-0.326
n, events	453	500		194	229		159	169		15	55	
Mean (SD)	0.6 (1.0)	0.8 (2.4)	-0.061	0.6 (1.0)	0.8 (1.0)	-0.107	0.7 (1.1)	0.7 (0.9)	-0.005	0.7 (0.9)	1.2 (1.4)	-0.428
Median	0.0	0.0		0.0	0.0		0.0	0.0		0.0	1.0	
Min; Max	[0.0;12.0]	[0.0;51.0]		[0.0;12.0]	[0.0;5.0]		[0.0;7.0]	[0.0;5.0]		[0.0;3.0]	[0.0;6.0]	
ED Visits	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
n, patients												
n, events												
Mean (SD)												
Median												
Min; Max												

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; mos = months; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

[a] Matching ratio 1:1 is applied

[b] Inpatient visits include number of hospitalisations

Table 6.128. bDMARD-Experienced: Baseline healthcare resource utilization by exposure duration - Incident Serious Infection cohort, Matched [SNDS]

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 843	TNFi[a] n = 820	Std. Diff.	Baricitinib n = 398	TNFi[a] n = 444	Std. Diff.	Baricitinib n = 359	TNFi[a] n = 308	Std. Diff.	Baricitinib n = 43	TNFi[a] n = 71	Std. Diff.
Physician Office Visits (rheumatologist visits excluded)												
n, patients (%)	478 (56.7)	511 (62.3)	-0.115	252 (63.3)	276 (62.2)	0.024	225 (62.7)	180 (58.4)	0.087	28 (65.1)	49 (69.0)	-0.083
n, events	1284	1517		734	952		720	533		81	166	
Mean (SD)	1.5 (2.2)	1.9 (2.6)	-0.136	1.8 (2.7)	2.1 (3.4)	-0.097	2.0 (2.8)	1.7 (2.5)	0.103	1.9 (2.7)	2.3 (2.8)	-0.167
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	
Min; Max	[0.0;20.0]	[0.0;20.0]		[0.0;25.0]	[0.0;27.0]		[0.0;19.0]	[0.0;17.0]		[0.0;16.0]	[0.0;11.0]	
Rheumatologist Visits												
n, patients (%)	517 (61.3)	501 (61.1)	0.005	244 (61.3)	268 (60.4)	0.019	229 (63.8)	192 (62.3)	0.03	29 (67.4)	53 (74.6)	-0.159
n, events	1170	1104		550	590		515	428		68	114	
Mean (SD)	1.4 (1.6)	1.3 (1.5)	0.027	1.4 (1.6)	1.3 (1.5)	0.035	1.4 (1.6)	1.4 (1.6)	0.028	1.6 (1.5)	1.6 (1.5)	-0.016
Median	1.0	1.0		1.0	1.0		1.0	1.0		2.0	1.0	
Min; Max	[0.0;11.0]	[0.0;8.0]		[0.0;8.0]	[0.0;8.0]		[0.0;9.0]	[0.0;13.0]		[0.0;5.0]	[0.0;7.0]	
Other Outpatient Visits												
n, patients (%)	791 (93.8)	759 (92.6)	0.051	370 (93.0)	416 (93.7)	-0.029	336 (93.6)	282 (91.6)	0.078	38 (88.4)	63 (88.7)	-0.011
n, events	16235	15932		7432	8235		8019	6103		561	1383	
Mean (SD)	19.3 (33.0)	19.4 (32.0)	-0.005	18.7 (29.3)	18.5 (30.4)	0.004	22.3 (35.2)	19.8 (31.0)	0.076	13.0 (17.9)	19.5 (38.8)	-0.213
Median	8.0	8.0		9.0	8.0		10.0	10.0		5.0	8.0	

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 843	TNFi[a] n = 820	Std. Diff.	Baricitinib n = 398	TNFi[a] n = 444	Std. Diff.	Baricitinib n = 359	TNFi[a] n = 308	Std. Diff.	Baricitinib n = 43	TNFi[a] n = 71	Std. Diff.
Min; Max	[0.0;322.0]	[0.0;255.0]		[0.0;242.0]	[0.0;275.0]		[0.0;257.0]	[0.0;242.0]		[0.0;62.0]	[0.0;280.0]	
Inpatient Visits[b]												
n, patients (%)	423 (50.2)	370 (45.1)	0.101	200 (50.3)	213 (48.0)	0.046	186 (51.8)	142 (46.1)	0.114	21 (48.8)	26 (36.6)	0.249
n, events	1244	1048		575	599		512	387		64	73	
Mean (SD)	1.5 (2.1)	1.3 (2.0)	0.096	1.4 (2.0)	1.3 (2.0)	0.048	1.4 (2.1)	1.3 (1.9)	0.085	1.5 (2.1)	1.0 (1.8)	0.236
Median	1.0	0.0		1.0	0.0		1.0	0.0		0.0	0.0	
Min; Max	[0.0;14.0]	[0.0;11.0]		[0.0;11.0]	[0.0;10.0]		[0.0;8.0]	[0.0;9.0]		[0.0;7.0]	[0.0;7.0]	
ED Visits	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
n, patients												
n, events												
Mean (SD)												
Median												
Min; Max												

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; mos = months; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor.

Note: Physician office visits do not include rheumatologist visits.

[a] Matching ratio 1:1 is applied

[b] Inpatient visits include number of hospitalisations

Table 6.129. bDMARD-Naïve: Baseline healthcare resource utilization by exposure duration - Incident Serious Infections cohort, Matched [SNDS]

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 732	TNFi[a] n = 705	Std. Diff.	Baricitinib n = 316	TNFi[a] n = 301	Std. Diff.	Baricitinib n = 246	TNFi[a] n = 263	Std. Diff.	Baricitinib n = 25	TNFi[a] n = 50	Std. Diff.
Physician Office Visits (rheumatologist visits excluded)												
n, patients (%)	451 (61.6)	435 (61.7)	-0.002	202 (63.9)	198 (65.8)	-0.039	168 (68.3)	166 (63.1)	0.109	20 (80.0)	35 (70.0)	0.233
n, events	1313.0	1270.0		562.0	539.0		543.0	469.0		50.0	111.0	
Mean (SD)	1.8 (2.8)	1.8 (4.3)	-0.002	1.8 (2.6)	1.8 (2.4)	-0.005	2.2 (3.2)	1.8 (2.3)	0.151	2.0 (2.1)	2.2 (3.1)	-0.083
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.5	
Min; Max	[0.0;41.0]	[0.0;85.0]		[0.0;24.0]	[0.0;19.0]		[0.0;31.0]	[0.0;18.0]		[0.0;9.0]	[0.0;19.0]	
Rheumatologist Visits												
n, patients (%)	450 (61.5)	423 (60.0)	0.030	203 (64.2)	195 (64.8)	-0.011	165 (67.1)	171 (65.0)	0.043	18 (72.0)	39 (78.0)	-0.139
n, events	963.0	921.0		435.0	440.0		387.0	415.0		40.0	89.0	
Mean (SD)	1.3 (1.4)	1.3 (1.5)	0.006	1.4 (1.5)	1.5 (1.5)	-0.057	1.6 (1.5)	1.6 (1.6)	-0.003	1.6 (1.2)	1.8 (1.6)	-0.127
Median	1.0	1.0		1.0	1.0		1.0	1.0		2.0	1.0	
Min; Max	[0.0;8.0]	[0.0;10.0]		[0.0;8.0]	[0.0;7.0]		[0.0;7.0]	[0.0;6.0]		[0.0;4.0]	[0.0;7.0]	
Other Outpatient Visits												
n, patients (%)	672 (91.8)	662 (93.9)	-0.082	296 (93.7)	278 (92.4)	0.052	227 (92.3)	252 (95.8)	-0.150	22 (88.0)	44 (88.0)	0.000
n, events	15111.0	14166.0		6319.0	6516.0		4581.0	4574.0		238.0	1041.0	
Mean (SD)	20.6 (35.6)	20.1 (35.0)	0.016	20.0 (34.4)	21.6 (34.7)	-0.048	18.6 (32.5)	17.4 (26.1)	0.042	9.5 (9.3)	20.8 (30.8)	-0.497
Median	7.0	7.0		8.0	9.0		6.0	7.0		8.0	11.0	

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 732	TNFi[a] n = 705	Std. Diff.	Baricitinib n = 316	TNFi[a] n = 301	Std. Diff.	Baricitinib n = 246	TNFi[a] n = 263	Std. Diff.	Baricitinib n = 25	TNFi[a] n = 50	Std. Diff.
Min; Max	[0.0;226.0]	[0.0;239.0]		[0.0;247.0]	[0.0;230.0]		[0.0;245.0]	[0.0;188.0]		[0.0;30.0]	[0.0;175.0]	
Inpatient Visits[b]												
n, patients (%)	323 (44.1)	314 (44.5)	-0.008	144 (45.6)	142 (47.2)	-0.032	107 (43.5)	125 (47.5)	-0.081	11 (44.0)	26 (52.0)	-0.161
n, events	498.0	501.0		204.0	221.0		167.0	178.0		15.0	40.0	
Mean (SD)	0.7 (1.1)	0.7 (1.2)	-0.027	0.6 (1.0)	0.7 (1.0)	-0.088	0.7 (1.0)	0.7 (0.9)	0.002	0.6 (0.9)	0.8 (1.1)	-0.201
Median	0.0	0.0		0.0	0.0		0.0	0.0		0.0	1.0	
Min; Max	[0.0;12.0]	[0.0;17.0]		[0.0;12.0]	[0.0;6.0]		[0.0;6.0]	[0.0;5.0]		[0.0;3.0]	[0.0;6.0]	
ED Visits	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
n, patients												
n, events												
Mean (SD)												
Median												
Min; Max												

Abbreviations: ED = emergency department; Max = maximum; Min = minimum; mos = months; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor. Note: Physician office visits do not include rheumatologist visits.

[a] Matching ratio 1:1 is applied

[b] Inpatient visits include number of hospitalisations

Table 6.130. bDMARD-Experienced: Baseline Healthcare Resource Utilization by Exposure Duration, Hospitalized Tuberculosis [SNDS]

Not applicable for SNDS data: no event

Table 6.131. bDMARD-Naïve: Baseline Healthcare Resource Utilization by Exposure Duration, Hospitalized Tuberculosis [SNDS]

Not applicable for SNDS data: no event

5.4 OUTCOMES

5.4.1 VENOUS THROMBOEMBOLISM (VTE)

Table 6.132. bDMARD-Experienced and bDMARD-Naïve: Clinical characteristics in patients with VTE, VTE matched cohort [SNDS]

	bDMARD-Experienced				bDMARD naïve			
Characteristics[b]	**Bari. Any n = 11**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**	**Bari. Any n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**
Age [in years]		-	-	-	-	-	-	-
N	11 (0)							
Mean (SD)	67.5 (8.3)							
Median	70.0							
Min; Max	[49.0;78.0]							
Sex, n (%)		-	-	-	-	-	-	-
Female	≤ 10							
Male	≤ 10							
Clinical conditions during baseline period, n (%)		-	-	-	-	-	-	-
Cancer, excluding NMSC	≤ 10							
NMSC	0 (0.0)							
Chronic lung disease, excluding cystic fibrosis[d]	≤ 10							
Cardiovascular conditions								
Atrial arrhythmia/fibrillation	0 (0.0)							
Cardiovascular revascularization	0 (0.0)							

	bDMARD-Experienced				bDMARD naïve			
Characteristics[b]	**Bari. Any n = 11**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**	**Bari. Any n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**
Congestive Heart Failure, hospitalized	0 (0.0)							
Coronary artery disease	0 (0.0)							
Unstable angina	0 (0.0)							
Ventricular arrhythmia	0 (0.0)							
Stroke	0 (0.0)							
Hemorrhagic	0 (0.0)							
Ischemic	0 (0.0)							
Unknown	0 (0.0)							
TIA								
Diabetes Mellitus[d]	≤ 10							
Treated insulin dependent	N/A							
Treated non insulin dependent	N/A							
Dyslipidemia (not available in SNDS)	N/A							
Hypertension (not available in SNDS)	N/A							
History of hypertension	N/A							
Current hypertension	N/A							
Immune disorders	≤ 10							
AIDS/HIV	0 (0.0)							
Antiphospholipid syndrome	0 (0.0)							

	bDMARD-Experienced				bDMARD naïve			
Characteristics[b]	**Bari. Any n = 11**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**	**Bari. Any n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**
SLE	≤ 10							
Primary Sjogren Syndrome	0 (0.0)							
Liver or pancreatic disorder[d]	0 (0.0)							
Obesity (not available in SNDS)	N/A							
Recent pregnancy	0 (0.0)							
RA Severity (CIRAS Index)	5.6 (0.6)							
Smoking (not available in SNDS)	N/A							
Surgery or trauma	0 (0.0)							
Other prescription medications during baseline period, n (%)	-	-	-	-	-	-	-	-
Antibiotics	≤ 10							
Antidiabetic agents	≤ 10							
Insulins	≤ 10							
Non-insulins	≤ 10							
Cardiovascular								
Antithrombotic agents	≤ 10							
Anticoagulant	≤ 10							
Antiplatelet	≤ 10							
Antihypertensives	≤ 10							
Angiotensin converting enzyme inhibitors (ACE)	≤ 10							
Angiotensin receptor blockers (ARB)	0 (0.0)							

	bDMARD-Experienced				bDMARD naïve			
Characteristics[b]	**Bari. Any n = 11**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**	**Bari. Any n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**
Beta blocker	0 (0.0)							
Calcium channel blocker	≤ 10							
Nitrates	0 (0.0)							
Acyclovir	0 (0.0)							
Valacyclovir	≤ 10							
Hormonal	≤ 10							
HRT	≤ 10							
Oral Contraceptives	0 (0.0)							
SERMs	0 (0.0)							
Topic with progestogens and/or estrogens	0 (0.0)							
Lipid-lowering agents	≤ 10							
HMG CoA reductase inhibitors	≤ 10							
Fibrates	≤ 10							
Bile acid sequestrants	0 (0.0)							
Nicotinic acid and derivatives	0 (0.0)							
Other lipid modifying agents	0 (0.0)							
Lipid modifying agents, combinations	≤ 10							
Rheumatoid arthritis-related								
Aspirin	0 (0.0)							
Cox-2 Inhibitor	0 (0.0)							

	bDMARD-Experienced				bDMARD naïve			
Characteristics[b]	**Bari. Any n = 11**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**	**Bari. Any n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**
NSAIDs	≤ 10							
Glucocorticosteroid	≤ 10							
Vaccines	≤ 10							
Antineoplastic agents	0 (0.0)							
Post-index Occurrence[c], n (%)		-	-	-	-	-	-	-
Cancer	0 (0.0)							
Hospitalization	0 (0.0)							
Surgery	0 (0.0)							

Abbreviations: HRT = hormone replacement therapy; IHD = ischemic heart disease; 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; TNFi = tumor 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 toVTE (Kline et al. 2017).

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

Table 6.133. bDMARD-Experienced and bDMARD-Naïve: Clinical characteristics in patients with VTE, VTE matched cohort [SNDS]

bDMARD-experienced and bDMARD naïve are grouped in the table above

Table 6.134. bDMARD-Experienced: Pattern of RA medication use in patients with VTE [SNDS]

	Unmatched					Matched				
Characteristics[a]	**Baricitinib n = 14**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi n ≤ 10**	**Total n = 22**	**Baricitinib n = 11**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[c] n ≤ 10**	**Total n = 19**
Baseline Medication, n (%)			-	-						
cDMARDs, during baseline period										
n, total (%)	≤ 10	≤ 10			13 (59.1)	≤ 10				12 (63.2)
Mean (SD)	0.6 (0.5)	0.6 (0.5)			0.6 (0.5)	0.6 (0.5)				0.6 (0.5)
Median	1.0	1.0			1.0	1.0				1.0
Min; Max	[0.0;1.0]	[0.0;1.0]			[0.0;1.0]	[0.0;1.0]				[0.0;1.0]
>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)			≤ 10	0 (0.0)				≤ 10
Chloroquine	0 (0.0)	0 (0.0)			0 (0.0)	0 (0.0)				0 (0.0)
Azathioprin	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)				≤ 10
Methotrexate	≤ 10	≤ 10			≤ 10	≤ 10				≤ 10
Mycophenolate mofetil	0 (0.0)	0 (0.0)			0 (0.0)	0 (0.0)				0 (0.0)
Sulfasalazin	≤ 10	≤ 10			≤ 10	≤ 10				≤ 10
Cyclosporin	0 (0.0)	0 (0.0)			0 (0.0)	0 (0.0)				0 (0.0)
Penicillamin	0 (0.0)	0 (0.0)			0 (0.0)	0 (0.0)				0 (0.0)
bDMARDs, during baseline period										
n, total (%)	14 (100.0)	11 (100.0)			22 (100.0)	11 (100.0)				19 (100.0)

	Unmatched					Matched				
Characteristics[a]	**Baricitinib n = 14**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi n ≤ 10**	**Total n = 22**	**Baricitinib n = 11**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[c] n ≤ 10**	**Total n = 19**
Mean (SD)	1.1 (0.3)	1.1 (0.3)			1.0 (0.2)	1.1 (0.3)				1.1 (0.2)
Median	1.0	1.0			1.0	1.0				1.0
Min; Max	[1.0;2.0]	[1.0;2.0]			[1.0;2.0]	[1.0;2.0]				[1.0;2.0]
cDMARDs, concomitant	≤ 10	≤ 10			≤ 10	≤ 10				≤ 10
Adalimumab[b]	≤ 10	≤ 10			≤ 10	≤ 10				≤ 10
Certolizumab pegol[b]	≤ 10	≤ 10			≤ 10	≤ 10				≤ 10
Etanercept[b]	≤ 10	≤ 10			≤ 10	≤ 10				≤ 10
Golimumab[b]	0 (0.0)	0 (0.0)			0 (0.0)	0 (0.0)				0 (0.0)
Infliximab[b]	≤ 10	≤ 10			≤ 10	≤ 10				≤ 10
Rituximab	≤ 10	≤ 10			≤ 10	0 (0.0)				0 (0.0)
Sarilumab	0 (0.0)	0 (0.0)			0 (0.0)	0 (0.0)				0 (0.0)
Abatacept	≤ 10	≤ 10			≤ 10	≤ 10				≤ 10
Tocilizumab	≤ 10	≤ 10			≤ 10	≤ 10				≤ 10
Anakinra	0 (0.0)	0 (0.0)			0 (0.0)	0 (0.0)				0 (0.0)
TNFi naïve at baseline	≤ 10	≤ 10	-	-	≤ 10	≤ 10				≤ 10
≥ 1 dispensing of bDMARD within 730 days before index date (excluded), n (%)	14 (100.0)	11 (100.0)			22 (100.0)	11 (100.0)				19 (100.0)
Post-index Medication, n (%)										
Methotrexate, concomitant	≤ 10	≤ 10			≤ 10	≤ 10				≤ 10

	Unmatched					Matched				
Characteristics[a]	**Baricitinib n = 14**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi n ≤ 10**	**Total n = 22**	**Baricitinib n = 11**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[c] n ≤ 10**	**Total n = 19**
Other Concomitant cDMARD	0 (0.0)	0 (0.0)			≤ 10	0 (0.0)				≤ 10
Dose change, baricitinib	≤ 10	≤ 10			≤ 10	≤ 10				≤ 10

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 = tumor 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] TNF inhibitors.

[c] Matching ratio 1:1 is applied

Table 6.135. bDMARD-Naïve: Pattern of RA medication use in patients with VTE [SNDS]

Characteristics[b]	Unmatched					Matched				
	Baricitinib n ≤ 10	Bari. 4 mg n ≤ 10	Bari. 2 mg n ≤ 10	TNFi n = 21	Total n = 30	Baricitinib n ≤ 10	Bari. 4 mg n ≤ 10	Bari. 2 mg n ≤ 10	TNFi[a] n ≤ 10	Total n = 11
Baseline Medication, n (%)	-	-	-			-	-	-	-	
cDMARDs, during baseline period										
n, total (%)				15 (71.4)	22 (73.3)					≤ 10
Mean (SD)				0.8 (0.6)	0.8 (0.6)					0.8 (0.6)
Median				1.0	1.0					1.0
Min; Max				[0.0;2.0]	[0.0;2.0]					[0.0;2.0]
>1 cDMARD concomitantly				0 (0.0)	≤ 10					≤ 10
Hydroxychloroquine				≤ 10	≤ 10					≤ 10
Chloroquine				0 (0.0)	0 (0.0)					0 (0.0)
Azathioprin				0 (0.0)	0 (0.0)					0 (0.0)
Leflunomide				≤ 10	≤ 10					0 (0.0)
Methotrexate				≤ 10	15 (50.0)					≤ 10
Mycophenolate mofetil				0 (0.0)	0 (0.0)					0 (0.0)
Sulfasalazin				≤ 10	≤ 10					≤ 10
Cyclosporin				0 (0.0)	0 (0.0)					0 (0.0)
Penicillamin				0 (0.0)	0 (0.0)					0 (0.0)
bDMARDs, during baseline period										
n, total (%)				0 (0.0)	0 (0.0)					0 (0.0)
Mean (SD)				0.0 (0.0)	0.0 (0.0)					0.0 (0.0)
Median				0.0	0.0					0.0

	Unmatched					Matched				
Characteristics[b]	**Baricitinib n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi n = 21**	**Total n = 30**	**Baricitinib n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**	**Total n = 11**
Min; Max				[0.0;0.0]	[0.0;0.0]					[0.0;0.0]
cDMARDs, concomitant				0 (0.0)	0 (0.0)					0 (0.0)
Adalimumab[c]				0 (0.0)	0 (0.0)					0 (0.0)
Certolizumab pegol[c]				0 (0.0)	0 (0.0)					0 (0.0)
Etanercept[c]				0 (0.0)	0 (0.0)					0 (0.0)
Golimumab[c]				0 (0.0)	0 (0.0)					0 (0.0)
Infliximab[c]				0 (0.0)	0 (0.0)					0 (0.0)
Rituximab				0 (0.0)	0 (0.0)					0 (0.0)
Sarilumab				0 (0.0)	0 (0.0)					0 (0.0)
Abatacept				0 (0.0)	0 (0.0)					0 (0.0)
Tocilizumab				0 (0.0)	0 (0.0)					0 (0.0)
Anakinra				0 (0.0)	0 (0.0)					0 (0.0)
TNFi naïve at baseline				21 (100.0)	30 (100.0)					11 (100.0)
≥ 1 dispensing of bDMARD within 730 days before index date (excluded), n (%)				≤ 10	≤ 10					≤ 10
Post-index Medication, n (%)	-	-	-			-	-	-	-	
Methotrexate, concomitant				≤ 10	14 (46.7)					≤ 10
Other Concomitant cDMARD				≤ 10	≤ 10					0 (0.0)
Dose change, baricitinib				-	≤ 10					≤ 10

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 = tumor 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.

Table 6.136. bDMARD-Experienced: Time to first VTE [SNDS]

	Unmatched					Matched				
	Baricitinib n = 14	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi n ≤ 10**	**Total n = 22**	**Baricitinib n = 11**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi [a] n ≤ 10**	**Total n = 19**
Time to first VTE (in days)			-	-			-	-	-	
N (missing)	14 (0)	11 (0)			22 (0)	11 (0)				19 (0)
Mean (SD)	290.0 (200.2)	299.7 (225.3)			258.8 (192.5)	280.1 (187.6)				248.2 (182.3)
Median	216.5	199.0			204.0	209.0				199.0
Min; Max	[75.0;650.0]	[75.0;650.0]			[37.0;650.0]	[75.0;632.0]				[37.0;632.0]

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

[a] Matching ratio 1:1 is applied

Table 6.137. bDMARD-Naïve: Time to first VTE [SNDS]

	Unmatched					Matched				
	Baricitinib n ≤ 10	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi n = 21**	**Total n = 30**	**Baricitinib n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi [a] n ≤ 10**	**Total n = 11**
Time to first VTE (in days)	-	-	-			-	-	-	-	
N (missing)				21 (0)	30 (0)					11 (0)
Mean (SD)				195.2 (178.5)	185.2 (160.1)					150.1 (106.0)
Median				144.0	143.0					142.0
Min; Max				[26.0;624.0]	[17.0;624.0]					[17.0;346.0]

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

[a] Matching ratio 1:1 is applied

Table 6.138. bDMARD-Experienced: Crude rates of incident VTE [SNDS]

	Unmatched					Matched				
VTE	**Bari. Any[a] n = 1982**	**Bari. 4 mg n = 1661**	**Bari. 2 mg n = 317**	**TNFi n = 2374**	**Total n = 4356**	**Bari. Any[b] n = 1600**	**Bari. 4 mg n = 1350**	**Bari. 2 mg n = 248**	**TNFi[a] n = 1600**	**Total n = 3200**
Overall										
Person-Years	1345	1137	205	1634	2979	1076	914	160	1095	2171
VTE	14	11	3	8	22	11	9	2	8	19
VTE/100 PY	1.0	1.0	1.5	0.5	0.7	1.0	1.0	1.3	0.7	0.9
95% CI	[0.6 ; 1.7]	[0.5 ; 1.7]	[0.3 ; 4.3]	[0.2 ; 1.0]	[0.5 ; 1.1]	[0.5 ; 1.8]	[0.5 ; 1.9]	[0.2 ; 4.5]	[0.3 ; 1.4]	[0.5 ; 1.4]
IRD	0.6					0.3				
IRD 95% CI	[-0.1 ; 1.2]					[-0.5 ; 1.1]				
Concomitant[b] MTX Use, n (%)	825 (41.6)	716 (43.1)	107 (33.8)	1079 (45.5)	1904 (43.7)	684 (42.8)	600 (44.4)	83 (33.5)	693 (43.3)	1377 (43.0)
Person-Years	628	545	81	854	1482	510	447	62	549	1059
VTE	5	5	0	2	7	4	4	0	2	6
VTE/100 PY	0.8	0.9	0	0.2	0.5	0.8	0.9	0	0.4	0.6
95% CI	[0.3 ; 1.9]	[0.3 ; 2.1]	[0.0 ; 4.5]	[0.0 ; 0.8]	[0.2 ; 1]	[0.2 ; 2]	[0.2 ; 2.3]	[0 ; 6]	[0 ; 1.3]	[0.2 ; 1.2]
IRD	0.6					0.4				
IRD 95% CI	[-0.1 ; 1.3]					[-0.5 ; 1.3]				
No concomitant[b] MTX Use, n (%)	1157 (58.4)	945 (56.9)	210 (66.2)	1295 (54.5)	2452 (56.3)	916 (57.3)	750 (55.6)	165 (66.5)	907 (56.7)	1823 (57.0)
Person-Years	718	592	124	780	1498	566	467	98	545	1112
VTE	9	6	3	6	15	7	5	2	6	13
VTE/100 PY	1.3	1.0	2.4	0.8	1.0	1.2	1.1	2	1.1	1.2
95% CI	[0.6 ; 2.4]	[0.4 ; 2.2]	[0.5 ; 7.1]	[0.3 ; 1.7]	[0.6 ; 1.7]	[0.5 ; 2.5]	[0.3 ; 2.5]	[0.2 ; 7.4]	[0.4 ; 2.4]	[0.6 ; 2]

	Unmatched					Matched				
	Bari. Any [a]	**Bari. 4 mg**	**Bari. 2 mg**	**TNFi**	**Total**	**Bari. Any[b]**	**Bari. 4 mg**	**Bari. 2 mg**	**TNFi[a]**	**Total**
VTE	**n = 1982**	**n = 1661**	**n = 317**	**n = 2374**	**n = 4356**	**n = 1600**	**n = 1350**	**n = 248**	**n = 1600**	**n = 3200**
IRD	0.5					0.1				
IRD 95% CI	[-0.5 ; 1.5]					[-1.1 ; 1.4]				

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

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

[b] 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.

Table 6.139. bDMARD-Naïve: Crude rates of incident VTE [SNDS]

	Unmatched					Matched				
VTE	**Bari. Any n = 1260**	**Bari. 4 mg n = 955**	**Bari. 2 mg n = 305**	**TNFi n = 7828**	**Total n = 9088**	**Bari. Any n = 1260**	**Bari. 4 mg n = 955**	**Bari. 2 mg n = 305**	**TNFi[a] n = 1260**	**Total n = 2520**
Overall										
Person-Years	769	597	172	5073	5842	769	597	172	781	1550
VTE	9	5	4	21	30	9	5	4	2	11
VTE/100 PY	1.2	0.8	2.3	0.4	0.5	1.2	0.8	2.3	0.3	0.7
95% CI	[0.5 ; 2.2]	[0.3 ; 2]	[0.6 ; 6]	[0.3 ; 0.6]	[0.3 ; 0.7]	[0.5 ; 2.2]	[0.3 ; 2]	[0.6 ; 6]	[0 ; 0.9]	[0.4 ; 1.3]
IRD	0.8					0.9			.	
IRD 95% CI	[0.2 ; 1.3]					[0.1 ; 1.8]				
Concomitant[c] MTX Use, n (%)	533 (42.3)	432 (45.2)	101 (33.1)	4305 (55.0)	4838 (53.2)	533 (42.3)	432 (45.2)	101 (33.1)	638 (50.6)	1171 (46.5)
Person-Years	382	314	67	3251	3632	382	314	67	468	850
VTE	4	3	1	10	14	4	3	1	1	5
VTE/100 PY	1.0	1.0	1.5	0.3	0.4	1	1	1.5	0.2	0.6
95% CI	[0.3 ; 2.7]	[0.2 ; 2.8]	[0.0 ; 8.3]	[0.1 ; 0.6]	[0.2 ; 0.6]	[0.3 ; 2.7]	[0.2 ; 2.8]	[0 ; 8.3]	[0 ; 1.2]	[0.2 ; 1.4]
IRD	0.7					0.8			.	
IRD 95% CI	[0.1 ; 1.4]					[-0.2 ; 1.9]				
No concomitant[c] MTX Use, n (%)	727 (57.7)	523 (54.8)	204 (66.9)	3523 (45.0)	4250 (46.8)	727 (57.7)	523 (54.8)	204 (66.9)	622 (49.4)	1349 (53.5)
Person-Years	387	283	105	1822	2209	387	283	105	312	700
VTE	5	2	3	11	16	5	2	3	1	6
VTE/100 PY	1.3	0.7	2.9	0.6	0.7	1.3	0.7	2.9	0.3	0.9
95% CI	[0.4 ; 3]	[0.1 ; 2.6]	[0.6 ; 8.4]	[0.3 ; 1.1]	[0.4 ; 1.2]	[0.4 ; 3]	[0.1 ; 2.6]	[0.6 ; 8.4]	[0 ; 1.8]	[0.3 ; 1.9]

	Unmatched					Matched				
	Bari. Any	**Bari. 4 mg**	**Bari. 2 mg**	**TNFi**	**Total**	**Bari. Any**	**Bari. 4 mg**	**Bari. 2 mg**	**TNFi[a]**	**Total**
VTE	**n = 1260**	**n = 955**	**n = 305**	**n = 7828**	**n = 9088**	**n = 1260**	**n = 955**	**n = 305**	**n = 1260**	**n = 2520**
IRD	0.7					1			.	
IRD 95% CI	[-0.2 ; 1.6]					[-0.4 ; 2.4]				

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

[a] Matching ratio 1:1 is applied

[b] n=3 subjects were dispensed both baricitinib 4mg and 2mg 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.

Table 6.140. bDMARD-Experienced and bDMARD naïve: Comparative risk of incident VTE, matched cohort [SNDS]

	bDMARD-Experienced			bDMARD naïve		
VTE	**TNFi**	**Baricitinib, HR [95% CI]**	**P-value**	**TNFi**	**Baricitinib, HR [95% CI]**	**P-value**
Base Model	Ref	1.39 [0.55 ; 3.49]	0.4821	Ref	4.51 [0.97 ; 20.94]	0.0542
Adjusted – Model [1]	Ref	1.39 [0.55 ; 3.49]	0.4821	Ref	4.51 [0.97 ; 20.94]	0.0542
Adjusted – Model [2]	Ref	1.37 [0.55 ; 3.43]	0.5000	Ref	4.42 [0.95 ; 20.64]	0.0587
Concomitant Glucocorticoid use	*Ref*	1.32 [0.51 ; 3.42]	0.5635	Ref	1.33 [0.41 ; 4.30]	0.6376
Concomitant cDMARD use	*Ref*	0.88 [0.36 ; 2.18]	0.7845	Ref	0.76 [0.24 ; 2.47]	0.6527
Adjusted – Model [3]	Ref	1.37 [0.55 ; 3.43]	0.4997	Ref	4.52 [0.97 ; 20.98]	0.0539
Concomitant Glucocorticoid use	*Ref*	1.32 [0.51 ; 3.41]	0.5697	Ref	1.31 [0.39 ; 4.38]	0.6568
Adjusted – Model [n]	Ref	N/A	N/A	Ref	N/A	N/A

Abbreviations: cDMARD = conventional disease-modifying antirheumatic drug; CI = confidence interval; HR = hazard ratio; Ref = referent group; VTE = venous thromboembolism.

Model [1] = propensity score-matched model with outcome and baricitinib exposure, adjusted for any variables that remain unbalanced after PS 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.

Models 1-n may include additional variables that remain unbalanced after propensity-score matching as well as concomitant cDMARD or glucocorticoid use separately.

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.

Table 6.141. bDMARD-Experienced and bDMARD naïve: Comparative Risk of Incident VTE, matched cohort [SNDS]

bDMARD-experienced and bDMARD naïve are grouped in the table above

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Table 6.142. bDMARD-Experienced and bDMARD naïve: Clinical characteristics in patients with MACE, MACE matched cohort [SNDS]

	bDMARD-Experienced				bDMARD naïve			
Characteristics[b]	**Bari. Any n = 16**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**	**Bari. Any n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**
Age [in years]			-	-	-	-	-	-
N	16 (0)	11 (0)						
Mean (SD)	67.9 (7.2)	63.9 (4.6)						
Median	66.5	64.0						
Min; Max	[55.0;80.0]	[55.0;70.0]						
Sex, n (%)			-	-	-	-	-	-
Female	≤ 10	≤ 10						
Male	11 (68.8)	≤ 10						
Clinical conditions during baseline period, n (%)			-	-	-	-	-	-
Cancer, excluding NMSC	0 (0.0)	0 (0.0)						
NMSC	0 (0.0)	0 (0.0)						
Chronic lung disease, excluding cystic fibrosis[d]	≤ 10	≤ 10						
Cardiovascular conditions								
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)						

	bDMARD-Experienced				bDMARD naïve			
Characteristics[b]	**Bari. Any n = 16**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**	**Bari. Any n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**
Coronary artery disease	≤ 10	≤ 10						
Unstable angina	0 (0.0)	0 (0.0)						
Ventricular arrhythmia	0 (0.0)	0 (0.0)						
Stroke	0 (0.0)	0 (0.0)						
Hemorrhagic	0 (0.0)	0 (0.0)						
Ischemic	0 (0.0)	0 (0.0)						
Unknown	0 (0.0)	0 (0.0)						
TIA	0 (0.0)	0 (0.0)						
Diabetes Mellitus[d]	≤ 10	≤ 10						
Treated insulin dependent	N/A	N/A						
Treated non insulin dependent	N/A	N/A						
Dyslipidemia (not available in SNDS)	N/A	N/A						
Hypertension (not available in SNDS)	N/A	N/A						
History of hypertension	N/A	N/A						
Current hypertension	N/A	N/A						
Immune disorders	≤ 10	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 Sjogren Syndrome	≤ 10	0 (0.0)						

	bDMARD-Experienced				bDMARD naïve			
Characteristics[b]	**Bari. Any n = 16**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**	**Bari. Any n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**
Liver or pancreatic disorder[d]	≤ 10	≤ 10						
Obesity (not available in SNDS)	N/A	N/A						
Recent pregnancy	0 (0.0)	0 (0.0)						
Smoking (not available in SNDS)								
Surgery or trauma	0 (0.0)	0 (0.0)						
Other prescription medications during baseline period, n (%)			-	-	-	-	-	-
Antibiotics	≤ 10	≤ 10						
Antidiabetic agents	≤ 10	≤ 10						
Insulins	≤ 10	≤ 10						
Non-insulins	≤ 10	≤ 10						
Cardiovascular								
Antithrombotic agents	≤ 10	≤ 10						
Anticoagulant	0 (0.0)	0 (0.0)						
Antiplatelet	≤ 10	≤ 10						
Antihypertensives	≤ 10	≤ 10						
Angiotensin converting enzyme inhibitors (ACE)	≤ 10	≤ 10						
Angiotensin receptor blockers (ARB)	≤ 10	≤ 10						
Beta blocker	≤ 10	≤ 10						
Calcium channel blocker	≤ 10	≤ 10						
Nitrates	≤ 10	≤ 10						

	bDMARD-Experienced				bDMARD naïve			
Characteristics[b]	**Bari. Any n = 16**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**	**Bari. Any n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**
Acyclovir	0 (0.0)	0 (0.0)						
Valacyclovir	≤ 10	0 (0.0)						
Hormonal	≤ 10	≤ 10						
HRT	≤ 10	≤ 10						
Oral Contraceptives	0 (0.0)	0 (0.0)						
SERMs	0 (0.0)	0 (0.0)						
Topic with progestogens and/or estrogens	0 (0.0)	0 (0.0)						
Lipid-lowering agents	≤ 10	≤ 10						
HMG CoA reductase inhibitors	≤ 10	≤ 10						
Fibrates	0 (0.0)	0 (0.0)						
Bile acid sequestrants	0 (0.0)	0 (0.0)						
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)						
Other lipid modifying agents	0 (0.0)	0 (0.0)						
Lipid modifying agents, combinations	0 (0.0)	0 (0.0)						
Rheumatoid arthritis-related								
Aspirin	0 (0.0)	0 (0.0)						
Cox-2 Inhibitor	≤ 10	≤ 10						
NSAIDs	≤ 10	≤ 10						
Glucocorticosteroid	12 (75.0)	≤ 10						
Vaccines	≤ 10	≤ 10						

	bDMARD-Experienced				bDMARD naïve			
Characteristics[b]	**Bari. Any n = 16**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**	**Bari. Any n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n ≤ 10**
Antineoplastic agents	0 (0.0)	0 (0.0)						
Post-index Occurrence[c], n (%)			-	-	-	-	-	-
Cancer	0 (0.0)	0 (0.0)						
Hospitalization	0 (0.0)	0 (0.0)						
Surgery	0 (0.0)	0 (0.0)						

Abbreviations: IHD = ischemic heart disease; 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 = tumor 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] Events in this category must have occurred in the 7 days immediately prior to MACE.

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

Table 6.143. bDMARD-Experienced and bDMARD naïve: Clinical characteristics in patients with MACE, MACE matched cohort [SNDS]

bDMARD-experienced and bDMARD naïve are grouped in the table above

Table 6.144. bDMARD-Experienced: Pattern of RA medication use in patients with MACE [SNDS]

	Unmatched					Matched				
Characteristics[a]	**Baricitinib n = 19**	**Bari. 4 mg n = 14**	**Bari. 2 mg n ≤ 10**	**TNFi n ≤ 10**	**Total n = 26**	**Baricitinib n = 16**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi[c] n ≤ 10**	**Total n = 22**
Baseline Medication, n (%)			-	-				-	-	
cDMARDs, during baseline period										
n, total (%)	12 (63.2)	≤ 10			16 (61.5)	≤ 10	≤ 10			12 (54.5)
Mean (SD)	0.6 (0.5)	0.6 (0.5)			0.6 (0.5)	0.6 (0.5)	0.5 (0.5)			0.5 (0.5)
Median	1.0	1.0			1.0	1.0	1.0			1.0
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]
>1 cDMARD concomitantly	0 (0.0)	0 (0.0)			0 (0.0)	0 (0.0)	0 (0.0)			0 (0.0)
Hydroxychloroquine	≤ 10	≤ 10			≤ 10	≤ 10	≤ 10			≤ 10
Chloroquine	0 (0.0)	0 (0.0)			0 (0.0)	0 (0.0)	0 (0.0)			0 (0.0)
Azathioprin	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
Methotrexate	≤ 10	≤ 10			≤ 10	≤ 10	≤ 10			≤ 10
Mycophenolate mofetil	0 (0.0)	0 (0.0)			0 (0.0)	0 (0.0)	0 (0.0)			0 (0.0)
Sulfasalazin	0 (0.0)	0 (0.0)			0 (0.0)	0 (0.0)	0 (0.0)			0 (0.0)
Cyclosporin	0 (0.0)	0 (0.0)			0 (0.0)	0 (0.0)	0 (0.0)			0 (0.0)
Penicillamin	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 (100.0)	14 (100.0)			26 (100.0)	16 (100.0)	11 (100.0)			22 (100.0)

	Unmatched					Matched				
Characteristics[a]	**Baricitinib n = 19**	**Bari. 4 mg n = 14**	**Bari. 2 mg n ≤ 10**	**TNFi n ≤ 10**	**Total n = 26**	**Baricitinib n = 16**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi[c] n ≤ 10**	**Total n = 22**
Mean (SD)	1.2 (0.4)	1.2 (0.4)			1.1 (0.3)	1.0 (0.0)	1.0 (0.0)			1.0 (0.0)
Median	1.0	1.0			1.0	1.0	1.0			1.0
Min; Max	[1.0;2.0]	[1.0;2.0]			[1.0;2.0]	[1.0;1.0]	[1.0;1.0]			[1.0;1.0]
cDMARDs, concomitant	11 (57.9)	≤ 10			15 (57.7)	≤ 10	≤ 10			11 (50.0)
Adalimumab[b]	≤ 10	≤ 10			≤ 10	≤ 10	≤ 10			≤ 10
Certolizumab pegol[b]	≤ 10	≤ 10			≤ 10	≤ 10	≤ 10			≤ 10
Etanercept[b]	≤ 10	≤ 10			≤ 10	≤ 10	≤ 10			≤ 10
Golimumab[b]	≤ 10	0 (0.0)			≤ 10	≤ 10	0 (0.0)			≤ 10
Infliximab[b]	≤ 10	≤ 10			≤ 10	≤ 10	≤ 10			≤ 10
Rituximab	≤ 10	≤ 10			≤ 10	≤ 10	≤ 10			≤ 10
Sarilumab	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
Tocilizumab	≤ 10	≤ 10			≤ 10	≤ 10	≤ 10			≤ 10
Anakinra	≤ 10	0 (0.0)			≤ 10	≤ 10	0 (0.0)			≤ 10
TNFi naïve at baseline	≤ 10	≤ 10			≤ 10	≤ 10	≤ 10			≤ 10
≥ 1 dispensing of bDMARD within 730 days before index date (excluded), n (%)	19 (100.0)	14 (100.0)			26 (100.0)	16 (100.0)	11 (100.0)			22 (100.0)
Post-index Medication, n (%)			-	-						
Methotrexate, concomitant	≤ 10	≤ 10			≤ 10	≤ 10	≤ 10			≤ 10

	Unmatched					Matched				
Characteristics[a]	**Baricitinib n = 19**	**Bari. 4 mg n = 14**	**Bari. 2 mg n ≤ 10**	**TNFi n ≤ 10**	**Total n = 26**	**Baricitinib n = 16**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi [c] n ≤ 10**	**Total n = 22**
Other Concomitant cDMARD	≤ 10	≤ 10			≤ 10	≤ 10	≤ 10			≤ 10
Dose change, baricitinib	≤ 10	≤ 10			≤ 10	≤ 10	≤ 10			≤ 10

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; DMARD = disease-modifying antirheumatic drugs; hosp = hospitalized; HRT = hormone replacement therapy; Max = maximum; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Min = minimum; mos = months; N = number of patients in the specified category; NMSC = non-melanoma skin cancer; RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulator; Std. Diff. = standardized difference; TNF = tumor necrosis factor; TNFi = tumor 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] TNF inhibitors.

[c] Matching ratio 1:1 is applied

Table 6.145. bDMARD-Naïve: Pattern of RA Medication Use in Patients with MACE [SNDS]

	Unmatched					Matched				
Characteristics[a]	**Baricitinib n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi n = 27**	**Total n = 36**	**Baricitinib n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[c] n ≤ 10**	**Total n = 16**
Baseline Medication, n (%)	-	-	-			-	-	-		
cDMARDs, during baseline period										
n, total (%)				21 (77.8)	26 (72.2)					≤ 10
Mean (SD)				0.9 (0.5)	0.8 (0.6)					0.7 (0.6)
Median				1.0	1.0					1.0
Min; Max				[0.0;2.0]	[0.0;2.0]					[0.0;2.0]
>1 cDMARD concomitantly				≤ 10	≤ 10					≤ 10
Hydroxychloroquine				≤ 10	≤ 10					≤ 10
Chloroquine				0 (0.0)	0 (0.0)					0 (0.0)
Azathioprin				0 (0.0)	0 (0.0)					0 (0.0)
Leflunomide				≤ 10	≤ 10					≤ 10
Methotrexate				20 (74.1)	23 (63.9)					≤ 10
Mycophenolate mofetil				0 (0.0)	0 (0.0)					0 (0.0)
Sulfasalazin				0 (0.0)	≤ 10					≤ 10
Cyclosporin				0 (0.0)	0 (0.0)					0 (0.0)
Penicillamin				0 (0.0)	0 (0.0)					0 (0.0)
bDMARDs, during baseline period										
n, total (%)				0 (0.0)	0 (0.0)					0 (0.0)

	Unmatched					Matched				
Characteristics[a]	**Baricitinib n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi n = 27**	**Total n = 36**	**Baricitinib n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[c] n ≤ 10**	**Total n = 16**
Mean (SD)				0.0 (0.0)	0.0 (0.0)					0.0 (0.0)
Median				0.0	0.0					0.0
Min; Max				[0.0;0.0]	[0.0;0.0]					[0.0;0.0]
cDMARDs, concomitant				0 (0.0)	0 (0.0)					0 (0.0)
Adalimumab[b]				0 (0.0)	0 (0.0)					0 (0.0)
Certolizumab pegol[b]				0 (0.0)	0 (0.0)					0 (0.0)
Etanercept[b]				0 (0.0)	0 (0.0)					0 (0.0)
Golimumab[b]				0 (0.0)	0 (0.0)					0 (0.0)
Infliximab[b]				0 (0.0)	0 (0.0)					0 (0.0)
Rituximab				0 (0.0)	0 (0.0)					0 (0.0)
Sarilumab				0 (0.0)	0 (0.0)					0 (0.0)
Abatacept				0 (0.0)	0 (0.0)					0 (0.0)
Tocilizumab				0 (0.0)	0 (0.0)					0 (0.0)
Anakinra				0 (0.0)	0 (0.0)					0 (0.0)
TNFi naïve at baseline				27 (100.0)	36 (100.0)					16 (100.0)
≥ 1 dispensing of bDMARD within 730 days before index date (excluded), n (%)				≤ 10	≤ 10					≤ 10
Post-index Medication, n (%)	-	-	-							
Methotrexate, concomitant				20 (74.1)	22 (61.1)					≤ 10

	Unmatched					Matched				
Characteristics[a]	**Baricitinib n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi n = 27**	**Total n = 36**	**Baricitinib n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi[c] n ≤ 10**	**Total n = 16**
Other Concomitant cDMARD				≤ 10	≤ 10					≤ 10
Dose change, baricitinib				0 (0.0)	≤ 10					≤ 10

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; DMARD = disease-modifying antirheumatic drugs; hosp = hospitalized; HRT = hormone replacement therapy; Max = maximum; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Min = minimum;
mos = months; N = number of patients in the specified category; NMSC = non-melanoma skin cancer;
RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulator; Std. Diff. = standardized difference; TNF = tumor necrosis factor; TNFi = tumor 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] TNF inhibitors.

[c] Matching ratio 1:1 is applied

Table 6.146. bDMARD-Experienced: Time to first MACE, [SNDS]

	Unmatched					Matched				
	Baricitinib n = 19	Bari. 4 mg n = 14	Bari. 2 mg n ≤ 10	TNFi n ≤ 10	Total n = 26	Baricitinib n = 16	Bari. 4 mg n = 11	Bari. 2 mg n ≤ 10	TNFi [a] n ≤ 10	Total n = 22
Time to first MACE (in days)										
N (missing)	19 (0)	14 (0)			26 (0)	16 (0)	11 (0)			22 (0)
Mean (SD)	210.8 (157.5)	206.1 (157.1)			210.9 (143.2)	217.5 (151.1)	214.5 (147.6)			217.8 (139.1)
Median	210.0	190.5			192.0	217.0	210.0			217.0
Min; Max	[4.0;586.0]	[7.0;586.0]			[4.0;586.0]	[4.0;586.0]	[56.0;586.0]			[4.0;586.0]

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke.

[a] Matching ratio 1:1 is applied

Table 6.147. bDMARD-Naïve: Time to first MACE [SNDS]

	Unmatched					matched				
	Baricitinib n ≤ 10	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi n = 27**	**Total n = 36**	**Baricitinib n ≤ 10**	**Bari. 4 mg n ≤ 10**	**Bari. 2 mg n ≤ 10**	**TNFi [a] n ≤ 10**	**Total n = 16**
Time to first MACE (in days)										
N (missing)				27 (0)	36 (0)					16 (0)
Mean (SD)				299.4 (260.3)	277.8 (253.2)					216.9 (216.6)
Median				221.0	165.0					106.5
Min; Max				[1.0;807.0]	[1.0;807.0]					[13.0;710.0]

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke.

[a] Matching ratio 1:1 is applied

Table 6.148. bDMARD-Experienced: Crude rates of incident MACE [SNDS]

	Unmatched					Matched				
MACE	Bari. Any [a] n = 1977	Bari. 4 mg n = 1659	Bari. 2 mg n = 314	TNFi n = 2370	Total n = 4347	Bari. Any[b] n = 1606	Bari. 4 mg n = 1360	Bari. 2 mg n = 244	TNFi[a] n = 1606	Total n = 3212
Overall (MI or stroke)										
Person-Years	1335	1131	202	1627	2962	1076	920	154	1095	2171
MACE	19	14	5	7	26	16	11	5	6	22
MACE/100 PY	1.4	1.2	2.5	0.4	0.9	1.5	1.2	3.2	0.5	1
95% CI	[0.9 ; 2.2]	[0.7 ; 2.1]	[0.8 ; 5.8]	[0.2 ; 0.9]	[0.6 ; 1.3]	[0.9 ; 2.4]	[0.6 ; 2.1]	[1.1 ; 7.6]	[0.2 ; 1.2]	[0.6 ; 1.5]
IRD	1					0.9			.	
IRD 95% CI	[0.3 ; 1.7]					[0.1 ; 1.8]				
Overall (MI)										
Person-Years	1335	1131	202	1627	2962	1076	920	154	1095	2171
MI	10	8	2	6	16	7	5	2	5	12
MI /100 PY	0.7	0.7	1.0	0.4	0.5	0.7	0.5	1.3	0.5	0.6
95% CI	[0.4 ; 1.4]	[0.3 ; 1.4]	[0.1 ; 3.6]	[0.1 ; 0.8]	[0.3 ; 0.9]	[0.3 ; 1.3]	[0.2 ; 1.3]	[0.2 ; 4.7]	[0.1 ; 1.1]	[0.3 ; 1]
IRD	0.4					0.2			.	
IRD 95% CI	[-0.2 ; 0.9]					[-0.4 ; 0.8]				
Overall (stroke)										
Person-Years	1335	1131	202	1627	2962	1076	920	154	1095	2171
Stroke	9	6	3	1	10	9	6	3	1	10
Stroke /100 PY	0.7	0.5	1.5	0.1	0.3	0.8	0.7	1.9	0.1	0.5
95% CI	[0.3 ; 1.3]	[0.2 ; 1.2]	[0.3 ; 4.4]	[0.0 ; 0.3]	[0.2 ; 0.6]	[0.4 ; 1.6]	[0.2 ; 1.4]	[0.4 ; 5.7]	[0 ; 0.5]	[0.2 ; 0.8]

	Unmatched					Matched				
MACE	**Bari. Any [a] n = 1977**	**Bari. 4 mg n = 1659**	**Bari. 2 mg n = 314**	**TNFi n = 2370**	**Total n = 4347**	**Bari. Any[b] n = 1606**	**Bari. 4 mg n = 1360**	**Bari. 2 mg n = 244**	**TNFi[a] n = 1606**	**Total n = 3212**
IRD	0.6					0.7			.	
IRD 95% CI	[0.2 ; 1]					[0.2 ; 1.3]				
Concomitant [b] MTX Use, n (%)	824 (41.7)	716 (43.2)	106 (33.8)	1082 (45.7)	1906 (43.8)	689 (42.9)	600 (44.1)	87 (35.7)	700 (43.6)	1389 (43.2)
Person-Years	623	543	79	853	1476	511	446	64	557	1069
MACE	7	5	2	3	10	5	3	2	2	7
MACE/100 PY	1.1	0.9	2.5	0.4	0.7	1	0.7	3.1	0.4	0.7
95% CI	[0.5 ; 2.3]	[0.3 ; 2.1]	[0.3 ; 9.2]	[0.1 ; 1.0]	[0.3 ; 1.2]	[0.3 ; 2.3]	[0.1 ; 2]	[0.4 ; 11.3]	[0 ; 1.3]	[0.3 ; 1.3]
IRD	0.8					0.6			.	
IRD 95% CI	[-0.1 ; 1.6]					[-0.4 ; 1.6]				
No concomitant [b] MTX Use, n (%)	1153 (58.3)	943 (56.8)	208 (66.2)	1288 (54.3)	2441 (56.2)	917 (57.1)	760 (55.9)	157 (64.3)	906 (56.4)	1823 (56.8)
Person-Years	713	588	123	773	1486	565	475	90	538	1102
MACE	12	9	3	4	16	11	8	3	4	15
MACE/100 PY	1.7	1.5	2.4	0.5	1.1	1.9	1.7	3.3	0.7	1.4
95% CI	[0.9 ; 2.9]	[0.7 ; 2.9]	[0.5 ; 7.1]	[0.1 ; 1.3]	[0.6 ; 1.7]	[1 ; 3.5]	[0.7 ; 3.3]	[0.7 ; 9.7]	[0.2 ; 1.9]	[0.8 ; 2.2]
IRD	1.2					1.2			.	
IRD 95% CI	[0.1 ; 2.2]					[-0.2 ; 2.6]				

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

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

[b] 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.

Table 6.149. bDMARD-Naïve: Crude Rates of Incident MACE [SNDS]

	Unmatched					Matched				
	Bari. Any	Bari. 4 mg	Bari. 2 mg	TNFi	Total	Bari. Any	Bari. 4 mg	Bari. 2 mg	TNFi[a]	Total
MACE	**n = 1259**	**n = 954**	**n = 305**	**n = 7805**	**n = 9064**	**n = 1257**	**n = 954**	**n = 303**	**n = 1257**	**n = 2514**
Overall (MI or stroke)										
Person-Years	766	596	170	5055	5821	765	596	169	830	1595
MACE	9	5	4	27	36	9	5	4	7	16
MACE/100 PY	1.2	0.8	2.3	0.5	0.6	1.2	0.8	2.4	0.8	1
95% CI	[0.5 ; 2.2]	[0.3 ; 2.0]	[0.6 ; 6.0]	[0.4 ; 0.8]	[0.4 ; 0.9]	[0.5 ; 2.2]	[0.3 ; 2]	[0.6 ; 6.1]	[0.3 ; 1.7]	[0.6 ; 1.6]
IRD	0.6					0.3			.	
IRD 95% CI	[0.04 ; 1.2]					[-0.7 ; 1.3]				
Overall (MI)										
Person-Years	766	596	170	5055	5821	765	596	169	830	1595
MI	6	4	2	17	23	6	4	2	4	10
MI /100 PY	0.8	0.7	1.2	0.3	0.4	0.8	0.7	1.2	0.5	0.6
95% CI	[0.3 ; 1.7]	[0.2 ; 1.7]	[0.1 ; 4.2]	[0.2 ; 0.5]	[0.3 ; 0.6]	[0.3 ; 1.7]	[0.2 ; 1.7]	[0.1 ; 4.3]	[0.1 ; 1.2]	[0.3 ; 1.2]
IRD	0.4					0.3			.	
IRD 95% CI	[-0.03 ; 0.9]					[-0.5 ; 1.1]				
Overall (stroke)										
Person-Years	766	596	170	5055	5821	765	596	169	830	1595
Stroke	3	1	2	10	13	3	1	2	3	6
Stroke /100 PY	0.4	0.2	1.2	0.2	0.2	0.4	0.2	1.2	0.4	0.4
95% CI	[0.1 ; 1.1]	[0.0 ; 0.9]	[0.1 ; 4.2]	[0.1 ; 0.4]	[0.1 ; 0.4]	[0.1 ; 1.1]	[0 ; 0.9]	[0.1 ; 4.3]	[0.1 ; 1.1]	[0.1 ; 0.8]
IRD	0.2					0.03			.	

	Unmatched					Matched				
MACE	**Bari. Any n = 1259**	**Bari. 4 mg n = 954**	**Bari. 2 mg n = 305**	**TNFi n = 7805**	**Total n = 9064**	**Bari. Any n = 1257**	**Bari. 4 mg n = 954**	**Bari. 2 mg n = 303**	**TNFi[a] n = 1257**	**Total n = 2514**
IRD 95% CI	[-0.2 ; 0.6]					[-0.6 ; 0.6]				
Concomitant[c] MTX Use, n (%)	533 (42.3)	432 (45.3)	101 (33.1)	4294 (55.0)	4827 (53.3)	533 (42.4)	432 (45.3)	101 (33.3)	647 (51.5)	1180 (46.9)
Person-Years	381	314	66	3239	3620	381	314	66	508	888
MACE	2	1	1	20	22	2	1	1	6	8
MACE/100 PY	0.5	0.3	1.5	0.6	0.6	0.5	0.3	1.5	1.2	0.9
95% CI	[0.1 ; 1.9]	[0.0 ; 1.8]	[0.0 ; 8.4]	[0.4 ; 1]	[0.4 ; 0.9]	[0.1 ; 1.9]	[0 ; 1.8]	[0 ; 8.4]	[0.4 ; 2.6]	[0.4 ; 1.8]
IRD	-0.1					-0.7			.	
IRD 95% CI	[-0.9 ; 0.7]					[-1.9 ; 0.6]				
No concomitant[c] MTX Use, n (%)	726 (57.7)	522 (54.7)	204 (66.9)	3511 (45.0)	4237 (46.7)	724 (57.6)	522 (54.7)	202 (66.7)	610 (48.5)	1334 (53.1)
Person-Years	385	281	104	1815	2201	384	281	103	322	706
MACE	7	4	3	7	14	7	4	3	1	8
MACE/100 PY	1.8	1.4	2.9	0.4	0.6	1.8	1.4	2.9	0.3	1.1
95% CI	[0.7 ; 3.7]	[0.4 ; 3.6]	[0.6 ; 8.4]	[0.2 ; 0.8]	[0.3 ; 1.1]	[0.7 ; 3.8]	[0.4 ; 3.6]	[0.6 ; 8.5]	[0 ; 1.7]	[0.5 ; 2.2]
IRD	1.4					1.5			.	
IRD 95% CI	[0.6 ; 2.3]					[-0.1 ; 3.1]				

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

[a] Matching ratio 1:1 is applied

[b] n=2 subjects were dispensed both baricitinib 4mg and 2mg 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.

Table 6.150. bDMARD-Experienced and bDMARD naïve: Comparative Risk of Incident MACE, matched cohort [SNDS]

	bDMARD-Experienced			bDMARD naïve		
MACE	**TNFi**	**Baricitinib, HR [95% CI]**	**P-value**	**TNFi**	**Baricitinib, HR [95% CI]**	**P-value**
Base Model	Ref	2.65 [1.07 ; 6.56]	0.0354	Ref	1.41 [0.51 ; 3.89]	0.5044
Adjusted – Model [1]	Ref	2.69 [1.09 ; 6.68]	0.0325	Ref	1.39 [0.51 ; 3.77]	0.5216
Methotrexate use during baseline	*Ref*	0.51 [0.20 ; 1.29]	0.1536	Ref	0.65 [0.25 ; 1.68]	0.3782
Adjusted – Model [2]	Ref	2.71 [1.08 ; 6.79]	0.0338	Ref	1.33 [0.48 ; 3.71]	0.5834
Methotrexate use during baseline	*Ref*	0.45 [0.17 ; 1.21]	0.1135	Ref	0.82 [0.30 ; 2.21]	0.6930
Concomitant Glucocorticoid use	*Ref*	1.05 [0.40 ; 2.72]	0.9256	Ref	0.76 [0.24 ; 2.39]	0.6325
Concomitant cDMARD use	*Ref*	1.26 [0.48 ; 3.32]	0.6333	Ref	0.58 [0.20 ; 1.66]	0.3058
Adjusted – Model [3]	Ref	2.68 [1.07 ; 6.71]	0.0347	Ref	1.39 [0.51 ; 3.79]	0.5173
Methotrexate use during baseline	*Ref*	0.51 [0.20 ; 1.28]	0.1507	Ref	0.65 [0.25 ; 1.68]	0.3765
Concomitant Glucocorticoid use	*Ref*	1.05 [0.41 ; 2.72]	0.9202	Ref	0.73 [0.23 ; 2.29]	0.5860
Adjusted – Model [n]	Ref	N/A	N/A	Ref	N/A	N/A

Abbreviations: cDMARD = conventional disease-modifying antirheumatic drug; CI = confidence interval; HR = hazard ratio; Ref = referent group; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke;

Model [1] = propensity score-matched model with outcome and baricitinib exposure, adjusted for any variables that remain unbalanced after PS matching (use of methotrexate during baseline period) .

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.

Models 1-n may include additional variables that remain unbalanced after propensity-score matching as well as concomitant cDMARD or glucocorticoid use separately.

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.

Table 6.151. bDMARD-Experienced and bDMARD naïve: Comparative Risk of Incident MACE, matched cohort [SNDS]

bDMARD-experienced and bDMARD naïve are grouped in the table above

5.4.2 SERIOUS INFECTIONS

Table 6.152. bDMARD-Experienced and bDMARD naïve: Clinical characteristics in patients with serious infection, Serious infection matched cohort [SNDS]

	bDMARD-Experienced				bDMARD naïve			
Characteristics[b]	**Bari. Any n = 19**	**Bari. 4 mg n = 12**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n = 21**	**Bari. Any n = 17**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n = 11**
Age [in years]			-				-	
N	19 (0)	12 (0)		21 (0)	17 (0)	11 (0)		11 (0)
Mean (SD)	65.5 (10.9)	61.0 (9.8)		64.4 (9.2)	69.0 (12.3)	65.4 (12.7)		70.8 (12.1)
Median	67.0	61.5		65.0	70.0	70.0		76.0
Min; Max	[34.0;83.0]	[34.0;73.0]		[43.0;80.0]	[43.0;85.0]	[43.0;79.0]		[47.0;83.0]
Sex, n (%)			-				-	
Female	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10
Male	13 (68.4)	≤ 10		16 (76.2)	11 (64.7)	≤ 10		≤ 10
Clinical conditions during baseline period, n (%)			-				-	
Cancer, excluding NMSC	0 (0.0)	0 (0.0)		0 (0.0)	≤ 10	0 (0.0)		0 (0.0)
NMSC	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)
Chronic lung disease, excluding cystic fibrosis[c]	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10
Cardiovascular conditions								

	bDMARD-Experienced				bDMARD naïve			
Characteristics[b]	**Bari. Any n = 19**	**Bari. 4 mg n = 12**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n = 21**	**Bari. Any n = 17**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n = 11**
Atrial arrhythmia/fibrillation	0 (0.0)	0 (0.0)		0 (0.0)	≤ 10	0 (0.0)		≤ 10
Cardiovascular revascularization	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)
Congestive Heart Failure, hospitalized	≤ 10	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)
Coronary artery disease	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10
Unstable angina	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)
Ventricular arrhythmia	0 (0.0)	0 (0.0)		0 (0.0)	≤ 10	≤ 10		0 (0.0)
Stroke	0 (0.0)	0 (0.0)		≤ 10	0 (0.0)	0 (0.0)		0 (0.0)
Hemorrhagic	0 (0.0)	0 (0.0)		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)	0 (0.0)		0 (0.0)
Unknown	0 (0.0)	0 (0.0)		≤ 10	0 (0.0)	0 (0.0)		0 (0.0)
TIA	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)
Diabetes Mellitus[c]	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10
Treated insulin dependent	N/A	N/A		N/A	N/A	N/A		N/A
Treated non insulin dependent	N/A	N/A		N/A	N/A	N/A		N/A
Dyslipidemia (not available in SNDS)	N/A	N/A		N/A	N/A	N/A		N/A

	bDMARD-Experienced				bDMARD naïve			
Characteristics[b]	**Bari. Any n = 19**	**Bari. 4 mg n = 12**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n = 21**	**Bari. Any n = 17**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n = 11**
Hypertension (not available in SNDS)	N/A	N/A		N/A	N/A	N/A		N/A
History of hypertension								
Current hypertension								
Immune disorders	0 (0.0)	0 (0.0)		≤ 10	0 (0.0)	0 (0.0)		0 (0.0)
AIDS/HIV	0 (0.0)	0 (0.0)		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)	0 (0.0)		0 (0.0)
SLE	0 (0.0)	0 (0.0)		≤ 10	0 (0.0)	0 (0.0)		0 (0.0)
Primary Sjogren Syndrome	0 (0.0)	0 (0.0)		≤ 10	0 (0.0)	0 (0.0)		0 (0.0)
Liver or pancreatic disorder[c]	≤ 10	≤ 10		0 (0.0)	0 (0.0)	0 (0.0)		≤ 10
Obesity (not available in SNDS)	N/A	N/A		N/A	N/A	N/A		
Recent pregnancy	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)
Smoking (not available in SNDS)	N/A	N/A		N/A	N/A	N/A		
Surgery or trauma	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)
Other prescription medications during baseline period, n (%)								
Antibiotics	11 (57.9)	≤ 10		11 (52.4)	≤ 10	≤ 10		≤ 10
Antidiabetic agents	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10
Insulins	≤ 10	0 (0.0)		≤ 10	0 (0.0)	0 (0.0)		≤ 10
Non-insulins	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10
Cardiovascular								
Antithrombotic agents	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10

	bDMARD-Experienced				bDMARD naïve			
Characteristics[b]	**Bari. Any n = 19**	**Bari. 4 mg n = 12**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n = 21**	**Bari. Any n = 17**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n = 11**
Anticoagulant	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10
Antiplatelet	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10
Antihypertensives	13 (68.4)	≤ 10		13 (61.9)	≤ 10	≤ 10		≤ 10
Angiotensin converting enzyme inhibitors (ACE)	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10
Angiotensin receptor blockers (ARB)	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10
Beta blocker	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10
Calcium channel blocker	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10
Nitrates	0 (0.0)	0 (0.0)		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)	0 (0.0)		0 (0.0)
Valacyclovir	≤ 10	≤ 10		≤ 10	0 (0.0)	0 (0.0)		0 (0.0)
Hormonal	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		0 (0.0)
HRT	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		0 (0.0)
Oral Contraceptives	0 (0.0)	0 (0.0)		≤ 10	0 (0.0)	0 (0.0)		0 (0.0)
SERMs	≤ 10	≤ 10		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)
Topic with progestogens and/or estrogens	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)
Lipid-lowering agents	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10
HMG CoA reductase inhibitors	≤ 10	0 (0.0)		≤ 10	≤ 10	≤ 10		≤ 10
Fibrates	≤ 10	≤ 10		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)	0 (0.0)		0 (0.0)

	bDMARD-Experienced				bDMARD naïve			
Characteristics[b]	**Bari. Any n = 19**	**Bari. 4 mg n = 12**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n = 21**	**Bari. Any n = 17**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n = 11**
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)		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)	0 (0.0)		0 (0.0)
Lipid modifying agents, combinations	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)
Rheumatoid arthritis-related								
Aspirin	0 (0.0)	0 (0.0)		≤ 10	0 (0.0)	0 (0.0)		0 (0.0)
Cox-2 Inhibitor	≤ 10	≤ 10		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)
NSAIDs	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10
Glucocorticosteroid	15 (78.9)	≤ 10		17 (81.0)	13 (76.5)	≤ 10		≤ 10
Vaccines	≤ 10	≤ 10		12 (57.1)	≤ 10	≤ 10		≤ 10
Antineoplastic agents	0 (0.0)	0 (0.0)		0 (0.0)	≤ 10	0 (0.0)		0 (0.0)
Post-index Occurrence[d], n (%)			-				-	
Cancer	0 (0.0)	0 (0.0)		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)	0 (0.0)		0 (0.0)
Surgery	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)

Abbreviations: IHD = ischemic heart disease; 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 = tumor necrosis facotr 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] CNAM algorithm based on the year preceding the year of inclusion

Table 6.153. bDMARD-Experienced and bDMARD naïve: Clinical characteristics in patients with serious infection, Serious infection matched cohort [SNDS]

bDMARD-experienced and bDMARD naïve are grouped in the table above

Table 6.154. bDMARD-Experienced: Pattern of RA medication use in patients with serious infection [SNDS]

	Unmatched					Matched				
Characteristics[a]	**Baricitinib n = 27**	**Bari. 4 mg n = 18**	**Bari. 2 mg n ≤ 10**	**TNFi n = 24**	**Total n = 51**	**Baricitinib n = 19**	**Bari. 4 mg n = 12**	**Bari. 2 mg n ≤ 10**	**TNFi[c] n = 21**	**Total n = 40**
Baseline Medication, n (%)								-		
cDMARDs, during baseline period										
n, total (%)	19 (70.4)	13 (72.2)		17 (70.8)	36 (70.6)	14 (73.7)	≤ 10		15 (71.4)	29 (72.5)
Mean (SD)	0.7 (0.5)	0.8 (0.5)		0.8 (0.5)	0.7 (0.5)	0.8 (0.5)	0.8 (0.6)		0.8 (0.5)	0.8 (0.5)
Median	1.0	1.0		1.0	1.0	1.0	1.0		1.0	1.0
Min; Max	[0.0;2.0]	[0.0;2.0]		[0.0;2.0]	[0.0;2.0]	[0.0;2.0]	[0.0;2.0]		[0.0;2.0]	[0.0;2.0]
>1 cDMARD concomitantly	≤ 10	≤ 10		0 (0.0)	≤ 10	≤ 10	≤ 10		0 (0.0)	≤ 10
Hydroxychloroquine	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10	≤ 10		≤ 10	≤ 10
Chloroquine	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Azathioprin	0 (0.0)	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	≤ 10
Methotrexate	12 (44.4)	≤ 10		13 (54.2)	25 (49.0)	≤ 10	≤ 10		11 (52.4)	21 (52.5)
Mycophenolate mofetil	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Sulfasalazin	≤ 10	≤ 10		0 (0.0)	≤ 10	≤ 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)	0 (0.0)
Penicillamin	0 (0.0)	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 (%)	27 (100.0)	18 (100.0)		24 (100.0)	51 (100.0)	19 (100.0)	12 (100.0)		21 (100.0)	40 (100.0)

	Unmatched					Matched				
Characteristics[a]	**Baricitinib n = 27**	**Bari. 4 mg n = 18**	**Bari. 2 mg n ≤ 10**	**TNFi n = 24**	**Total n = 51**	**Baricitinib n = 19**	**Bari. 4 mg n = 12**	**Bari. 2 mg n ≤ 10**	**TNFi[c] n = 21**	**Total n = 40**
Mean (SD)	1.1 (0.3)	1.1 (0.3)		1.1 (0.3)	1.1 (0.3)	1.1 (0.2)	1.1 (0.3)		1.1 (0.4)	1.1 (0.3)
Median	1.0	1.0		1.0	1.0	1.0	1.0		1.0	1.0
Min; Max	[1.0;2.0]	[1.0;2.0]		[1.0;2.0]	[1.0;2.0]	[1.0;2.0]	[1.0;2.0]		[1.0;2.0]	[1.0;2.0]
cDMARDs, concomitant	18 (66.7)	13 (72.2)		15 (62.5)	33 (64.7)	13 (68.4)	≤ 10		14 (66.7)	27 (67.5)
Adalimumab[b]	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10	≤ 10		≤ 10	≤ 10
Certolizumab pegol[b]	≤ 10	≤ 10		0 (0.0)	≤ 10	≤ 10	≤ 10		0 (0.0)	≤ 10
Etanercept[b]	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10	≤ 10		≤ 10	≤ 10
Golimumab[b]	0 (0.0)	0 (0.0)		≤ 10	≤ 10	0 (0.0)	0 (0.0)		≤ 10	≤ 10
Infliximab[b]	≤ 10	≤ 10		0 (0.0)	≤ 10	≤ 10	≤ 10		0 (0.0)	≤ 10
Rituximab	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10	0 (0.0)		≤ 10	≤ 10
Sarilumab	≤ 10	≤ 10		0 (0.0)	≤ 10	≤ 10	≤ 10		0 (0.0)	≤ 10
Abatacept	11 (40.7)	≤ 10		≤ 10	18 (35.3)	≤ 10	≤ 10		≤ 10	15 (37.5)
Tocilizumab	≤ 10	≤ 10		≤ 10	12 (23.5)	≤ 10	≤ 10		≤ 10	≤ 10
Anakinra	≤ 10	0 (0.0)		≤ 10	≤ 10	≤ 10	0 (0.0)		≤ 10	≤ 10
TNFi naïve at baseline	19 (70.4)	11 (61.1)		13 (54.2)	32 (62.7)	13 (68.4)	≤ 10		11 (52.4)	24 (60.0)
≥ 1 dispensing of bDMARD within 730 days before index date (excluded), n (%)	27 (100.0)	18 (100.0)		24 (100.0)	51 (100.0)	19 (100.0)			21 (100.0)	40 (100.0)
Post-index Medication, n (%)								-		
Methotrexate, concomitant	11 (40.7)	≤ 10		12 (50.0)	23 (45.1)	≤ 10	≤ 10		≤ 10	19 (47.5)

Characteristics[a]	Unmatched					Matched				
	Baricitinib n = 27	Bari. 4 mg n = 18	Bari. 2 mg n ≤ 10	TNFi n = 24	Total n = 51	Baricitinib n = 19	Bari. 4 mg n = 12	Bari. 2 mg n ≤ 10	TNFi[c] n = 21	Total n = 40
Other Concomitant cDMARD	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10	≤ 10		≤ 10	≤ 10
Dose change, baricitinib	≤ 10	≤ 10		0 (0.0)	≤ 10	≤ 10	≤ 10		0 (0.0)	≤ 10

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug; N = number of patients in the specified category; TB = tuberculosis; TNFi = tumor 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] TNF inhibitors.

[c] Matching ratio 1:1 is applied

Table 6.155. bDMARD-Naïve: Pattern of RA medication use in patients with serious infection [SNDS]

	Unmatched					Matched				
Characteristics[a]	**Baricitinib n = 17**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi n = 44**	**Total n = 61**	**Baricitinib n = 17**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n = 11**	**Total n = 28**
Baseline Medication, n (%)								-		
cDMARDs, during baseline period										
n, total (%)	≤ 10	≤ 10		36 (81.8)	46 (75.4)	≤ 10	≤ 10		≤ 10	20 (71.4)
Mean (SD)	0.8 (0.8)	1.0 (0.9)		0.9 (0.5)	0.9 (0.6)	0.8 (0.8)	1.0 (0.9)		1.1 (0.7)	0.9 (0.8)
Median	1.0	1.0		1.0	1.0	1.0	1.0		1.0	1.0
Min; Max	[0.0;3.0]	[0.0;3.0]		[0.0;3.0]	[0.0;3.0]	[0.0;3.0]	[0.0;3.0]		[0.0;3.0]	[0.0;3.0]
>1 cDMARD concomitantly	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10	≤ 10		≤ 10	≤ 10
Hydroxychloroquine	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10	≤ 10		≤ 10	≤ 10
Chloroquine	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Azathioprin	0 (0.0)	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	11 (18.0)	≤ 10	≤ 10		≤ 10	≤ 10
Methotrexate	≤ 10	≤ 10		26 (59.1)	33 (54.1)	≤ 10	≤ 10		≤ 10	13 (46.4)
Mycophenolate mofetil	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Sulfasalazin	≤ 10	≤ 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)	0 (0.0)
Penicillamin	0 (0.0)	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 (%)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)

	Unmatched					Matched				
Characteristics[a]	**Baricitinib n = 17**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi n = 44**	**Total n = 61**	**Baricitinib n = 17**	**Bari. 4 mg n = 11**	**Bari. 2 mg n ≤ 10**	**TNFi[a] n = 11**	**Total n = 28**
Mean (SD)	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 (0.0)	0.0 (0.0)
Median	0.0	0.0		0.0	0.0	0.0	0.0		0.0	0.0
Min; Max	[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;0.0]	[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)	0 (0.0)
Adalimumab[b]	0 (0.0)	0 (0.0)		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)		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)		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)		0 (0.0)	0 (0.0)
Infliximab[b]	0 (0.0)	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)	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)	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)	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)	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)	0 (0.0)
TNFi naïve at baseline	17 (100.0)	11 (100.0)		44 (100.0)	61 (100.0)	17 (100.0)	11 (100.0)		11 (100.0)	28 (100.0)
≥ 1 dispensing of bDMARD within 730 days before index date (excluded), n (%)	≤ 10	≤ 10		≤ 10	15 (24.6)	≤ 10	≤ 10		≤ 10	≤ 10
Post-index Medication, n (%)								-		
Methotrexate, concomitant	≤ 10	≤ 10		20 (45.5)	25 (41.0)	≤ 10	≤ 10		≤ 10	≤ 10

Characteristics[a]	Unmatched					Matched				
	Baricitinib n = 17	Bari. 4 mg n = 11	Bari. 2 mg n ≤ 10	TNFi n = 44	Total n = 61	Baricitinib n = 17	Bari. 4 mg n = 11	Bari. 2 mg n ≤ 10	TNFi[a] n = 11	Total n = 28
Other Concomitant cDMARD	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10	≤ 10		≤ 10	≤ 10
Dose change, baricitinib	≤ 10	≤ 10		0 (0.0)	≤ 10	≤ 10	≤ 10		0 (0.0)	≤ 10

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; DMARD = disease-modifying antirheumatic drugs; hosp = hospitalized; HRT = hormone replacement therapy; Max = maximum; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Min = minimum;
mos = months; N = number of patients in the specified category; NMSC = non-melanoma skin cancer;
RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulator; Std. Diff. = standardized difference; TNF = tumor necrosis factor; TNFi = tumor 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.

Table 6.156. bDMARD-Experienced: Time to first serious infection [SNDS]

	Unmatched					Matched				
	Baricitinib n = 27	**Bari. 4 mg n = 18**	**Bari. 2 mg n ≤ 10**	**TNFi n = 24**	**Total n = 51**	**Baricitinib n = 19**	**Bari. 4 mg n = 12**	**Bari. 2 mg n ≤ 10**	**TNFi [a] n = 21**	**Total n = 40**
Time to first serious infection (in days)										
N (missing)	27 (0)	18 (0)		24 (0)	51 (0)	19 (0)	12 (0)		21 (0)	40 (0)
Mean (SD)	213.9 (189.3)	260.7 (210.0)		184.4 (196.8)	200.0 (191.5)	207.4 (181.9)	263.8 (207.6)		185.6 (208.7)	196.0 (194.2)
Median	144.0	180.0		111.5	129.0	144.0	251.5		105.0	125.0
Min; Max	[6.0;628.0]	[10.0;628.0]		[4.0;743.0]	[4.0;743.0]	[10.0;628.0]	[10.0;628.0]		[4.0;743.0]	[4.0;743.0]

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor.

[a] Matching ratio 1:1 is applied

Table 6.157. bDMARD-Naïve: Time to first serious infection [SNDS]

	Unmatched					Matched				
	Baricitinib n = 17	Bari. 4 mg n = 11	Bari. 2 mg n ≤ 10	TNFi n = 44	Total n = 61	Baricitinib n = 17	Bari. 4 mg n = 11	Bari. 2 mg n ≤ 10	TNFi [a] n = 11	Total n = 28
Time to first serious infection (in days)										
N (missing)	17 (0)	11 (0)		44 (0)	61 (0)	17 (0)	11 (0)		11 (0)	28 (0)
Mean (SD)	207.8 (200.1)	234.7 (198.3)		148.9 (142.0)	165.3 (160.7)	207.8 (200.1)	234.7 (198.3)		199.2 (169.9)	204.4 (185.6)
Median	111.0	136.0		124.5	121.0	111.0	136.0		154.0	132.0
Min; Max	[6.0;629.0]	[35.0;629.0]		[1.0;599.0]	[1.0;629.0]	[6.0;629.0]	[35.0;629.0]		[38.0;599.0]	[6.0;629.0]

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor.

[a] Matching ratio 1:1 is applied

Table 6.158. bDMARD-Experienced: Crude rates of first serious infection [SNDS]

	Unmatched					Matched				
SI	**Bari. Any[b] n = 2044**	**Bari. 4 mg n = 1708**	**Bari. 2 mg n = 332**	**TNFi n = 2432**	**Total n = 4476**	**Bari. Any[b] n = 1643**	**Bari. 4 mg n = 1376**	**Bari. 2 mg n = 264**	**TNFi[a] n = 1643**	**Total n = 3286**
Overall										
Person-Years	1384	1167	213	1670	3053	1095	921	173	1137	2232
SI	27	18	9	24	51	19	12	7	21	40
SI/100 PY	2.0	1.5	4.2	1.4	1.7	1.7	1.3	4.1	1.8	1.8
95% CI	[1.3 ; 2.8]	[0.9 ; 2.4]	[1.9 ; 8.0]	[0.9 ; 2.1]	[1.2 ; 2.2]	[1 ; 2.7]	[0.7 ; 2.3]	[1.6 ; 8.4]	[1.1 ; 2.8]	[1.3 ; 2.4]
IRD	0.5					-0.1			.	
IRD 95% CI	[-0.4 ; 1.4]					[-1.2 ; 1]				
Concomitant[b] MTX Use, n (%)	854 (41.8)	739 (43.3)	113 (34.0)	1104 (45.4)	1958 (43.7)	718 (43.7)	620 (45.1)	96 (36.4)	708 (43.1)	1426 (43.4)
Person-Years	648	561	86	872	1520	541	465	75	562	1103
SI	11	7	4	12	23	9	6	3	10	19
SI/100 PY	1.7	1.2	4.7	1.4	1.5	1.7	1.3	4	1.8	1.7
95% CI	[0.8 ; 3.0]	[0.5 ; 2.6]	[1.3 ; 11.9]	[0.7 ; 2.4]	[1 ; 2.3]	[0.8 ; 3.2]	[0.5 ; 2.8]	[0.8 ; 11.7]	[0.9 ; 3.3]	[1 ; 2.7]
IRD	0.3					-0.1			.	
IRD 95% CI	[-0.9 ; 1.6]					[-1.7 ; 1.4]				
No concomitant[b] MTX Use, n (%)	1190 (58.2)	969 (56.7)	219 (66.0)	1328 (54.6)	2518 (56.3)	925 (56.3)	756 (54.9)	168 (63.6)	935 (56.9)	1860 (56.6)
Person-Years	736	606	127	797	1533	554	456	98	575	1129
SI	16	11	5	12	28	10	6	4	11	21
SI/100 PY	2.2	1.8	3.9	1.5	1.8	1.8	1.3	4.1	1.9	1.9
95% CI	[1.2 ; 3.5]	[0.9 ; 3.2]	[1.3 ; 9.2]	[0.8 ; 2.6]	[1.2 ; 2.6]	[0.9 ; 3.3]	[0.5 ; 2.9]	[1.1 ; 10.5]	[1 ; 3.4]	[1.2 ; 2.8]
IRD	0.7					-0.1			.	

	Unmatched					Matched				
	Bari. Any[b]	**Bari. 4 mg**	**Bari. 2 mg**	**TNFi**	**Total**	**Bari. Any[b]**	**Bari. 4 mg**	**Bari. 2 mg**	**TNFi[a]**	**Total**
SI	**n = 2044**	**n = 1708**	**n = 332**	**n = 2432**	**n = 4476**	**n = 1643**	**n = 1376**	**n = 264**	**n = 1643**	**n = 3286**
IRD 95% CI	[-0.7 ; 2]					[-1.7 ; 1.5]				

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

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

[b] 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.

Table 6.159. bDMARD-Naïve: Crude rates of first serious infection [SNDS]

	Unmatched					Matched				
SI	**Bari. Any n = 1322**	**Bari. 4 mg n = 988**	**Bari. 2 mg n = 334**	**TNFi n = 8019**	**Total n = 9341**	**Bari. Any n = 1319**	**Bari. 4 mg n = 985**	**Bari. 2 mg n = 334**	**TNFi[a] n = 1319**	**Total n = 2638**
Overall										
Person-Years	805	618	187	5198	6002	802	615	187	876	1677
SI	17	11	6	44	61	17	11	6	11	28
SI/100 PY	2.1	1.8	3.2	0.8	1	2.1	1.8	3.2	1.3	1.7
95% CI	[1.2 ; 3.4]	[0.9 ; 3.2]	[1.2 ; 7]	[0.6 ; 1.1]	[0.7 ; 1.3]	[1.2 ; 3.4]	[0.9 ; 3.2]	[1.2 ; 7]	[0.6 ; 2.2]	[1.1 ; 2.4]
IRD	1.3			.		0.9			.	
IRD 95% CI	[0.5 ; 2]					[-0.4 ; 2.1]				
Concomitant[b] MTX Use, n (%)	549 (41.5)	442 (44.7)	107 (32.0)	4404 (54.9)	4953 (53.0)	548 (41.5)	441 (44.8)	107 (32.0)	687 (52.1)	1235 (46.8)
Person-Years	388	319	69	3322	3709	387	318	69	545	933
SI	5	4	1	20	25	5	4	1	5	10
SI/100 PY	1.3	1.3	1.4	0.6	0.7	1.3	1.3	1.4	0.9	1.1
95% CI	[0.4 ; 3]	[0.3 ; 3.2]	[0 ; 8.1]	[0.4 ; 0.9]	[0.4 ; 1]	[0.4 ; 3]	[0.3 ; 3.2]	[0 ; 8.1]	[0.3 ; 2.1]	[0.5 ; 2]
IRD	0.7			.		0.4			.	
IRD 95% CI	[-0.2 ; 1.5]					[-1 ; 1.7]				
No concomitant[b] MTX Use, n (%)	773 (58.5)	546 (55.3)	227 (68.0)	3615 (45.1)	4388 (47.0)	771 (58.5)	544 (55.2)	227 (68.0)	632 (47.9)	1403 (53.2)
Person-Years	417	299	118	1876	2293	414	297	118	330	745
SI	12	7	5	24	36	12	7	5	6	18
SI/100 PY	2.9	2.3	4.2	1.3	1.6	2.9	2.4	4.2	1.8	2.4
95% CI	[1.5 ; 5]	[0.9 ; 4.8]	[1.4 ; 9.9]	[0.8 ; 1.9]	[1.1 ; 2.2]	[1.5 ; 5.1]	[0.9 ; 4.9]	[1.4 ; 9.9]	[0.7 ; 4]	[1.4 ; 3.8]
IRD	1.6			.		1.1			.	

	Unmatched					Matched				
	Bari. Any	**Bari. 4 mg**	**Bari. 2 mg**	**TNFi**	**Total**	**Bari. Any**	**Bari. 4 mg**	**Bari. 2 mg**	**TNFi[a]**	**Total**
SI	**n = 1322**	**n = 988**	**n = 334**	**n = 8019**	**n = 9341**	**n = 1319**	**n = 985**	**n = 334**	**n = 1319**	**n = 2638**
IRD 95% CI	[0.3 ; 2.9]					[-1.2 ; 3.3]				

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

[a] Matching ratio 1:1 is applied

[b] 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.

Table 6.160. bDMARD-Experienced: Serious infection per patient during all available follow-up [SNDS]

Number of serious Infections per Person during the follow-up, n (%)	Unmatched			Matched		
	Baricitinib n = 2044	TNFi n = 2432	Total n = 4476	Baricitinib n = 1659	TNFi [a] n = 1659	Total n = 3318
0	2017 (98.7)	2408 (99.0)	4425 (98.9)	1642 (99.0)	1639 (98.8)	3281 (98.9)
1	24 (1.2)	22 (0.9)	46 (1.0)	14 (0.8)	18 (1.1)	32 (1.0)
2	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
3	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 = tumor necrosis factor inhibitor.

[a] Matching ratio 1:1 is applied

Table 6.161. bDMARD-Naïve: Serious infection per patient during all available follow-up [SNDS]

Number of serious Infections per Person during the follow-up, n (%)	Unmatched			Matched		
	Baricitinib n = 1322	TNFi n = 8019	Total n = 9341	Baricitinib n = 1322	TNFi [a] n = 1322	Total n = 2644
0	1305 (98.7)	7975 (99.5)	9280 (99.3)	1305 (98.7)	1312 (99.2)	2617 (99.0)
1	15 (1.1)	41 (0.5)	56 (0.6)	15 (1.1)	≤ 10	24 (0.9)
2	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
3	≤ 10	0 (0.0)	≤ 10	≤ 10	0 (0.0)	≤ 10

Abbreviations: N = number of patients in the specified category; TNFi = tumor necrosis factor inhibitor.

[a] Matching ratio 1:1 is applied

Table 6.162. bDMARD-Experienced and bDMARD naïve: Comparative risk of first serious infection, matched cohort [SNDS]

	bDMARD-Experienced			bDMARD naïve		
Serious infections	**TNFi**	**Baricitinib, HR [95% CI]**	**P-value**	**TNFi**	**Baricitinib, HR [95% CI]**	**P-value**
Base Model	Ref	0.95 [0.51 ; 1.77]	0.8702	Ref	1.68 [0.78 ; 3.62]	0.1809
Adjusted – Model [1]	Ref	0.95 [0.51 ; 1.77]	0.8688	Ref	1.63 [0.76 ; 3.49]	0.2087
Methotrexate use during baseline	*Ref*	1.02 [0.54 ; 1.91]	0.9574	Ref	0.59 [0.28 ; 1.23]	0.1601
Adjusted – Model [2]	Ref	0.97 [0.52 ; 1.81]	0.9207	Ref	1.58 [0.74 ; 3.37]	0.2379
Methotrexate use during baseline	Ref	0.73 [0.33 ; 1.61]	0.4380	Ref	0.7 [0.35 ; 1.41]	0.3189
Concomitant Glucocorticoid use	*Ref*	0.81 [0.39 ; 1.67]	0.5699	Ref	0.61 [0.24 ; 1.53]	0.2921
Concomitant cDMARD use	*Ref*	1.9 [0.87 ; 4.18]	0.1081	Ref	0.67 [0.32 ; 1.37]	0.2692
Adjusted – Model [3]	Ref	0.95 [0.51 ; 1.78]	0.8835	Ref	1.63 [0.76 ; 3.5]	0.2064
Methotrexate use during baseline	*Ref*	1.02 [0.54 ; 1.92]	0.9520	Ref	0.59 [0.28 ; 1.23]	0.1574
Concomitant Glucocorticoid use	*Ref*	0.83 [0.4 ; 1.73]	0.6259	Ref	0.59 [0.24 ; 1.48]	0.2637
Adjusted – Model [n]	Ref	N/A	N/A	Ref	N/A	N/A

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

Model [1] = propensity score-matched model with outcome and baricitinib exposure, adjusted for any variables that remain unbalanced after PS matching (use of methotrexate during baseline period) .

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.

Models 1-n may include additional variables that remain unbalanced after propensity-score matching as well as concomitant cDMARD or glucocorticoid use separately.

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.

Table 6.163. bDMARD-Experienced and bDMARD naïve: Comparative risk of first serious infection, matched cohort [SNDS]

bDMARD-experienced and bDMARD naïve are grouped in the table above

Table 6.164. bDMARD-Experienced and Naïve: Incidence rates of first hospitalized TB [SNDS]

NA for SNDS: no event

6 SENSITIVITY ANALYSES - VTE: POTENTIAL CLASS EFFECTS OF JAK MEDICATIONS

6.1 BASELINE CHARACTERISTICS

Table 6.165. Class Effect: Baseline demographics - Unmatched cohort [SNDS]

Characteristics	JAK n = 5663	TNFi n = 9747	Std. Diff. (Any vs TNFi)
Age at index date [in years]			**0.288**
N (missing)	5663 (0)	9747 (0)	
Mean (SD)	58.8 (13.0)	54.9 (14.2)	
Median	59.0	56.0	
Min; Max	[18.0;92.0]	[18.0;94.0]	
Age (in years), in categories, n (%)			
[18-30[	109 (1.9)	417 (4.3)	
[30-40[	365 (6.4)	1192 (12.2)	
[40-50[	797 (14.1)	1663 (17.1)	
[50-60[	1599 (28.2)	2641 (27.1)	
[60-65[	828 (14.6)	1191 (12.2)	
≥65	1965 (34.7)	2643 (27.1)	
Sex, n (%)			**-0.134**
Male	1171 (20.7)	2567 (26.3)	
Female	4492 (79.3)	7180 (73.7)	

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor.

Table 6.166. Class Effect: Clinical characteristics during baseline period - VTE cohort, Matched [SNDS]

Characteristics	JAK n = 4153	TNFi [a] n = 4153	Std. Diff. (Any vs TNFi)
Age at index date [in years]			0.011
N (missing)	4153 (0)	4153 (0)	
Mean (SD)	58.1 (13.2)	58.0 (13.4)	
Median	59.0	59.0	
Min; Max	[18.0;91.0]	[18.0;94.0]	
Age (in years), in categories, n (%)			
[18-30[	94 (2.3)	102 (2.5)	
[30-40[	304 (7.3)	297 (7.2)	
[40-50[	616 (14.8)	595 (14.3)	
[50-60[	1185 (28.5)	1174 (28.3)	
[60-65[	579 (13.9)	584 (14.1)	
≥65	1375 (33.1)	1401 (33.7)	
Sex, n (%)			-0.013
Male	918 (22.1)	941 (22.7)	
Female	3235 (77.9)	3212 (77.3)	

Abbreviations: N = number of patients in the specified category; Std. Diff = standardized difference; TNFi = tumor necrosis factor inhibitor; VTE = venous thrombotic event, HRT = hormone replacement therapy.

[a] Variable matching ratio 1:1 is applied

Table 6.167. Class Effect: Clinical history at baseline - Unmatched cohort [SNDS]

Characteristics[a]	JAK n = 5663	TNFi n = 9747	Std. Diff. (Any vs TNFi)
Clinical conditions during baseline period, n (%)			
Cancer, excluding NMSC	167 (2.9)	291 (3.0)	-0.002
NMSC	13 (0.2)	21 (0.2)	0.003
Chronic lung disease, excluding cystic fibrosis[c]	769 (13.6)	987 (10.1)	**0.107**
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	52 (0.9)	51 (0.5)	0.047
Cardiovascular revascularization procedure	13 (0.2)	23 (0.2)	-0.001
Congestive Heart Failure, hospitalized	23 (0.4)	29 (0.3)	0.018
Coronary artery disease	233 (4.1)	336 (3.4)	0.035
Unstable angina	≤ 10	15 (0.2)	-0.013
Ventricular arrhythmia	37 (0.7)	63 (0.6)	0.001
Stroke	50 (0.9)	56 (0.6)	0.036
Hemorrhagic	≤ 10	≤ 10	0.008
Ischemic	14 (0.2)	15 (0.2)	0.021
Unknown	38 (0.7)	42 (0.4)	0.032
TIA	≤ 10	≤ 10	0.008
Diabetes Mellitus[c]	599 (10.6)	830 (8.5)	0.070
Treated insulin dependent	N/A	N/A	
Treated non insulin dependent	N/A	N/A	
Dyslipidemia (not available in SNDS)	N/A	N/A	
Hypertension (not available in SNDS)			
History of hypertension	N/A	N/A	

Characteristics[a]	JAK n = 5663	TNFi n = 9747	Std. Diff. (Any vs TNFi)
Current hypertension	N/A	N/A	
Immune disorders	209 (3.7)	269 (2.8)	0.053
AIDS/HIV	≤ 10	11 (0.1)	-0.037
Antiphospholipid syndrome	N/A	N/A	
SLE	51 (0.9)	50 (0.5)	0.046
Primary Sjogren Syndrome	167 (2.9)	216 (2.2)	0.046
Liver or pancreatic disorder[c]	161 (2.8)	239 (2.5)	0.024
Obesity (not available in SNDS)	N/A	N/A	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date)	14 (0.2)	138 (1.4)	**-0.129**
RA Severity (CIRAS Index)			-0.221
Mean (± SD)	6.5 (1.4)	6.8 (1.6)	
Smoking (not available in SNDS)	N/A	N/A	
DMARDs, n (%)			
cDMARDs, during baseline period			
n, total (%)	3779 (66.7)	6993 (71.7)	**-0.109**
Mean (SD)	0.7 (0.6)	0.8 (0.6)	**-0.103**
Median	1.0	1.0	
Min; Max	[0.0;4.0]	[0.0;4.0]	
>1 cDMARD concomitantly	285 (5.0)	549 (5.6)	-0.027
Hydroxychloroquine	289 (5.1)	468 (4.8)	0.014
Chloroquine	≤ 10	≤ 10	-0.008

Characteristics[a]	JAK n = 5663	TNFi n = 9747	Std. Diff. (Any vs TNFi)
Azathioprine	19 (0.3)	33 (0.3)	-0.001
Leflunomide	689 (12.2)	953 (9.8)	0.077
Methotrexate	2962 (52.3)	5843 (59.9)	**-0.155**
Mycophenolate mofetil	≤ 10	≤ 10	0.024
Sulfasalazine	179 (3.2)	418 (4.3)	-0.060
Cyclosporin	≤ 10	≤ 10	0.017
Penicillamine	≤ 10	≤ 10	-0.002
bDMARDs, during baseline period			
n, total (%)	3424 (60.5)	2162 (22.2)	**0.844**
Mean (SD)	0.7 (0.6)	0.2 (0.4)	**0.833**
Median	1.0	0.0	
Min; Max	[0.0;3.0]	[0.0;2.0]	
cDMARDs, concomitant	1873 (33.1)	1200 (12.3)	**0.512**
Adalimumab[b]	419 (7.4)	390 (4.0)	**0.147**
Certolizumab pegol[b]	288 (5.1)	136 (1.4)	**0.210**
Etanercept[b]	678 (12.0)	609 (6.2)	**0.200**
Golimumab[b]	251 (4.4)	138 (1.4)	**0.180**
Infliximab[b]	142 (2.5)	178 (1.8)	0.047
Rituximab	193 (3.4)	33 (0.3)	**0.228**
Sarilumab	68 (1.2)	26 (0.3)	**0.110**
Abatacept	913 (16.1)	424 (4.4)	**0.396**
Tocilizumab	870 (15.4)	325 (3.3)	**0.422**
Anakinra	26 (0.5)	17 (0.2)	0.051

Characteristics[a]	JAK n = 5663		TNFi n = 9747		Std. Diff. (Any vs TNFi)
TNFi naïve at baseline	4001	(70.7)	8316	(85.3)	**-0.360**
JAK at index date	5663	(100.0)	0	(0.0)	-
Tofacitinib	2445	(43.2)	0	(0.0)	-
Baricitinib	3218	(56.8)	0	(0.0)	-
Other prescription medications during baseline period, n (%)					
Antibiotics	2378	(42.0)	3687	(37.8)	0.085
Antidiabetic agents	570	(10.1)	782	(8.0)	0.071
Insulins	229	(4.0)	283	(2.9)	0.062
Non-insulins	456	(8.1)	652	(6.7)	0.052
Cardiovascular					
Antithrombotic agents	866	(15.3)	1336	(13.7)	0.045
Anticoagulant	262	(4.6)	444	(4.6)	0.003
Antiplatelet	652	(11.5)	955	(9.8)	0.056
Antihypertensives	1973	(34.8)	2784	(28.6)	**0.135**
Angiotensin converting enzyme inhibitors (ACE)	536	(9.5)	784	(8.0)	0.050
Angiotensin receptor blockers (ARB)	751	(13.3)	1138	(11.7)	0.048
Beta blocker	825	(14.6)	1139	(11.7)	0.085
Calcium channel blocker	578	(10.2)	778	(8.0)	0.077
Nitrates	53	(0.9)	84	(0.9)	0.008
Acyclovir	29	(0.5)	55	(0.6)	-0.007
Valacyclovir	204	(3.6)	297	(3.0)	0.031
Hormonal	727	(12.8)	1424	(14.6)	-0.052

Characteristics[a]	JAK n = 5663		TNFi n = 9747		Std. Diff. (Any vs TNFi)
HRT	428	(7.6)	648	(6.6)	0.035
Oral Contraceptives	287	(5.1)	739	(7.6)	**-0.103**
SERMs	21	(0.4)	33	(0.3)	0.005
Topic with progestogens and/or estrogens	13	(0.2)	54	(0.6)	-0.052
Lipid-lowering agents	945	(16.7)	1321	(13.6)	0.088
HMG CoA reductase inhibitors	774	(13.7)	1065	(10.9)	0.084
Fibrates	72	(1.3)	109	(1.1)	0.014
Bile acid sequestrants	23	(0.4)	31	(0.3)	0.015
Nicotinic acid and derivatives	0	(0.0)	0	(0.0)	0.000
Other lipid modifying agents	43	(0.8)	87	(0.9)	-0.015
Lipid modifying agents, combinations	75	(1.3)	97	(1.0)	0.031
Rheumatoid arthritis-related					
Aspirin	77	(1.4)	113	(1.2)	0.018
Cox-2 Inhibitor	309	(5.5)	608	(6.2)	-0.033
NSAIDs	2068	(36.5)	3991	(40.9)	-0.091
Glucocorticosteroid	4115	(72.7)	6383	(65.5)	**0.156**
Vaccines	1689	(29.8)	3645	(37.4)	**-0.161**
Antineoplastic agents	18	(0.3)	24	(0.2)	0.014

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; cDMARD = classical disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; Chronic lung disease =asthma, chronic obstructive lung disease, interstitial lung disease, pulmonary fibrosis; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; JAKi = Janus kinase inhibitor; 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. = standard difference; TIA = transient ischemic attack; TNFi = tumor 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] TNF inhibitors

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

Table 6.168. Class Effect: Clinical characteristics during baseline period - VTE cohort, Matched [SNDS]

Characteristics[b]	JAK n = 4153	TNFi[a] n = 4153	Std. Diff. (Any vs TNFi)
Clinical conditions during baseline period, n (%)			
Cancer, excluding NMSC	126 (3.0)	124 (3.0)	0.003
NMSC	≤ 10	≤ 10	0.011
Chronic lung disease, excluding cystic fibrosis[d]	562 (13.5)	471 (11.3)	0.066
Cardiovascular conditions			
Atrial arrhythmia/fibrillation	35 (0.8)	31 (0.7)	0.011
Cardiovascular revascularization procedure	≤ 10	≤ 10	0
Congestive Heart Failure, hospitalized	19 (0.5)	19 (0.5)	0
Coronary artery disease	187 (4.5)	163 (3.9)	0.029
Unstable angina	≤ 10	≤ 10	-0.024
Ventricular arrhythmia	26 (0.6)	32 (0.8)	-0.017
Stroke	32 (0.8)	30 (0.7)	0.006
Hemorrhagic	≤ 10	≤ 10	-0.025
Ischemic	≤ 10	≤ 10	0.017
Unknown	24 (0.6)	21 (0.5)	0.01
TIA	≤ 10	≤ 10	0
Diabetes Mellitus[d]	403 (9.7)	401 (9.7)	0.002
Treated insulin dependent	N/A	N/A	
Treated non insulin dependent	N/A	N/A	
Dyslipidemia (not available in SNDS)	N/A	N/A	
Hypertension (not available in SNDS)			
History of hypertension	N/A	N/A	

Characteristics[b]	JAK n = 4153	TNFi[a] n = 4153	Std. Diff. (Any vs TNFi)
Current hypertension	N/A	N/A	
Immune disorders	137 (3.3)	147 (3.5)	-0.013
AIDS/HIV	≤ 10	≤ 10	-0.03
Antiphospholipid syndrome	N/A	N/A	
SLE	38 (0.9)	20 (0.5)	0.052
Primary Sjogren Syndrome	104 (2.5)	125 (3.0)	-0.031
Liver or pancreatic disorder[d]	103 (2.5)	119 (2.9)	-0.024
Obesity (not available in SNDS)	N/A	N/A	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date)	14 (0.3)	18 (0.4)	-0.016
RA Severity (CIRAS Index)			0.005
Mean (± SD)	6.5 (1.4)	6.5 (1.5)	
Smoking (not available in SNDS)	N/A	N/A	
DMARDs, n (%)			
cDMARDs, during baseline period			
n, total (%)	2875 (69.2)	2831 (68.2)	0.023
Mean (SD)	0.8 (0.6)	0.7 (0.6)	0.045
Median	1.0	1.0	
Min; Max	[0.0;4.0]	[0.0;4.0]	
>1 cDMARD concomitantly	237 (5.7)	189 (4.6)	0.052
Hydroxychloroquine	232 (5.6)	190 (4.6)	0.046
Chloroquine	≤ 10	≤ 10	-0.022
Azathioprin	≤ 10	17 (0.4)	-0.03

Characteristics[b]	JAK n = 4153	TNFi[a] n = 4153	Std. Diff. (Any vs TNFi)
Leflunomid	501 (12.1)	437 (10.5)	0.049
Methotrexate	2298 (55.3)	2278 (54.9)	0.01
Mycophenolate mofetil	≤ 10	≤ 10	0.013
Sulfasalazin	149 (3.6)	156 (3.8)	-0.009
Cyclosporin	≤ 10	≤ 10	0
Penicillamin	≤ 10	≤ 10	-0.013
bDMARDs, during baseline period			
n, total (%)	1915 (46.1)	1924 (46.3)	-0.004
Mean (SD)	0.5 (0.6)	0.5 (0.6)	-0.006
Median	0.0	0.0	
Min; Max	[0.0;3.0]	[0.0;2.0]	
cDMARDs, concomitant	1124 (27.1)	1064 (25.6)	0.033
Adalimumab[c]	288 (6.9)	305 (7.3)	-0.016
Certolizumab pegol[c]	135 (3.3)	130 (3.1)	0.007
Etanercept[c]	499 (12.0)	535 (12.9)	-0.026
Golimumab[c]	130 (3.1)	136 (3.3)	-0.008
Infliximab[c]	109 (2.6)	118 (2.8)	-0.013
Rituximab	45 (1.1)	33 (0.8)	0.03
Sarilumab	27 (0.7)	25 (0.6)	0.006
Abatacept	415 (10.0)	417 (10.0)	-0.002
Tocilizumab	347 (8.4)	323 (7.8)	0.021
Anakinra	20 (0.5)	16 (0.4)	0.015
TNFi naïve at baseline	3025 (72.8)	2949 (71.0)	0.041

Characteristics[b]	JAK n = 4153		TNFi[a] n = 4153		Std. Diff. (Any vs TNFi)
JAK at index date	4153	(100.0)	0	(0.0)	
Tofacitinib	1814	(43.7)	0	(0.0)	
Baricitinib	2339	(56.3)	0	(0.0)	
Other prescription medications during baseline period, n (%)					
Antibiotics	1701	(41.0)	1645	(39.6)	0.028
Antidiabetic agents	381	(9.2)	384	(9.2)	-0.003
Insulins	152	(3.7)	134	(3.2)	0.024
Non-insulins	309	(7.4)	321	(7.7)	-0.011
Cardiovascular					
Antithrombotic agents	624	(15.0)	632	(15.2)	-0.005
Anticoagulant	190	(4.6)	186	(4.5)	0.005
Antiplatelet	471	(11.3)	470	(11.3)	0.001
Antihypertensives	1402	(33.8)	1400	(33.7)	0.001
Angiotensin converting enzyme inhibitors (ACE)	388	(9.3)	398	(9.6)	-0.008
Angiotensin receptor blockers (ARB)	543	(13.1)	569	(13.7)	-0.018
Beta blocker	586	(14.1)	584	(14.1)	0.001
Calcium channel blocker	399	(9.6)	406	(9.8)	-0.006
Nitrates	39	(0.9)	53	(1.3)	-0.032
Acyclovir	20	(0.5)	25	(0.6)	-0.016
Valacyclovir	137	(3.3)	142	(3.4)	-0.007
Hormonal	543	(13.1)	538	(13.0)	0.004
HRT	311	(7.5)	298	(7.2)	0.012

Characteristics[b]	JAK n = 4153		TNFi[a] n = 4153		Std. Diff. (Any vs TNFi)
Oral Contraceptives	226	(5.4)	224	(5.4)	0.002
SERMs	15	(0.4)	11	(0.3)	0.017
Topic with progestogens and/or estrogens	≤ 10		19	(0.5)	-0.047
Lipid-lowering agents	666	(16.0)	658	(15.8)	0.005
HMG CoA reductase inhibitors	543	(13.1)	535	(12.9)	0.006
Fibrates	47	(1.1)	50	(1.2)	-0.007
Bile acid sequestrants	19	(0.5)	18	(0.4)	0.004
Nicotinic acid and derivatives	0	(0.0)	0	(0.0)	0
Other lipid modifying agents	28	(0.7)	43	(1.0)	-0.039
Lipid modifying agents, combinations	59	(1.4)	47	(1.1)	0.026
Rheumatoid arthritis-related					
Aspirin	53	(1.3)	58	(1.4)	-0.011
Cox-2 Inhibitor	218	(5.2)	263	(6.3)	-0.046
NSAIDs	1535	(37.0)	1636	(39.4)	-0.05
Glucocorticosteroid	2905	(69.9)	2912	(70.1)	-0.004
Vaccines	1329	(32.0)	1310	(31.5)	0.01
Antineoplastic agents	13	(0.3)	14	(0.3)	-0.004

Abbreviations: AIDS = acquired immunodeficiency syndrome; bDMARD = biologic disease-modifying antirheumatic drugs; CIRAS = claims-based index for RA severity; cDMARD = classical disease-modifying antirheumatic drugs; Concom. cDMARDs = concomitant cDMARDs; Chronic lung disease =asthma, chronic obstructive lung disease, interstitial lung disease, pulmonary fibrosis; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; JAKi = Janus kinase inhibitor; 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. = standard difference; TIA = transient ischemic attack; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Variable 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] TNF inhibitors.

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

Table 6.169. Class Effect: Baseline healthcare resource utilization during baseline period - Unmatched cohort [SNDS]

Type of resource use during baseline period[a]	JAK n = 5663	TNFi n = 9747	Std. Diff. (Any vs TNFi)
Physician Office Visits (rheumatologist visits excluded)			
n, patients (%)	3425 (60.5)	6128 (62.9)	-0.049
n, events	9634	19306	
Mean (SD)	1.7 (2.5)	2.0 (3.1)	-0.099
Median	1.0	1.0	
Min; Max	[0.0;41.0]	[0.0;85.0]	
Rheumatologist Visits			
n, patients (%)	3498 (61.8)	6203 (63.6)	-0.039
n, events	7764	13993	
Mean (SD)	1.4 (1.5)	1.4 (1.5)	-0.043
Median	1.0	1.0	
Min; Max	[0.0;11.0]	[0.0;13.0]	
Other Outpatient Visits			
n, patients (%)	5295 (93.5)	8885 (91.2)	0.088
n, events	109686	149027	
Mean (SD)	19.4 (32.8)	15.3 (26.2)	**0.137**
Median	8.0	6.0	
Min; Max	[0.0;322.0]	[0.0;283.0]	
Inpatient Visits[b]			
n, patients (%)	2716 (48.0)	4574 (46.9)	0.021
n, events	6738	7767	

Type of resource use during baseline period[a]	JAK n = 5663	TNFi n = 9747	Std. Diff. (Any vs TNFi)
Mean (SD)	1.2 (2.1)	0.8 (1.6)	**0.212**
Median	0.0	0.0	
Min; Max	[0.0;74.0]	[0.0;76.0]	
ED Visits	N/A	N/A	
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 = standardized difference; TNFi = tumor necrosis factor inhibitor JAKi = Janus kinase inhibitor

Note: Physician office visits do not include rheumatologist visits.

[a] Index date excluded

[b] Inpatient visits include number of hospitalisations

Table 6.170. Class Effect: Baseline healthcare resource utilization during baseline period - VTE cohort, Matched [SNDS]

Type of resource use during baseline period[b]	JAK n = 4153	TNFi [a] n = 4143	Std. Diff. (Any vs TNFi)
Physician Office Visits (rheumatologist visits excluded)			
n, patients (%)	2548 (61.4)	2536 (61.1)	0.006
n, events	7283.0	7394.0	
Mean (SD)	1.8 (2.6)	1.8 (2.8)	-0.010
Median	1.0	1.0	
Min; Max	[0.0;41.0]	[0.0;49.0]	
Rheumatologist Visits			
n, patients (%)	2605 (62.7)	2654 (63.9)	-0.025
n, events	5716.0	5958.0	
Mean (SD)	1.4 (1.5)	1.4 (1.5)	-0.039
Median	1.0	1.0	
Min; Max	[0.0;9.0]	[0.0;13.0]	
Other Outpatient Visits			
n, patients (%)	3862 (93.0)	3815 (91.9)	0.043
n, events	76661.0	68955.0	
Mean (SD)	18.5 (31.4)	16.6 (28.1)	0.062
Median	7.0	7.0	
Min; Max	[0.0;266.0]	[0.0;280.0]	
Inpatient Visits[c]			
n, patients (%)	1868 (45.0)	1838 (44.3)	0.015
n, events	3964.0	3796.0	

Type of resource use during baseline period[b]	JAK n = 4153	TNFi [a] n = 4143	Std. Diff. (Any vs TNFi)
Mean (SD)	1.0 (1.9)	0.9 (1.9)	0.021
Median	0.0	0.0	
Min; Max	[0.0;74.0]	[0.0;76.0]	
ED Visits	N/A	N/A	
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 = standardized difference; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism JAKi = Janus kinase inhibitor

Note: Physician office visits do not include rheumatologist visits.

[a] Variable matching ratio 1:1 is applied

[b] Index date excluded

[c] Inpatient visits include number of hospitalisations

Table 6.171. Class Effect: Baseline Prevalence of Outcomes [SNDS]

Prevalence of outcome at baseline in each concerned cohort[a]	Unmatched		
	JAK	TNFi	Std. Diff. (Any vs TNFi)
VTE, N population	5668	9756	
VTE, n events (%)	≤ 10	≤ 10	-0.001

Abbreviations: JAKi = Janus kinase inhibitor; 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 = standard difference; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism, defined based on the case definitions.

[a] Baseline prevalence was calculated only for unmatched VTE cohort

6.2 CHARACTERISTICS OF PATIENTS UNDER FOLLOW-UP

Table 6.172. Class Effect: Duration of follow-up period - Unmatched cohort [SNDS]

	JAK n = 5663	TNFi n = 9747	Std. Diff. (Any vs TNFi)
Duration of follow-up period (in days)			
N (missing)	5663 (0)	9747 (0)	
Mean (SD)	230.5 (187.3)	243.0 (207.2)	-0.063
Median	172.0	172.0	
Min; Max	[0.0;831.0]	[0.0;851.0]	
Reason for censoring, n (%)			
Switch	879 (15.5)	1261 (12.9)	0.074
Discontinuation	2025 (35.8)	4511 (46.3)	-0.215
Outcome	36 (0.6)	29 (0.3)	0.050
Death	21 (0.4)	15 (0.2)	0.042
End of study (31/12/2019)	2702 (47.7)	3931 (40.3)	0.149

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor JAKi = Janus kinase inhibitor

Table 6.173. Class Effect: Duration of follow-up period (in days) - VTE cohort, Matched [SNDS]

	JAK n = 4153	TNFi [a] n = 4153	Std. Diff. (Any vs TNFi)
Duration of follow-up period (in days)			
N (missing)	4153 (0)	4153 (0)	
Mean (SD)	225.7 (185.6)	247.0 (208.0)	-0.108
Median	168.0	175.0	
Min; Max	[0.0;831.0]	[0.0;851.0]	
Reason for censoring, n (%)			
Switch	566 (13.6)	642 (15.5)	-0.052
Discontinuation	1520 (36.6)	1844 (44.4)	-0.159
Outcome	28 (0.7)	14 (0.3)	0.048
Death	15 (0.4)	≤ 10	0.022
End of study (31/12/2019)	2024 (48.7)	1643 (39.6)	0.186

Abbreviations: Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor; VTE = venous thrombotic event JAKi = Janus kinase inhibitor

[a] Variable matching ratio 1:1 is applied

6.3 CHARACTERISTICS OF PATIENTS BY EXPOSURE DURATION

6.3.1 BASELINE CHARACTERISTICS BY EXPOSURE DURATION

Table 6.174. Class Effect: Baseline characteristics by exposure duration, Unmatched cohort [SNDS]

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	JAK n = 2966	TNFi n = 5082		JAK n = 1450	TNFi n = 2417		JAK n = 1165	TNFi n = 1871		JAK n = 82	TNFi n = 377	Std. Diff.
Age [in years]			0.308			0.308			0.229			0.119
N (missing)	2966 (0)	5082 (0)		1450 (0)	2417 (0)		1165 (0)	1871 (0)		82 (0)	377 (0)	
Mean (SD)	58.6 (13.5)	54.3 (14.4)		59.5 (12.6)	55.4 (14.1)		58.6 (12.1)	55.6 (13.8)		58.2 (11.6)	56.7 (13.0)	
Median	59.0	55.0		60.0	56.0		59.0	57.0		60.0	57.0	
Min; Max	[18.0;91.0]	[18.0;94.0]		[18.0;89.0]	[18.0;91.0]		[19.0;92.0]	[18.0;93.0]		[30.0;77.0]	[19.0;84.0]	
Sex, n (%)			-0.158			-0.157			-0.045			-0.091
Male	566 (19.1)	1303 (25.6)		305 (21.0)	671 (27.8)		280 (24.0)	486 (26.0)		20 (24.4)	107 (28.4)	
Female	2400 (80.9)	3779 (74.4)		1145 (79.0)	1746 (72.2)		885 (76.0)	1385 (74.0)		62 (75.6)	270 (71.6)	
Clinical conditions during baseline period, n (%)												
Cancer, excluding NMSC	92 (3.1)	140 (2.8)	0.021	42 (2.9)	80 (3.3)	-0.024	31 (2.7)	61 (3.3)	-0.035	≤ 10	≤ 10	-0.014
NMSC	≤ 10	≤ 10	-0.007	≤ 10	≤ 10	0.048	0 (0.0)	≤ 10	-0.066	0 (0.0)	≤ 10	-0.073
Chronic lung disease, excluding cystic fibrosis[c]	434 (14.6)	510 (10.0)	0.140	189 (13.0)	271 (11.2)	0.056	138 (11.8)	169 (9.0)	0.092	≤ 10	37 (9.8)	-0.002
Cardiovascular conditions												

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	JAK n = 2966	TNFi n = 5082		JAK n = 1450	TNFi n = 2417		JAK n = 1165	TNFi n = 1871		JAK n = 82	TNFi n = 377	Std. Diff.
Atrial arrhythmia/fibrillation	31 (1.0)	27 (0.5)	0.058	11 (0.8)	11 (0.5)	0.039	≤ 10	12 (0.6)	0.025	0 (0.0)	≤ 10	-0.073
Cardiovascular revascularization	≤ 10	14 (0.3)	-0.015	≤ 10	≤ 10	-0.025	≤ 10	≤ 10	0.050	0 (0.0)	0 (0.0)	0.000
Congestive Heart Failure, hospitalized	15 (0.5)	16 (0.3)	0.030	≤ 10	≤ 10	-0.010	≤ 10	≤ 10	0.014	0 (0.0)	0 (0.0)	0.000
Coronary artery disease	116 (3.9)	170 (3.3)	0.030	65 (4.5)	91 (3.8)	0.036	47 (4.0)	63 (3.4)	0.035	≤ 10	12 (3.2)	0.139
Unstable angina	≤ 10	≤ 10	-0.001	≤ 10	≤ 10	-0.007	0 (0.0)	≤ 10	-0.066	0 (0.0)	0 (0.0)	0.000
Ventricular arrhythmia	21 (0.7)	36 (0.7)	0.000	≤ 10	11 (0.5)	0.004	≤ 10	13 (0.7)	0.009	0 (0.0)	≤ 10	-0.127
Stroke	25 (0.8)	26 (0.5)	0.040	16 (1.1)	16 (0.7)	0.047	≤ 10	12 (0.6)	0.016	0 (0.0)	≤ 10	-0.103
Hemorrhagic	≤ 10	≤ 10	0.023	≤ 10	≤ 10	0.004	0 (0.0)	≤ 10	-0.033	0 (0.0)	0 (0.0)	0.000
Ischemic	≤ 10	≤ 10	0.006	≤ 10	≤ 10	0.056	≤ 10	≤ 10	0.003	0 (0.0)	0 (0.0)	0.000
Unknown	18 (0.6)	18 (0.4)	0.037	12 (0.8)	12 (0.5)	0.041	≤ 10	≤ 10	0.020	0 (0.0)	≤ 10	-0.103
TIA	≤ 10	≤ 10	-0.011	≤ 10	0 (0.0)	0.053	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Diabetes Mellitus[c]	310 (10.5)	443 (8.7)	0.059	156 (10.8)	212 (8.8)	0.067	125 (10.7)	145 (7.7)	0.103	≤ 10	30 (8.0)	0.063
Treated insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Treated non insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Dyslipidemia (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	JAK n = 2966	TNFi n = 5082		JAK n = 1450	TNFi n = 2417		JAK n = 1165	TNFi n = 1871		JAK n = 82	TNFi n = 377	Std. Diff.
Hypertension (not available in SNDS)												
History of hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Current hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Immune disorders	128 (4.3)	152 (3.0)	0.071	40 (2.8)	63 (2.6)	0.009	39 (3.3)	44 (2.4)	0.060	≤ 10	≤ 10	-0.014
AIDS/HIV	0 (0.0)	≤ 10	-0.053	0 (0.0)	≤ 10	-0.029	≤ 10	≤ 10	-0.007	0 (0.0)	≤ 10	-0.073
Antiphospholipid syndrome	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
SLE	36 (1.2)	34 (0.7)	0.056	≤ 10	≤ 10	0.021	≤ 10	≤ 10	0.052	≤ 10	≤ 10	0.042
Primary Sjogren Syndrome	99 (3.3)	117 (2.3)	0.063	36 (2.5)	56 (2.3)	0.011	31 (2.7)	37 (2.0)	0.045	≤ 10	≤ 10	-0.032
Liver or pancreatic disorder[c]	79 (2.7)	117 (2.3)	0.023	44 (3.0)	69 (2.9)	0.011	35 (3.0)	47 (2.5)	0.030	≤ 10	≤ 10	0.130
Obesity (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date)	≤ 10	73 (1.4)	-0.137	≤ 10	36 (1.5)	-0.12	≤ 10	26 (1.4)	-0.126	0 (0.0)	≤ 10	-0.127
RA Severity (CIRAS Index)			-0.178			-0.275			-0.271			-0.159
Mean (SD)	6.5 (1.4)	6.7 (1.6)		6.4 (1.3)	6.8 (1.6)		6.5 (1.4)	6.9 (1.5)		6.6 (1.3)	6.8 (1.5)	
DMARDs, n (%)												

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	JAK n = 2966	TNFi n = 5082		JAK n = 1450	TNFi n = 2417		JAK n = 1165	TNFi n = 1871		JAK n = 82	TNFi n = 377	Std. Diff.
cDMARDs, during baseline period												
n, total (%)	1897 (64.0)	3429 (67.5)	-0.074	1005 (69.3)	1806 (74.7)	-0.121	818 (70.2)	1453 (77.7)	-0.17	59 (72.0)	305 (80.9)	-0.212
Mean (SD)	0.7 (0.6)	0.7 (0.6)	-0.074	0.8 (0.6)	0.8 (0.6)	-0.114	0.8 (0.6)	0.9 (0.6)	-0.157	0.9 (0.7)	0.9 (0.5)	-0.053
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	
Min; Max	[0.0;3.0]	[0.0;4.0]		[0.0;3.0]	[0.0;4.0]		[0.0;4.0]	[0.0;3.0]		[0.0;3.0]	[0.0;3.0]	
>1 cDMARD concomitantly	143 (4.8)	244 (4.8)	0.001	75 (5.2)	138 (5.7)	-0.024	60 (5.2)	133 (7.1)	-0.082	≤ 10	34 (9.0)	-0.017
Hydroxychloroquine	140 (4.7)	232 (4.6)	0.007	80 (5.5)	110 (4.6)	0.044	61 (5.2)	101 (5.4)	-0.007	≤ 10	25 (6.6)	0.114
Chloroquine	0 (0.0)	≤ 10	-0.034	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	≤ 10	0 (0.0)	0.157
Azathioprin	≤ 10	16 (0.3)	-0.002	≤ 10	≤ 10	-0.005	≤ 10	≤ 10	-0.014	≤ 10	0 (0.0)	0.157
Leflunomide	369 (12.4)	496 (9.8)	0.085	177 (12.2)	227 (9.4)	0.091	128 (11.0)	191 (10.2)	0.025	15 (18.3)	39 (10.3)	0.228
Methotrexate	1468 (49.5)	2824 (55.6)	-0.122	791 (54.6)	1537 (63.6)	-0.185	663 (56.9)	1219 (65.2)	-0.17	40 (48.8)	263 (69.8)	-0.437
Mycophenolate mofetil	≤ 10	≤ 10	0.023	≤ 10	≤ 10	0.012	≤ 10	0 (0.0)	0.042	0 (0.0)	0 (0.0)	0.000
Sulfasalazin	86 (2.9)	208 (4.1)	-0.065	44 (3.0)	103 (4.3)	-0.066	43 (3.7)	95 (5.1)	-0.068	≤ 10	12 (3.2)	0.186
Cyclosporin	≤ 10	≤ 10	0.023	0 (0.0)	0 (0.0)	0.000	≤ 10	≤ 10	0.012	0 (0.0)	0 (0.0)	0.000
Penicillamin	≤ 10	0 (0.0)	0.026	0 (0.0)	≤ 10	-0.029	0 (0.0)	≤ 10	-0.033	0 (0.0)	0 (0.0)	0.000
bDMARDs, during baseline period												
n, total (%)	1732 (58.4)	1071 (21.1)	0.825	860 (59.3)	560 (23.2)	0.789	776 (66.6)	427 (22.8)	0.981	56 (68.3)	104 (27.6)	0.892
Mean (SD)	0.7 (0.6)	0.2 (0.4)	0.815	0.7 (0.6)	0.2 (0.5)	0.777	0.7 (0.6)	0.2 (0.4)	0.967	0.8 (0.7)	0.3 (0.5)	0.923
Median	1.0	0.0		1.0	0.0		1.0	0.0		1.0	0.0	
Min; Max	[0.0;3.0]	[0.0;2.0]		[0.0;3.0]	[0.0;2.0]		[0.0;3.0]	[0.0;2.0]		[0.0;2.0]	[0.0;2.0]	

Characteristics[a]	<6 mos				6 mos to <12 mos				12 mos to <24 mos				≥24 mos			
	JAK n = 2966		TNFi n = 5082		JAK n = 1450		TNFi n = 2417		JAK n = 1165		TNFi n = 1871		JAK n = 82		TNFi n = 377	Std. Diff.
cDMARDs, concomitant	898	(30.3)	558	(11.0)	0.491	493	(34.0)	319	(13.2)	0.505	449	(38.5)	253	(13.5)	0.595	33 (40.2)	70 (18.6)	0.490
Adalimumab[b]	211	(7.1)	184	(3.6)	0.156	102	(7.0)	102	(4.2)	0.122	98	(8.4)	74	(4.0)	0.186	≤ 10	30 (8.0)	0.063
Certolizumab pegol[b]	148	(5.0)	66	(1.3)	0.213	76	(5.2)	36	(1.5)	0.209	56	(4.8)	25	(1.3)	0.202	≤ 10	≤ 10	0.312
Etanercept[b]	365	(12.3)	314	(6.2)	0.213	165	(11.4)	156	(6.5)	0.174	144	(12.4)	114	(6.1)	0.218	≤ 10	25 (6.6)	-0.075
Golimumab[b]	134	(4.5)	74	(1.5)	0.181	59	(4.1)	27	(1.1)	0.187	55	(4.7)	28	(1.5)	0.187	≤ 10	≤ 10	0.074
Infliximab[b]	71	(2.4)	92	(1.8)	0.041	39	(2.7)	42	(1.7)	0.065	30	(2.6)	34	(1.8)	0.052	≤ 10	≤ 10	-0.014
Rituximab	87	(2.9)	15	(0.3)	0.211	49	(3.4)	13	(0.5)	0.206	46	(3.9)	≤ 10		0.275	11 (13.4)	≤ 10	0.507
Sarilumab	50	(1.7)	17	(0.3)	0.135	18	(1.2)	≤ 10		0.097	0	(0.0)	0	(0.0)	0	0 (0.0)	0 (0.0)	0.000
Abatacept	435	(14.7)	199	(3.9)	0.377	247	(17.0)	117	(4.8)	0.398	213	(18.3)	96	(5.1)	0.418	18 (22.0)	12 (3.2)	0.59
Tocilizumab	423	(14.3)	157	(3.1)	0.405	215	(14.8)	88	(3.6)	0.394	218	(18.7)	68	(3.6)	0.493	14 (17.1)	12 (3.2)	0.473
Anakinra	14	(0.5)	≤ 10		0.061	≤ 10		≤ 10		0.021	≤ 10		≤ 10		0.061	0 (0.0)	0 (0.0)	0
TNFi naïve at baseline	2095	(70.6)	4363	(85.9)	-0.375	1042	(71.9)	2058	(85.1)	-0.328	804	(69.0)	1598	(85.4)	-0.399	60 (73.2)	297 (78.8)	-0.132
Other prescription medications during baseline period, n (%)																		
Antibiotics	1232	(41.5)	1921	(37.8)	0.077	608	(41.9)	966	(40.0)	0.04	503	(43.2)	692	(37.0)	0.127	35 (42.7)	108 (28.6)	0.296
Antidiabetic agents	293	(9.9)	414	(8.1)	0.061	148	(10.2)	192	(7.9)	0.079	119	(10.2)	144	(7.7)	0.088	≤ 10	32 (8.5)	0.122
Insulins	131	(4.4)	166	(3.3)	0.060	54	(3.7)	61	(2.5)	0.069	41	(3.5)	45	(2.4)	0.066	≤ 10	11 (2.9)	0.042
Non-insulins	220	(7.4)	339	(6.7)	0.029	128	(8.8)	165	(6.8)	0.075	99	(8.5)	120	(6.4)	0.079	≤ 10	28 (7.4)	0.123
Cardiovascular																		

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	JAK n = 2966	TNFi n = 5082		JAK n = 1450	TNFi n = 2417		JAK n = 1165	TNFi n = 1871		JAK n = 82	TNFi n = 377	Std. Diff.
Antithrombotic agents	446 (15.0)	711 (14.0)	0.03	227 (15.7)	326 (13.5)	0.062	174 (14.9)	236 (12.6)	0.067	19 (23.2)	63 (16.7)	0.162
Anticoagulant	145 (4.9)	240 (4.7)	0.008	65 (4.5)	105 (4.3)	0.007	49 (4.2)	73 (3.9)	0.015	≤ 10	26 (6.9)	-0.145
Antiplatelet	333 (11.2)	509 (10.0)	0.039	173 (11.9)	233 (9.6)	0.074	129 (11.1)	170 (9.1)	0.066	17 (20.7)	43 (11.4)	0.256
Antihypertensives	996 (33.6)	1426 (28.1)	0.120	529 (36.5)	690 (28.5)	0.17	411 (35.3)	564 (30.1)	0.110	37 (45.1)	104 (27.6)	0.371
Angiotensin converting enzyme inhibitors (ACE)	262 (8.8)	427 (8.4)	0.015	148 (10.2)	187 (7.7)	0.087	113 (9.7)	142 (7.6)	0.075	13 (15.9)	28 (7.4)	0.265
Angiotensin receptor blockers (ARB)	397 (13.4)	552 (10.9)	0.077	196 (13.5)	303 (12.5)	0.029	150 (12.9)	239 (12.8)	0.003	≤ 10	44 (11.7)	-0.062
Beta blocker	421 (14.2)	589 (11.6)	0.078	208 (14.3)	271 (11.2)	0.094	177 (15.2)	233 (12.5)	0.079	19 (23.2)	46 (12.2)	0.291
Calcium channel blocker	278 (9.4)	397 (7.8)	0.056	160 (11.0)	199 (8.2)	0.095	129 (11.1)	153 (8.2)	0.098	11 (13.4)	29 (7.7)	0.187
Nitrates	32 (1.1)	44 (0.9)	0.022	≤ 10	20 (0.8)	-0.053	14 (1.2)	19 (1.0)	0.018	≤ 10	≤ 10	0.111
Acyclovir	19 (0.6)	29 (0.6)	0.009	≤ 10	18 (0.7)	-0.044	≤ 10	≤ 10	0.025	0 (0.0)	≤ 10	-0.147
Valacyclovir	96 (3.2)	162 (3.2)	0.003	57 (3.9)	71 (2.9)	0.055	50 (4.3)	51 (2.7)	0.085	≤ 10	13 (3.4)	-0.148
Hormonal	372 (12.5)	762 (15.0)	-0.071	196 (13.5)	350 (14.5)	-0.028	147 (12.6)	256 (13.7)	-0.032	12 (14.6)	56 (14.9)	-0.006
HRT	223 (7.5)	361 (7.1)	0.016	111 (7.7)	145 (6.0)	0.066	87 (7.5)	117 (6.3)	0.048	≤ 10	25 (6.6)	0.072
Oral Contraceptives	139 (4.7)	391 (7.7)	-0.125	84 (5.8)	180 (7.4)	-0.067	59 (5.1)	137 (7.3)	-0.094	≤ 10	31 (8.2)	-0.083
SERMs	≤ 10	≤ 10	0.027	≤ 10	15 (0.6)	-0.040	≤ 10	≤ 10	0.000	≤ 10	0 (0.0)	0.157

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	JAK n = 2966	TNFi n = 5082		JAK n = 1450	TNFi n = 2417		JAK n = 1165	TNFi n = 1871		JAK n = 82	TNFi n = 377	Std. Diff.
Topic with progestogens and/or estrogens	≤ 10	26 (0.5)	-0.045	≤ 10	19 (0.8)	-0.083	≤ 10	≤ 10	-0.021	0 (0.0)	≤ 10	-0.103
Lipid-lowering agents	462 (15.6)	683 (13.4)	0.061	259 (17.9)	321 (13.3)	0.127	205 (17.6)	261 (13.9)	0.1	19 (23.2)	56 (14.9)	0.213
HMG CoA reductase inhibitors	374 (12.6)	549 (10.8)	0.056	218 (15.0)	264 (10.9)	0.123	166 (14.2)	207 (11.1)	0.096	16 (19.5)	45 (11.9)	0.209
Fibrates	34 (1.1)	58 (1.1)	0.001	17 (1.2)	23 (1.0)	0.022	21 (1.8)	24 (1.3)	0.042	0 (0.0)	≤ 10	-0.147
Bile acid sequestrants	13 (0.4)	17 (0.3)	0.017	≤ 10	≤ 10	0.014	≤ 10	≤ 10	0.014	0 (0.0)	≤ 10	-0.073
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Other lipid modifying agents	25 (0.8)	55 (1.1)	-0.025	≤ 10	16 (0.7)	-0.014	≤ 10	15 (0.8)	0.006	0 (0.0)	≤ 10	-0.073
Lipid modifying agents, combinations	37 (1.2)	47 (0.9)	0.031	18 (1.2)	20 (0.8)	0.041	17 (1.5)	25 (1.3)	0.011	≤ 10	≤ 10	0.150
Rheumatoid arthritis-related												
Aspirin	38 (1.3)	60 (1.2)	0.009	18 (1.2)	35 (1.4)	-0.018	19 (1.6)	15 (0.8)	0.076	≤ 10	≤ 10	0.131
Cox-2 Inhibitor	159 (5.4)	311 (6.1)	-0.033	81 (5.6)	145 (6.0)	-0.018	66 (5.7)	118 (6.3)	-0.027	≤ 10	34 (9.0)	-0.221
NSAIDs	1078 (36.3)	2008 (39.5)	-0.065	545 (37.6)	1024 (42.4)	-0.098	418 (35.9)	814 (43.5)	-0.156	27 (32.9)	145 (38.5)	-0.116
Glucocorticosteroid	2176 (73.4)	3205 (63.1)	0.223	1058 (73.0)	1658 (68.6)	0.096	824 (70.7)	1273 (68.0)	0.058	57 (69.5)	247 (65.5)	0.085
Vaccines	816 (27.5)	1729 (34.0)	-0.141	495 (34.1)	992 (41.0)	-0.143	353 (30.3)	792 (42.3)	-0.252	25 (30.5)	132 (35.0)	-0.097
Antineoplastic agents	13 (0.4)	16 (0.3)	0.020	≤ 10	≤ 10	0.010	≤ 10	≤ 10	-0.033	≤ 10	0 (0.0)	0.157

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs;
Concom. cDMARDs = concomitant cDMARDs; DMARD = disease-modifying antirheumatic drugs; hosp = hospitalized; HRT = hormone replacement therapy; Max = maximum; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Min = minimum;
mos = months; N = number of patients in the specified category; NMSC = non-melanoma skin cancer;
RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulator; Std. Diff. = standardized difference; TNF = tumor necrosis factor; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Matching ratio 1:1 is applied

[b] TNF inhibitors.

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

Table 6.175. Class Effect: Baseline characteristics by exposure duration - VTE Cohort, Matched [SNDS]

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	JAK n = 2224	TNFi n = 2145		JAK n = 1058	TNFi n = 1036		JAK n = 817	TNFi n = 810		JAK n = 54	TNFi n = 162	Std. Diff.
Age [in years]			0.034			0.05			-0.089			-0.156
N (missing)	2224 (0)	2145 (0)		1058 (0)	1036 (0)		817 (0)	810 (0)		54 (0)	162 (0)	
Mean (SD)	57.8 (13.7)	57.3 (13.8)		59.2 (12.8)	58.6 (13.3)		57.7 (12.3)	58.8 (12.6)		56.8 (12.3)	58.7 (11.7)	
Median	58.0	58.0		59.5	59.0		58.0	60.0		59.5	59.0	
Min; Max	[18.0;91.0]	[18.0;94.0]		[18.0;89.0]	[18.0;91.0]		[19.0;88.0]	[19.0;93.0]		[30.0;77.0]	[22.0;84.0]	
Sex, n (%)			-0.047			0.014			0.029			0.129
Male	450 (20.2)	475 (22.1)		242 (22.9)	231 (22.3)		211 (25.8)	199 (24.6)		15 (27.8)	36 (22.2)	
Female	1774 (79.8)	1670 (77.9)		816 (77.1)	805 (77.7)		606 (74.2)	611 (75.4)		39 (72.2)	126 (77.8)	
Clinical conditions during baseline period, n (%)												
Cancer, excluding NMSC	71 (3.2)	62 (2.9)	0.018	32 (3.0)	35 (3.4)	-0.02	21 (2.6)	23 (2.8)	-0.017	≤ 10	≤ 10	0.071
NMSC	≤ 10	≤ 10	0.024	≤ 10	≤ 10	0.049	0 (0.0)	≤ 10	-0.07	0 (0.0)	≤ 10	-0.112
Chronic lung disease, excluding cystic fibrosis[c]	326 (14.7)	247 (11.5)	0.093	141 (13.3)	119 (11.5)	0.056	89 (10.9)	90 (11.1)	-0.007	≤ 10	15 (9.3)	0.061
Cardiovascular conditions												
Atrial arrhythmia/fibrillation	22 (1.0)	16 (0.7)	0.026	≤ 10	≤ 10	0.035	≤ 10	≤ 10	-0.054	0 (0.0)	≤ 10	-0.112
Cardiovascular revascularization	≤ 10	≤ 10	-0.021	≤ 10	≤ 10	-0.045	≤ 10	0 (0.0)	0.099	0 (0.0)	0 (0.0)	0
Congestive Heart Failure, hospitalized	11 (0.5)	≤ 10	0.004	≤ 10	≤ 10	-0.016	≤ 10	≤ 10	-0.001	0 (0.0)	0 (0.0)	0

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	JAK n = 2224	TNFi n = 2145		JAK n = 1058	TNFi n = 1036		JAK n = 817	TNFi n = 810		JAK n = 54	TNFi n = 162	Std. Diff.
Coronary artery disease	94 (4.2)	79 (3.7)	0.028	58 (5.5)	49 (4.7)	0.034	32 (3.9)	32 (4.0)	-0.002	≤ 10	≤ 10	0.197
Unstable angina	≤ 10	≤ 10	-0.013	≤ 10	≤ 10	-0.021	0 (0.0)	≤ 10	-0.07	0 (0.0)	0 (0.0)	0
Ventricular arrhythmia	13 (0.6)	18 (0.8)	-0.03	≤ 10	≤ 10	0.012	≤ 10	≤ 10	-0.001	0 (0.0)	≤ 10	-0.158
Stroke	18 (0.8)	≤ 10	0.05	≤ 10	≤ 10	-0.002	≤ 10	≤ 10	-0.065	0 (0.0)	≤ 10	-0.158
Hemorrhagic	≤ 10	≤ 10	-0.001	≤ 10	≤ 10	-0.045	0 (0.0)	≤ 10	-0.05	0 (0.0)	0 (0.0)	0
Ischemic	≤ 10	≤ 10	0.01	≤ 10	≤ 10	0.058	≤ 10	≤ 10	-0.029	0 (0.0)	0 (0.0)	0
Unknown	14 (0.6)	≤ 10	0.061	≤ 10	≤ 10	-0.002	≤ 10	≤ 10	-0.058	0 (0.0)	≤ 10	-0.158
TIA	≤ 10	≤ 10	-0.031	≤ 10	0 (0.0)	0.062	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Diabetes Mellitus[c]	207 (9.3)	217 (10.1)	-0.027	110 (10.4)	95 (9.2)	0.041	81 (9.9)	73 (9.0)	0.031	≤ 10	16 (9.9)	-0.021
Treated insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Treated non insulin dependent	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Dyslipidemia (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Hypertension (not available in SNDS)												
History of hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Current hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Immune disorders	86 (3.9)	85 (4.0)	-0.005	25 (2.4)	35 (3.4)	-0.061	25 (3.1)	25 (3.1)	-0.002	≤ 10	≤ 10	0.05
AIDS/HIV	0 (0.0)	≤ 10	-0.053	0 (0.0)	0 (0.0)	0	≤ 10	≤ 10	0	0 (0.0)	0 (0.0)	0

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	JAK n = 2224	TNFi n = 2145		JAK n = 1058	TNFi n = 1036		JAK n = 817	TNFi n = 810		JAK n = 54	TNFi n = 162	Std. Diff.
Antiphospholipid syndrome	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
SLE	27 (1.2)	14 (0.7)	0.058	≤ 10	≤ 10	0.015	≤ 10	≤ 10	0.07	≤ 10	≤ 10	0.112
Primary Sjogren Syndrome	64 (2.9)	70 (3.3)	-0.022	22 (2.1)	32 (3.1)	-0.064	18 (2.2)	22 (2.7)	-0.033	0 (0.0)	≤ 10	-0.112
Liver or pancreatic disorder[c]	55 (2.5)	57 (2.7)	-0.012	29 (2.7)	37 (3.6)	-0.048	17 (2.1)	22 (2.7)	-0.042	≤ 10	≤ 10	0.113
Obesity (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date)	≤ 10	≤ 10	-0.032	≤ 10	≤ 10	-0.002	≤ 10	≤ 10	-0.001	0 (0.0)	0 (0.0)	0
RA Severity (CIRAS Index)			0.001			-0.006			0.047			-0.004
Mean (SD)	6.5 (1.5)	6.5 (1.5)		6.5 (1.4)	6.5 (1.4)		6.6 (1.4)	6.5 (1.4)		6.7 (1.4)	6.7 (1.3)	
DMARDs, n (%)												
cDMARDs, during baseline period												
n, total (%)	1459 (65.6)	1379 (64.3)	0.028	763 (72.1)	728 (70.3)	0.041	612 (74.9)	598 (73.8)	0.025	41 (75.9)	126 (77.8)	-0.044
Mean (SD)	0.7 (0.6)	0.7 (0.6)	0.035	0.8 (0.6)	0.8 (0.6)	0.059	0.8 (0.6)	0.8 (0.5)	0.065	1.0 (0.8)	0.8 (0.5)	0.219
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	
Min; Max	[0.0;3.0]	[0.0;3.0]		[0.0;3.0]	[0.0;4.0]		[0.0;4.0]	[0.0;3.0]		[0.0;3.0]	[0.0;2.0]	
>1 cDMARD concomitantly	115 (5.2)	85 (4.0)	0.058	65 (6.1)	46 (4.4)	0.076	51 (6.2)	50 (6.2)	0.003	≤ 10	≤ 10	0.229

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	JAK n = 2224	TNFi n = 2145		JAK n = 1058	TNFi n = 1036		JAK n = 817	TNFi n = 810		JAK n = 54	TNFi n = 162	Std. Diff.
Hydroxychloroquine	114 (5.1)	103 (4.8)	0.015	63 (6.0)	41 (4.0)	0.092	48 (5.9)	38 (4.7)	0.053	≤ 10	≤ 10	0.284
Chloroquine	0 (0.0)	≤ 10	-0.053	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	≤ 10	0 (0.0)	0.194
Azathioprin	≤ 10	≤ 10	-0.011	≤ 10	≤ 10	-0.029	≤ 10	≤ 10	-0.082	0 (0.0)	0 (0.0)	0
Leflunomide	274 (12.3)	230 (10.7)	0.05	129 (12.2)	111 (10.7)	0.046	87 (10.6)	87 (10.7)	-0.003	11 (20.4)	≤ 10	0.452
Methotrexate	1147 (51.6)	1086 (50.6)	0.019	612 (57.8)	591 (57.0)	0.016	511 (62.5)	488 (60.2)	0.047	28 (51.9)	113 (69.8)	-0.373
Mycophenolate mofetil	0 (0.0)	0 (0.0)	0	≤ 10	≤ 10	-0.001	≤ 10	0 (0.0)	0.05	0 (0.0)	0 (0.0)	0
Sulfasalazin	71 (3.2)	82 (3.8)	-0.034	35 (3.3)	40 (3.9)	-0.03	38 (4.7)	31 (3.8)	0.041	≤ 10	≤ 10	0.328
Cyclosporin	≤ 10	≤ 10	-0.001	0 (0.0)	0 (0.0)	0	≤ 10	≤ 10	0	0 (0.0)	0 (0.0)	0
Penicillamin	≤ 10	0 (0.0)	0.03	0 (0.0)	≤ 10	-0.044	0 (0.0)	≤ 10	-0.05	0 (0.0)	0 (0.0)	0
bDMARDs, during baseline period												
n, total (%)	990 (44.5)	958 (44.7)	-0.003	468 (44.2)	490 (47.3)	-0.062	428 (52.4)	387 (47.8)	0.092	29 (53.7)	89 (54.9)	-0.025
Mean (SD)	0.5 (0.5)	0.5 (0.5)	-0.006	0.5 (0.6)	0.5 (0.6)	-0.069	0.6 (0.6)	0.5 (0.5)	0.106	0.6 (0.6)	0.6 (0.6)	-0.022
Median	0.0	0.0		0.0	0.0		1.0	0.0		1.0	1.0	
Min; Max	[0.0;2.0]	[0.0;2.0]		[0.0;3.0]	[0.0;2.0]		[0.0;2.0]	[0.0;2.0]		[0.0;2.0]	[0.0;2.0]	
cDMARDs, concomitant	535 (24.1)	499 (23.3)	0.019	291 (27.5)	276 (26.6)	0.019	279 (34.1)	228 (28.1)	0.13	19 (35.2)	61 (37.7)	-0.051
Adalimumab[b]	141 (6.3)	143 (6.7)	-0.013	70 (6.6)	78 (7.5)	-0.036	74 (9.1)	59 (7.3)	0.065	≤ 10	25 (15.4)	-0.327
Certolizumab pegol[b]	68 (3.1)	66 (3.1)	-0.001	37 (3.5)	31 (3.0)	0.029	27 (3.3)	24 (3.0)	0.02	≤ 10	≤ 10	0
Etanercept[b]	272 (12.2)	275 (12.8)	-0.018	116 (11.0)	135 (13.0)	-0.064	108 (13.2)	102 (12.6)	0.019	≤ 10	23 (14.2)	-0.293
Golimumab[b]	67 (3.0)	73 (3.4)	-0.022	31 (2.9)	27 (2.6)	0.02	30 (3.7)	27 (3.3)	0.018	≤ 10	≤ 10	-0.088
Infliximab[b]	54 (2.4)	68 (3.2)	-0.045	32 (3.0)	24 (2.3)	0.044	22 (2.7)	24 (3.0)	-0.016	≤ 10	≤ 10	0.05

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	JAK n = 2224	TNFi n = 2145		JAK n = 1058	TNFi n = 1036		JAK n = 817	TNFi n = 810		JAK n = 54	TNFi n = 162	Std. Diff.
Rituximab	19 (0.9)	15 (0.7)	0.018	12 (1.1)	13 (1.3)	-0.011	11 (1.3)	≤ 10	0.124	≤ 10	≤ 10	0.197
Sarilumab	21 (0.9)	16 (0.7)	0.022	≤ 10	≤ 10	-0.036	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0
Abatacept	202 (9.1)	195 (9.1)	0	104 (9.8)	115 (11.1)	-0.042	99 (12.1)	95 (11.7)	0.012	≤ 10	12 (7.4)	0.335
Tocilizumab	178 (8.0)	155 (7.2)	0.029	81 (7.7)	88 (8.5)	-0.031	82 (10.0)	68 (8.4)	0.057	≤ 10	12 (7.4)	0.128
Anakinra	12 (0.5)	≤ 10	0.041	≤ 10	≤ 10	-0.014	≤ 10	≤ 10	-0.023	0 (0.0)	0 (0.0)	0
TNFi naïve at baseline	1639 (73.7)	1531 (71.4)	0.052	779 (73.6)	745 (71.9)	0.039	565 (69.2)	576 (71.1)	-0.043	42 (77.8)	97 (59.9)	0.394
Other prescription medications during baseline period, n (%)												
Antibiotics	904 (40.6)	848 (39.5)	0.023	437 (41.3)	445 (43.0)	-0.033	339 (41.5)	303 (37.4)	0.084	21 (38.9)	49 (30.2)	0.183
Antidiabetic agents	195 (8.8)	207 (9.7)	-0.031	104 (9.8)	85 (8.2)	0.057	75 (9.2)	76 (9.4)	-0.007	≤ 10	16 (9.9)	0.097
Insulins	83 (3.7)	85 (4.0)	-0.012	40 (3.8)	22 (2.1)	0.098	28 (3.4)	23 (2.8)	0.034	≤ 10	≤ 10	-0.043
Non-insulins	151 (6.8)	165 (7.7)	-0.035	91 (8.6)	77 (7.4)	0.043	60 (7.3)	64 (7.9)	-0.021	≤ 10	15 (9.3)	0.118
Cardiovascular												
Antithrombotic agents	324 (14.6)	324 (15.1)	-0.015	174 (16.4)	160 (15.4)	0.027	111 (13.6)	120 (14.8)	-0.035	15 (27.8)	28 (17.3)	0.253
Anticoagulant	107 (4.8)	99 (4.6)	0.009	53 (5.0)	48 (4.6)	0.018	28 (3.4)	31 (3.8)	-0.021	≤ 10	≤ 10	-0.061
Antiplatelet	243 (10.9)	241 (11.2)	-0.01	129 (12.2)	115 (11.1)	0.034	86 (10.5)	93 (11.5)	-0.031	13 (24.1)	21 (13.0)	0.289
Antihypertensives	730 (32.8)	708 (33.0)	-0.004	385 (36.4)	357 (34.5)	0.04	265 (32.4)	278 (34.3)	-0.04	22 (40.7)	57 (35.2)	0.115
Angiotensin converting enzyme inhibitors (ACE)	194 (8.7)	208 (9.7)	-0.034	118 (11.2)	100 (9.7)	0.049	67 (8.2)	73 (9.0)	-0.029	≤ 10	17 (10.5)	0.181
Angiotensin receptor blockers (ARB)	303 (13.6)	270 (12.6)	0.031	145 (13.7)	156 (15.1)	-0.039	91 (11.1)	120 (14.8)	-0.11	≤ 10	23 (14.2)	-0.22

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	JAK n = 2224	TNFi n = 2145		JAK n = 1058	TNFi n = 1036		JAK n = 817	TNFi n = 810		JAK n = 54	TNFi n = 162	Std. Diff.
Beta blocker	302 (13.6)	291 (13.6)	0	153 (14.5)	149 (14.4)	0.002	120 (14.7)	120 (14.8)	-0.004	11 (20.4)	24 (14.8)	0.146
Calcium channel blocker	195 (8.8)	207 (9.7)	-0.031	110 (10.4)	104 (10.0)	0.012	88 (10.8)	74 (9.1)	0.055	≤ 10	21 (13.0)	-0.057
Nitrates	24 (1.1)	27 (1.3)	-0.017	≤ 10	13 (1.3)	-0.098	≤ 10	12 (1.5)	-0.022	≤ 10	≤ 10	0.112
Acyclovir	14 (0.6)	12 (0.6)	0.009	≤ 10	≤ 10	-0.062	≤ 10	≤ 10	0.028	0 (0.0)	≤ 10	-0.194
Valacyclovir	73 (3.3)	72 (3.4)	-0.004	36 (3.4)	38 (3.7)	-0.014	28 (3.4)	26 (3.2)	0.012	0 (0.0)	≤ 10	-0.277
Hormonal	282 (12.7)	282 (13.1)	-0.014	150 (14.2)	139 (13.4)	0.022	102 (12.5)	95 (11.7)	0.023	≤ 10	22 (13.6)	0.086
HRT	166 (7.5)	159 (7.4)	0.002	78 (7.4)	75 (7.2)	0.005	62 (7.6)	52 (6.4)	0.046	≤ 10	12 (7.4)	0.067
Oral Contraceptives	113 (5.1)	119 (5.5)	-0.021	71 (6.7)	54 (5.2)	0.063	38 (4.7)	41 (5.1)	-0.019	≤ 10	≤ 10	0.049
SERMs	≤ 10	≤ 10	0.049	≤ 10	≤ 10	-0.029	≤ 10	≤ 10	0.018	0 (0.0)	0 (0.0)	0
Topic with progestogens and/or estrogens	≤ 10	≤ 10	-0.061	≤ 10	≤ 10	-0.045	≤ 10	≤ 10	0	0 (0.0)	≤ 10	-0.112
Lipid-lowering agents	325 (14.6)	328 (15.3)	-0.019	194 (18.3)	163 (15.7)	0.069	136 (16.6)	139 (17.2)	-0.014	11 (20.4)	28 (17.3)	0.079
HMG CoA reductase inhibitors	262 (11.8)	268 (12.5)	-0.022	163 (15.4)	136 (13.1)	0.065	109 (13.3)	107 (13.2)	0.004	≤ 10	24 (14.8)	0.051
Fibrates	21 (0.9)	24 (1.1)	-0.017	12 (1.1)	≤ 10	0.017	14 (1.7)	15 (1.9)	-0.01	0 (0.0)	≤ 10	-0.112
Bile acid sequestrants	11 (0.5)	≤ 10	0.004	≤ 10	≤ 10	0.013	≤ 10	≤ 10	-0.019	0 (0.0)	0 (0.0)	0
Nicotinic acid and derivatives	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)	0
Other lipid modifying agents	15 (0.7)	29 (1.4)	-0.068	≤ 10	≤ 10	0.011	≤ 10	≤ 10	-0.027	0 (0.0)	0 (0.0)	0
Lipid modifying agents, combinations	29 (1.3)	21 (1.0)	0.031	15 (1.4)	≤ 10	0.042	13 (1.6)	13 (1.6)	-0.001	≤ 10	≤ 10	0.113

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	JAK n = 2224	TNFi n = 2145		JAK n = 1058	TNFi n = 1036		JAK n = 817	TNFi n = 810		JAK n = 54	TNFi n = 162	Std. Diff.
Rheumatoid arthritis-related												
Aspirin	26 (1.2)	26 (1.2)	-0.004	15 (1.4)	22 (2.1)	-0.054	≤ 10	≤ 10	0.023	≤ 10	≤ 10	0.16
Cox-2 Inhibitor	111 (5.0)	134 (6.2)	-0.055	53 (5.0)	62 (6.0)	-0.043	51 (6.2)	53 (6.5)	-0.012	≤ 10	14 (8.6)	-0.12
NSAIDs	817 (36.7)	843 (39.3)	-0.053	410 (38.8)	400 (38.6)	0.003	289 (35.4)	332 (41.0)	-0.116	19 (35.2)	61 (37.7)	-0.051
Glucocorticosteroid	1560 (70.1)	1461 (68.1)	0.044	756 (71.5)	763 (73.6)	-0.049	555 (67.9)	576 (71.1)	-0.069	34 (63.0)	112 (69.1)	-0.131
Vaccines	649 (29.2)	624 (29.1)	0.002	398 (37.6)	365 (35.2)	0.05	267 (32.7)	283 (34.9)	-0.048	15 (27.8)	38 (23.5)	0.099
Antineoplastic agents	≤ 10	≤ 10	0.005	≤ 10	≤ 10	-0.045	≤ 10	≤ 10	-0.029	≤ 10	0 (0.0)	0.194

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs;
Concom. cDMARDs = concomitant cDMARDs; DMARD = disease-modifying antirheumatic drugs; hosp = hospitalized; HRT = hormone replacement therapy; Max = maximum;
MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Min = minimum;
mos = months; N = number of patients in the specified category; NMSC = non-melanoma skin cancer;
RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulator; Std. Diff. = standardized difference; TNF = tumor necrosis factor; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Matching ratio 1:1 is applied

[b] TNF inhibitors.

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

6.3.2 BASELINE HEALTHCARE RESOURCE UTILIZATION BY EXPOSURE DURATION

Table 6.176. Class Effect: Baseline healthcare resource utilization by exposure duration, Unmatched cohort [SNDS]

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	JAK n = 2966	TNFi n = 5082	Std. Diff.	JAK n = 1450	TNFi n = 2417	Std. Diff.	JAK n = 1165	TNFi n = 1871	Std. Diff.	JAK n = 82	TNFi n = 377	Std. Diff.
Physician Office Visits (rheumatologist visits excluded)												
n, patients (%)	1763 (59.4)	3155 (62.1)	-0.054	891 (61.4)	1531 (63.3)	-0.039	711 (61.0)	1171 (62.6)	-0.032	60 (73.2)	271 (71.9)	0.029
n, events	4925	9977		2499	4843		2047	3487		163	999	
Mean (SD)	1.7 (2.4)	2.0 (3.2)	-0.106	1.7 (2.6)	2.0 (3.1)	-0.097	1.8 (2.7)	1.9 (2.7)	-0.04	2.0 (2.4)	2.6 (3.3)	-0.233
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.5	2.0	
Min; Max	[0.0;41.0]	[0.0;85.0]		[0.0;31.0]	[0.0;49.0]		[0.0;31.0]	[0.0;25.0]		[0.0;16.0]	[0.0;22.0]	
Rheumatologist Visits												
n, patients (%)	1793 (60.5)	3079 (60.6)	-0.003	907 (62.6)	1567 (64.8)	-0.047	737 (63.3)	1271 (67.9)	-0.098	61 (74.4)	286 (75.9)	-0.034
n, events	3958	6769		2022	3603		1639	2944		145	677	
Mean (SD)	1.3 (1.5)	1.3 (1.5)	0.002	1.4 (1.5)	1.5 (1.5)	-0.062	1.4 (1.5)	1.6 (1.6)	-0.108	1.8 (1.4)	1.8 (1.6)	-0.018
Median	1.0	1.0		1.0	1.0		1.0	1.0		2.0	2.0	
Min; Max	[0.0;11.0]	[0.0;10.0]		[0.0;8.0]	[0.0;10.0]		[0.0;9.0]	[0.0;13.0]		[0.0;6.0]	[0.0;10.0]	
Other Outpatient Visits												
n, patients (%)	2778 (93.7)	4587 (90.3)	0.125	1353 (93.3)	2219 (91.8)	0.057	1090 (93.6)	1735 (92.7)	0.033	74 (90.2)	344 (91.2)	-0.035
n, events	58933	77389		27639	37002		21786	28984		1328	5652	
Mean (SD)	19.9 (34.0)	15.2 (27.1)	0.151	19.1 (32.5)	15.3 (25.1)	0.129	18.7 (30.6)	15.5 (25.3)	0.114	16.2 (25.5)	15.0 (25.5)	0.047

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	JAK n = 2966	TNFi n = 5082	Std. Diff.	JAK n = 1450	TNFi n = 2417	Std. Diff.	JAK n = 1165	TNFi n = 1871	Std. Diff.	JAK n = 82	TNFi n = 377	Std. Diff.
Median	8.0	6.0		8.0	7.0		8.0	7.0		7.0	7.0	
Min; Max	[0.0;322.0]	[0.0;283.0]		[0.0;266.0]	[0.0;275.0]		[0.0;257.0]	[0.0;242.0]		[0.0;152.0]	[0.0;280.0]	
Inpatient Visits[a]												
n, patients (%)	1412 (47.6)	2294 (45.1)	0.050	693 (47.8)	1202 (49.7)	-0.039	568 (48.8)	906 (48.4)	0.007	43 (52.4)	172 (45.6)	0.137
n, events	3475	3878		1686	2066		1479	1541		98	282	
Mean (SD)	1.2 (2.2)	0.8 (1.5)	0.218	1.2 (1.8)	0.9 (1.9)	0.164	1.3 (1.9)	0.8 (1.7)	0.243	1.2 (1.7)	0.7 (1.2)	0.309
Median	0.0	0.0		0.0	0.0		0.0	0.0		1.0	0.0	
Min; Max	[0.0;74.0]	[0.0;51.0]		[0.0;12.0]	[0.0;76.0]		[0.0;10.0]	[0.0;56.0]		[0.0;7.0]	[0.0;7.0]	
ED Visits	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
n, patients												
n, events												
Mean (SD)												
Median												
Min; Max												

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs;
Concom. cDMARDs = concomitant cDMARDs; DMARD = disease-modifying antirheumatic drugs; hosp = hospitalized; HRT = hormone replacement therapy; Max = maximum;
MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Min = minimum;
mos = months; N = number of patients in the specified category; NMSC = non-melanoma skin cancer;
RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulator; Std. Diff. = standardized difference; TNF = tumor necrosis factor; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Inpatient visits include number of hospitalisations

Table 6.177. Class Effect: Baseline healthcare resource utilization by exposure duration - VTE Cohort, Matched [SNDS]

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	JAK n = 2224	TNFi n = 2145	Std. Diff.	JAK n = 1058	TNFi n = 1036	Std. Diff.	JAK n = 817	TNFi n = 810	Std. Diff.	JAK n = 54	TNFi n = 162	Std. Diff.
Physician Office Visits (rheumatologist visits excluded)												
n, patients (%)	1338 (60.2)	1307 (60.9)	-0.016	662 (62.6)	647 (62.5)	0.003	507 (62.1)	470 (58.0)	0.082	41 (75.9)	112 (69.1)	0.153
n, events	3809.0	3687.0		1884.0	2057.0		1478.0	1257.0		112.0	393.0	
Mean (SD)	1.7 (2.5)	1.7 (2.6)	-0.002	1.8 (2.6)	2.0 (3.5)	-0.066	1.8 (2.8)	1.6 (2.3)	0.101	2.1 (2.5)	2.4 (3.2)	-0.124
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.5	2.0	
Min; Max	[0.0;41.0]	[0.0;29.0]		[0.0;31.0]	[0.0;49.0]		[0.0;31.0]	[0.0;23.0]		[0.0;16.0]	[0.0;19.0]	
Rheumatologist Visits												
n, patients (%)	1350 (60.7)	1315 (61.3)	-0.012	685 (64.7)	660 (63.7)	0.022	534 (65.4)	550 (67.9)	-0.054	36 (66.7)	129 (79.6)	-0.296
n, events	2913.0	2889.0		1531.0	1537.0		1195.0	1233.0		77.0	299.0	
Mean (SD)	1.3 (1.5)	1.3 (1.5)	-0.025	1.4 (1.5)	1.5 (1.6)	-0.023	1.5 (1.5)	1.5 (1.6)	-0.039	1.4 (1.3)	1.8 (1.6)	-0.288
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.5	2.0	
Min; Max	[0.0;8.0]	[0.0;10.0]		[0.0;8.0]	[0.0;8.0]		[0.0;9.0]	[0.0;13.0]		[0.0;5.0]	[0.0;10.0]	
Other Outpatient Visits												
n, patients (%)	2074 (93.3)	1949 (90.9)	0.089	977 (92.3)	970 (93.6)	-0.05	763 (93.4)	750 (92.6)	0.031	48 (88.9)	146 (90.1)	-0.04
n, events	42804.0	35171.0		19470.0	17577.0		13573.0	13702.0		814.0	2505.0	
Mean (SD)	19.2 (32.9)	16.4 (28.4)	0.093	18.4 (32.3)	17.0 (27.5)	0.048	16.6 (25.7)	16.9 (27.5)	-0.011	15.1 (24.6)	15.5 (30.8)	-0.014

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	JAK n = 2224	TNFi n = 2145	Std. Diff.	JAK n = 1058	TNFi n = 1036	Std. Diff.	JAK n = 817	TNFi n = 810	Std. Diff.	JAK n = 54	TNFi n = 162	Std. Diff.
Median	7.0	7.0		7.0	7.0		7.0	7.0		6.0	6.0	
Min; Max	[0.0;261.0]	[0.0;255.0]		[0.0;266.0]	[0.0;275.0]		[0.0;236.0	[0.0;242.0]		[0.0;152.0]	[0.0;280.0]	
Inpatient Visits[a]												
n, patients (%)	996 (44.8)	908 (42.3)	0.05	489 (46.2)	511 (49.3)	-0.062	358 (43.8)	358 (44.2)	-0.008	25 (46.3)	61 (37.7)	0.176
n, events	2123.0	1856.0		980.0	1106.0		805.0	722.0		56.0	112.0	
Mean (SD)	1.0 (2.2)	0.9 (1.5)	0.048	0.9 (1.5)	1.1 (2.8)	-0.064	1.0 (1.7)	0.9 (1.5)	0.06	1.0 (1.6)	0.7 (1.3)	0.24
Median	0.0	0.0		0.0	0.0		0.0	0.0		0.0	0.0	
Min; Max	[0.0;74.0]	[0.0;16.0]		[0.0;12.0]	[0.0;76.0]		[0.0;10.0]	[0.0;9.0]		[0.0;6.0]	[0.0;7.0]	
ED Visits	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
n, patients												
n, events												
Mean (SD)												
Median												
Min; Max												

Abbreviations: bDMARD = biologic disease-modifying antirheumatic drugs; cDMARD = classical disease-modifying antirheumatic drugs;
Concom. cDMARDs = concomitant cDMARDs; DMARD = disease-modifying antirheumatic drugs; hosp = hospitalized; HRT = hormone replacement therapy; Max = maximum;
MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Min = minimum;
mos = months; N = number of patients in the specified category; NMSC = non-melanoma skin cancer;
RA = rheumatoid arthritis; SD = standard deviation; SERMs = selective estrogen receptor modulator; Std. Diff. = standardized difference; TNF = tumor necrosis factor; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Inpatient visits include number of hospitalisations

6.4 OUTCOME

Table 6.178. Class Effect: Clinical characteristics during baseline period in patients with VTE, VTE matched cohort [SNDS]

Characteristics[b]	JAK n = 28	TNFi[a] n = 14	Total n = 42
Age [in years]			
N	28 (0)	14 (0)	42 (0)
Mean (SD)	67.8 (11.7)	64.7 (12.7)	66.7 (12.0)
Median	69.5	65.0	67.5
Min; Max	[48.0;89.0]	[43.0;88.0]	[43.0;89.0]
Sex, n (%)			
Female	≤ 10	≤ 10	≤ 10
Male	23 (82.1)	≤ 10	32 (76.2)
Clinical conditions during baseline period, n (%)			
Cancer, excluding NMSC	≤ 10	0 (0.0)	≤ 10
NMSC	≤ 10	≤ 10	≤ 10
Chronic lung disease, excluding cystic fibrosis[c]			
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	≤ 10	≤ 10	≤ 10
Unstable angina	0 (0.0)	≤ 10	≤ 10
Ventricular arrhythmia	≤ 10	0 (0.0)	≤ 10
Stroke	0 (0.0)	0 (0.0)	0 (0.0)

Characteristics[b]	JAK n = 28	TNFi[a] n = 14	Total n = 42
Hemorrhagic	0 (0.0)	0 (0.0)	0 (0.0)
Ischemic	0 (0.0)	0 (0.0)	0 (0.0)
Unknown	0 (0.0)	0 (0.0)	0 (0.0)
TIA	0 (0.0)	0 (0.0)	0 (0.0)
Diabetes Mellitus[c]	≤ 10	≤ 10	≤ 10
Treated insulin dependent	N/A	N/A	N/A
Treated non insulin dependent	N/A	N/A	N/A
Dyslipidemia (not available in SNDS)	N/A	N/A	N/A
Hypertension (not available in SNDS)			
History of hypertension	N/A	N/A	N/A
Current hypertension	N/A	N/A	N/A
Immune disorders	≤ 10	0 (0.0)	≤ 10
AIDS/HIV	0 (0.0)	0 (0.0)	0 (0.0)
Antiphospholipid syndrome	N/A	N/A	N/A
SLE	≤ 10	0 (0.0)	≤ 10
Primary Sjogren Syndrome	≤ 10	0 (0.0)	≤ 10
Liver or pancreatic disorder[c]	0 (0.0)	0 (0.0)	0 (0.0)
Obesity (not available in SNDS)	N/A	N/A	N/A
Recent pregnancy	0 (0.0)	0 (0.0)	0 (0.0)
RA Severity (CIRAS Index)			
Mean (± SD)	5.6 (0.9)	6.3 (1.5)	5.8 (1.2)
Smoking (not available in SNDS)	N/A	N/A	N/A
Surgery or trauma	≤ 10	≤ 10	≤ 10

Characteristics[b]	JAK n = 28	TNFi[a] n = 14	Total n = 42
Other prescription medications during baseline period, n (%)			
Antibiotics	16 (57.1)	≤ 10	25 (59.5)
Antidiabetic agents	≤ 10	0 (0.0)	≤ 10
Insulins	0 (0.0	0 (0.0	0 (0.0
Non-insulins	≤ 10	0 (0.0)	≤ 10
Cardiovascular			
Antithrombotic agents	≤ 10	≤ 10	≤ 10
Anticoagulant	≤ 10	≤ 10	≤ 10
Antiplatelet	≤ 10	≤ 10	≤ 10
Antihypertensives	13 (46.4)	≤ 10	18 (42.9)
Angiotensin converting enzyme inhibitors (ACE)	≤ 10	≤ 10	≤ 10
Angiotensin receptor blockers (ARB)	≤ 10	0 (0.0)	≤ 10
Beta blocker	≤ 10	≤ 10	≤ 10
Calcium channel blocker	≤ 10	≤ 10	≤ 10
Nitrates	≤ 10	0 (0.0)	≤ 10
Acyclovir	0 (0.0)	0 (0.0)	0 (0.0)
Valacyclovir	≤ 10	0 (0.0)	≤ 10
Hormonal	≤ 10	≤ 10	≤ 10
HRT	≤ 10	0 (0.0)	≤ 10
Oral Contraceptives	0 (0.0)	≤ 10	≤ 10
SERMs	0 (0.0)	0 (0.0)	0 (0.0)
Topic with progestogens and/or estrogens	0 (0.0)	0 (0.0)	0 (0.0)

Characteristics[b]	JAK n = 28	TNFi[a] n = 14	Total n = 42
Lipid-lowering agents	≤ 10	≤ 10	12 (28.6)
HMG CoA reductase inhibitors	≤ 10	≤ 10	≤ 10
Fibrates	≤ 10	0 (0.0)	≤ 10
Bile acid sequestrants	0 (0.0)	0 (0.0)	0 (0.0)
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)
Other lipid modifying agents	0 (0.0)	0 (0.0)	0 (0.0)
Lipid modifying agents, combinations	0 (0.0)	≤ 10	≤ 10
Rheumatoid arthritis-related			
Aspirin	0 (0.0)	0 (0.0)	0 (0.0)
Cox-2 Inhibitor	0 (0.0)	≤ 10	≤ 10
NSAIDs	≤ 10	≤ 10	≤ 10
Glucocorticosteroid	26 (92.9)	≤ 10	36 (85.7)
Vaccines	13 (46.4)	≤ 10	18 (42.9)
Antineoplastic agents	0 (0.0)	0 (0.0)	0 (0.0)
Post-index Occurrence[d], n (%)			
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)

Abbreviations: HRT = hormone replacement therapy; IHD = ischemic heart disease; 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; TNFi = tumor necrosis factor inhibitor; VTE = Venous thromboembolism.

[a] Variable 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] CNAM algorithm based on the year preceding the year of inclusion

[d] Except for cancer diagnosed within 90 days of VTE diagnosis, events in this category must have occurred in the 4 weeks immediately prior toVTE (Kline et al. 2017).

Table 6.179. Class Effect: Pattern of RA medication use in patients with VTE [SNDS]

Characteristics[b]	Unmatched		Matched		
	JAK n = 36	TNFi n = 29	JAK n = 28	TNFi[a] n = 14	Total n = 42
Baseline Medication, n (%)					
cDMARDs, during baseline period					
n, total (%)	26 (72.2)	20 (69.0)	19 (67.9)	≤ 10	28 (66.7)
Mean (SD)	0.8 (0.6)	0.8 (0.6)	0.8 (0.6)	0.7 (0.6)	0.8 (0.6)
Median	1.0	1.0	1.0	1.0	1.0
Min; Max	[0.0;2.0]	[0.0;2.0]	[0.0;2.0]	[0.0;2.0]	[0.0;2.0]
>1 cDMARD concomitantly	≤ 10	0 (0.0)	≤ 10	0 (0.0)	≤ 10
Hydroxychloroquine	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
Chloroquine	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Azathioprin	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Leflunomide	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
Methotrexate	22 (61.1)	11 (37.9)	15 (53.6)	≤ 10	20 (47.6)
Mycophenolate mofetil	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sulfasalazin	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
Cyclosporin	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Penicillamin	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
bDMARDs, during baseline period					
n, total (%)	22 (61.1)	≤ 10	14 (50.0)	≤ 10	22 (52.4)
Mean (SD)	0.6 (0.5)	0.3 (0.5)	0.5 (0.6)	0.6 (0.5)	0.5 (0.6)
Median	1.0	0.0	0.5	1.0	1.0
Min; Max	[0.0;2.0]	[0.0;1.0]	[0.0;2.0]	[0.0;1.0]	[0.0;2.0]

Characteristics[b]	Unmatched		Matched		
	JAK n = 36	TNFi n = 29	JAK n = 28	TNFi[a] n = 14	Total n = 42
cDMARDs, concomitant	11 (30.6)	≤ 10	≤ 10	≤ 10	11 (26.2)
Adalimumab[c]	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
Certolizumab pegol[c]	≤ 10	0 (0.0)	≤ 10	0 (0.0)	≤ 10
Etanercept[c]	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
Golimumab[c]	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infliximab[c]	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
Rituximab	≤ 10	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)
Abatacept	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
Tocilizumab	≤ 10	0 (0.0)	≤ 10	0 (0.0)	≤ 10
Anakinra	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TNFi naïve at baseline	26 (72.2)	24 (82.8)	19 (67.9)	≤ 10	28 (66.7)
Post-index Medication, n (%)					
Methotrexate, concomitant	17 (47.2)	12 (41.4)	13 (46.4)	≤ 10	19 (45.2)
Other Concomitant cDMARD	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
Dose change, baricitinib	≤ 10	N/A	≤ 10	0 (0.0)	≤ 10

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 = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

[a] Variable 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.

Table 6.180. Class Effect: Time to first VTE [SNDS]

	Unmatched		Matched		
	JAK n = 36	**TNFi n = 29**	**JAK n = 28**	**TNFi[a] n = 14**	**Total n = 42**
Time to first VTE (in days)					
N (missing)	36 (0)	29 (0)	28 (0)	14 (0)	42 (0)
Mean (SD)	226.3 (189.8)	197.7 (175.0)	206.9 (180.1)	198.5 (161.7)	204.1 (172.3)
Median	176.0	144.0	147.0	135.0	147.0
Min; Max	[4.0;650.0]	[26.0;624.0]	[17.0;632.0]	[26.0;555.0]	[17.0;632.0]

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

[a] Variable matching ratio 1:1 is applied

Table 6.181. Class Effect: Crude rates of incident VTE [SNDS]

	Unmatched		Matched		
	JAK	TNFi	JAK	TNFi[a]	Total
VTE	**n = 5663**	**n = 9747**	**n = 4153**	**n = 4153**	**n = 8306**
Overall					
Person-Years	3577	6490	2568	2810	5378
VTE	36	29	28	14	42
VTE /100 PY	1.0	0.4	1.1	0.5	0.8
95% CI	[0.7 ; 1.4]	[0.3 ; 0.6]	[0.7 ; 1.6]	[0.3 ; 0.8]	[0.6 ; 1.1]
IRD	0.6		0.6	.	
IRD 95% CI	[0.2 ; 0.9]		[0.1 ; 1.1]		
Concomitant[b] MTX Use, n (%)	2402 (42.4)	5165 (53.0)	1847 (44.5)	2059 (49.6)	3906 (47.0)
Person-Years	1724	3996	1318	1616	2934
VTE	17	12	13	6	19
VTE /100 PY	1.0	0.3	1	0.4	0.6
95% CI	[0.6 ; 1.6]	[0.2 ; 0.5]	[0.5 ; 1.7]	[0.1 ; 0.8]	[0.4 ; 1]
IRD	0.7		0.6	.	
IRD 95% CI	[0.3 ; 1.1]		[0.03 ; 1.2]		
No concomitant[b] MTX Use, n (%)	3261 (57.6)	4582 (47.0)	2306 (55.5)	2094 (50.4)	4400 (53.0)
Person-Years	1853	2494	1250	1194	2444
VTE	19	17	15	8	23
VTE /100 PY	1.0	0.7	1.2	0.7	0.9
95% CI	[0.6 ; 1.6]	[0.4 ; 1.1]	[0.7 ; 2]	[0.3 ; 1.3]	[0.6 ; 1.4]
IRD	0.3		0.5	.	

	Unmatched		Matched		
	JAK	**TNFi**	**JAK**	**TNFi[a]**	**Total**
VTE	**n = 5663**	**n = 9747**	**n = 4153**	**n = 4153**	**n = 8306**
IRD 95% CI	[-0.2 ; 0.9]		[-0.2 ; 1.3]		

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

[a] Variable matching ratio 1:1 is applied

[b] 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.

Table 6.182. Class Effect: Comparative risk of incident VTE , matched cohort [SNDS]

VTE	TNFi	JAK, HR [95% CI]	P-value
Base Model	Ref	2.18 [1.14 ; 4.16]	0.0188
Adjusted – Model [1]	Ref	2.18 [1.14 ; 4.16]	0.0188
Adjusted – Model [2]	Ref	2.15 [1.12 ; 4.10]	0.0207
Concomitant Glucocorticoid use	*Ref*	1.39 [0.74 ; 2.61]	0.3015
Concomitant cDMARD use	*Ref*	0.80 [0.43 ; 1.46]	0.4591
Adjusted – Model [3]	Ref	2.16 [1.13 ; 4.13]	0.0197
Concomitant Glucocorticoid use	*Ref*	1.38 [0.74 ; 2.59]	0.3148
Adjusted – Model [n]	Ref	N/A	.

Abbreviations: cDMARD = conventional disease-modifying antirheumatic drug; CI = confidence interval; HR = hazard ratio; Ref = referent group; VTE = venous thromboembolism.

Model [1] = propensity score-matched model with outcome and baricitinib exposure, adjusted for any variables that remain unbalanced after PS 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.

Models 1-n may include additional variables that remain unbalanced after propensity-score matching as well as concomitant cDMARD or glucocorticoid use separately.

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.

7 SENSITIVITY ANALYSES - VTE: INCLUDING PATIENTS WITH PRIOR TOFACITINIB EXPOSURE

The sensitivity analyses « VTE: “including patients with prior tofacitinib exposure » have not been conducted due to the small number of total patients added (< 10%, cf figure 6.1 in section 1.1 and table 6.16 in section 1.2. Therefore all tables below have not been performed.

Table 6.183. Any Prior JAKi Use: Baseline demographics, Unmatched cohort [SNDS]

Table 6.184. Any Prior JAKi Use: Baseline demographics VTE cohort, Matched [SNDS]

Table 6.185. Any Prior JAKi Use: Clinical history at baseline, Unmatched cohort [SNDS]

Table 6.186. Any Prior JAKi Use: Clinical characteristics VTE cohort, Matched [SNDS]

Table 6.187. Any Prior JAKi Use: Clinical characteristics MACE cohort, Matched [SNDS]

Table 6.188. Any Prior JAKi Use: Baseline healthcare resource utilization, Unmatched cohort [SNDS]

Table 6.189. Any Prior JAKi Use: Baseline healthcare resource utilization VTE cohort, Matched [SNDS]

Table 6.190. Any Prior JAKi Use: Duration of follow-up period (days), Unmatched cohort [SNDS]

Table 6.191. Any Prior JAKi Use: Duration of follow-up period (days) VTE cohort, Matched [SNDS]

Table 6.192. Any Prior JAKi Use: Baseline characteristics by exposure duration, Unmatched cohort [SNDS]

Table 6.193. Any Prior JAKi Use: Baseline characteristics by exposure duration, VTE Cohort, Matched [SNDS]

Table 6.194. Any Prior JAKi Use: Baseline healthcare resource utilization by exposure duration, Unmatched cohort [SNDS]

Table 6.195. Any Prior JAKi Use: Baseline healthcare resource utilization by exposure duration, VTE cohort [SNDS]

8 APPENDICES

8.1 PROPENSITY SCORE, MAIN ANALYSES

8.1.1 APPENDIX 1. PROPENSITY SCORE, VTE COHORT

Table A.1. Baricitinib vs TNFi PS model (pre-defined variables + variables with standardized difference ≥ 0.10), VTE cohort

	TNFi n=10202	Baricitinib n=3242	Total n=13444	Baricitinib vs TNFi OR [95%CI]	p
CIRAS score (during the year preceding index date)					0.0057
≤5.5	2122 (20.8)	823 (25.4)	2945 (21.9)	1	
]5.5-6.5]	2663 (26.1)	1002 (30.9)	3665 (27.3)	1.00 [0.88 - 1.14]	
]6.5-7.5]	2201 (21.6)	746 (23.0)	2947 (21.9)	1.07 [0.93 - 1.23]	
>7.5	3216 (31.5)	671 (20.7)	3887 (28.9)	0.85 [0.73 - 0.98]	
Age (in years), in categories, n (%)					<0.0001
≥ 65	2766 (27.1)	1142 (35.2)	3908 (29.1)	1	
[18-30[	435 (4.3)	70 (2.2)	505 (3.8)	0.45 [0.33 - 0.61]	
[30-40[	1231 (12.1)	208 (6.4)	1439 (10.7)	0.47 [0.38 - 0.57]	
[40-50[	1743 (17.1)	462 (14.3)	2205 (16.4)	0.66 [0.56 - 0.77]	
[50-60[	2776 (27.2)	899 (27.7)	3675 (27.3)	0.81 [0.71 - 0.91]	
[60-65[	1251 (12.3)	461 (14.2)	1712 (12.7)	0.90 [0.78 - 1.04]	
Sex, n (%)					<0.0001
Female	7534 (73.8)	2597 (80.1)	10131 (75.4)	1	

	TNFi n=10202	Baricitinib n=3242	Total n=13444	Baricitinib vs TNFi OR [95%CI]	p
Male	2668 (26.2)	645 (19.9)	3313 (24.6)	0.71 [0.64 - 0.79]	
Cancer during baseline period, n (%)					0.6031
No	9883 (96.9)	3142 (96.9)	13025 (96.9)	1	
Yes	319 (3.1)	100 (3.1)	419 (3.1)	0.94 [0.73 - 1.20]	
Atrial arrhythmia/fibrillation, Ventricular arrhythmia or Congestive Heart Failure, hospitalized during baseline period, n (%)					0.3799
No	10064 (98.6)	3179 (98.1)	13243 (98.5)	1	
Yes	138 (1.4)	63 (1.9)	201 (1.5)	1.17 [0.83 - 1.64]	
Immune disorders during baseline period, n (%)					0.0859
No	9920 (97.2)	3119 (96.2)	13039 (97.0)	1	
Yes	282 (2.8)	123 (3.8)	405 (3.0)	1.24 [0.97 - 1.58]	
Diabete during the year preceding the year of index date, n (%)					0.6110
No	9318 (91.3)	2921 (90.1)	12239 (91.0)	1	
Yes	884 (8.7)	321 (9.9)	1205 (9.0)	0.96 [0.82 - 1.12]	

	TNFi n=10202	Baricitinib n=3242	Total n=13444	Baricitinib vs TNFi OR [95%CI]	p
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date), n (%)					0.0243
No	10058 (98.6)	3234 (99.8)	13292 (98.9)	1	
Yes	144 (1.4)	8 (0.2)	152 (1.1)	0.42 [0.20 - 0.89]	
≥1 recent surgery, n (%)					0.3246
No	9762 (95.7)	3118 (96.2)	12880 (95.8)	1	
Yes	440 (4.3)	124 (3.8)	564 (4.2)	1.13 [0.89 - 1.43]	
≥1 recent Trauma, n (%)					0.8777
No	10135 (99.3)	3221 (99.4)	13356 (99.3)	1	
Yes	67 (0.7)	21 (0.6)	88 (0.6)	0.96 [0.56 - 1.65]	
Aspirin (analgesic) (during baseline period, index date excluded), n (%)					0.8145
No	10085 (98.9)	3201 (98.7)	13286 (98.8)	1	
Yes	117 (1.1)	41 (1.3)	158 (1.2)	0.95 [0.64 - 1.42]	
Anticoagulant (during baseline period, index date excluded), n (%)					0.6907
No	9737 (95.4)	3100 (95.6)	12837 (95.5)	1	
Yes	465 (4.6)	142 (4.4)	607 (4.5)	1.05 [0.84 - 1.31]	

	TNFi n=10202	Baricitinib n=3242	Total n=13444	Baricitinib vs TNFi OR [95%CI]	p
Glucocorticosteroid (during baseline period, index date excluded), n (%)					<0.0001
0	3493 (34.2)	883 (27.2)	4376 (32.5)	1	
1	1585 (15.5)	435 (13.4)	2020 (15.0)	1.07 [0.93 - 1.24]	
[2-4]	2466 (24.2)	865 (26.7)	3331 (24.8)	1.39 [1.23 - 1.56]	
≥ 5	2658 (26.1)	1059 (32.7)	3717 (27.6)	1.69 [1.51 - 1.90]	
Methotrexate (during baseline period, index date excluded), n (%)					<0.0001
0	4108 (40.3)	1563 (48.2)	5671 (42.2)	1	
1	506 (5.0)	155 (4.8)	661 (4.9)	0.92 [0.75 - 1.13]	
[2-4]	2200 (21.6)	685 (21.1)	2885 (21.5)	0.93 [0.83 - 1.04]	
≥ 5	3388 (33.2)	839 (25.9)	4227 (31.4)	0.75 [0.68 - 0.84]	
Oral Contraceptives (during baseline period, index date excluded), n (%)					0.3462
No	9429 (92.4)	3085 (95.2)	12514 (93.1)	1	
Yes	773 (7.6)	157 (4.8)	930 (6.9)	0.90 [0.73 - 1.12]	
HRT (during baseline period, index date excluded), n (%)					0.6562
No	9518 (93.3)	2997 (92.4)	12515 (93.1)	1	
Yes	684 (6.7)	245 (7.6)	929 (6.9)	0.96 [0.81 - 1.14]	

	TNFi n=10202	Baricitinib n=3242	Total n=13444	Baricitinib vs TNFi OR [95%CI]	p
SERMs (during baseline period, index date excluded), n (%)					0.4178
No	10168 (99.7)	3233 (99.7)	13401 (99.7)	1	
Yes	34 (0.3)	9 (0.3)	43 (0.3)	0.72 [0.33 - 1.59]	
Total hospital medical costs (in euros) per patient (during baseline period, index date excluded), n (%)					0.5001
For an increase of one unit	10202 (100.0)	3242 (100.0)	13444 (100.0)	1.00 [1.00 - 1.00]	
Total non-hospital medical costs (in euros) per patient (during baseline period, index date excluded), n (%)					0.2968
For an increase of one unit	10202 (100.0)	3242 (100.0)	13444 (100.0)	1.00 [1.00 - 1.00]	
Etanercept (during baseline period index date excluded), n (%)					<0.0001
No	9538 (93.5)	2883 (88.9)	12421 (92.4)	1	
Yes	664 (6.5)	359 (11.1)	1023 (7.6)	2.43 [2.09 - 2.83]	
Infliximab (during baseline period index date excluded), n (%)					<0.0001
No	10017 (98.2)	3150 (97.2)	13167 (97.9)	1	
Yes	185 (1.8)	92 (2.8)	277 (2.1)	1.95 [1.44 - 2.63]	

	TNFi n=10202	Baricitinib n=3242	Total n=13444	Baricitinib vs TNFi OR [95%CI]	p
Adalimumab (during baseline period index date excluded), n (%)					<0.0001
No	9794 (96.0)	2989 (92.2)	12783 (95.1)	1	
Yes	408 (4.0)	253 (7.8)	661 (4.9)	2.81 [2.35 - 3.36]	
Certolizumab pegol (during baseline period index date excluded), n (%)					<0.0001
No	10052 (98.5)	3085 (95.2)	13137 (97.7)	1	
Yes	150 (1.5)	157 (4.8)	307 (2.3)	4.86 [3.79 - 6.22]	
Golimumab (during baseline period index date excluded), n (%)					<0.0001
No	10056 (98.6)	3110 (95.9)	13166 (97.9)	1	
Yes	146 (1.4)	132 (4.1)	278 (2.1)	4.22 [3.26 - 5.47]	
Tocilizumab (during baseline period index date excluded), n (%)					<0.0001
No	9813 (96.2)	2736 (84.4)	12549 (93.3)	1	
Yes	389 (3.8)	506 (15.6)	895 (6.7)	5.18 [4.42 - 6.08]	
Abatacept (during baseline period index date excluded), n (%)					<0.0001
No	9712 (95.2)	2686 (82.9)	12398 (92.2)	1	
Yes	490 (4.8)	556 (17.1)	1046 (7.8)	4.35 [3.76 - 5.04]	

	TNFi n=10202	Baricitinib n=3242	Total n=13444	Baricitinib vs TNFi OR [95%CI]	p
Rituximab (during baseline period index date excluded), n (%)					<0.0001
No	10164 (99.6)	3120 (96.2)	13284 (98.8)	1	
Yes	38 (0.4)	122 (3.8)	160 (1.2)	15.41 [10.47 - 22.68]	
Anakinra (during baseline period index date excluded), n (%)					0.0007
No	10185 (99.8)	3226 (99.5)	13411 (99.8)	1	
Yes	17 (0.2)	16 (0.5)	33 (0.2)	3.54 [1.70 - 7.38]	
Sarilumab (during baseline period index date excluded), n (%)					<0.0001
No	10175 (99.7)	3195 (98.6)	13370 (99.4)	1	
Yes	27 (0.3)	47 (1.4)	74 (0.5)	5.74 [3.43 - 9.59]	
Vaccines (during baseline period index date excluded), n (%)					<0.0001
No	6406 (62.8)	2284 (70.5)	8690 (64.6)	1	
Yes	3796 (37.2)	958 (29.5)	4754 (35.4)	0.80 [0.73 - 0.88]	
Number of hospitalisations (during baseline period index date excluded), n (%)					0.0001

	TNFi n=10202	Baricitinib n=3242	Total n=13444	Baricitinib vs TNFi OR [95%CI]	p
0	5400 (52.9)	1649 (50.9)	7049 (52.4)	1	
1	3187 (31.2)	755 (23.3)	3942 (29.3)	0.86 [0.77 - 0.97]	
2	899 (8.8)	302 (9.3)	1201 (8.9)	0.95 [0.79 - 1.14]	
≥3	716 (7.0)	536 (16.5)	1252 (9.3)	1.31 [1.06 - 1.62]	
Number of Physician Office Visits (rheumatologist visits excluded) (during baseline period index date excluded), n (%)					0.0004
0	3777 (37.0)	1259 (38.8)	5036 (37.5)	1	
1	2244 (22.0)	768 (23.7)	3012 (22.4)	1.04 [0.93 - 1.17]	
[2-3]	2336 (22.9)	721 (22.2)	3057 (22.7)	0.91 [0.81 - 1.03]	
[4-6]	1205 (11.8)	345 (10.6)	1550 (11.5)	0.78 [0.67 - 0.92]	
>6	640 (6.3)	149 (4.6)	789 (5.9)	0.70 [0.56 - 0.87]	

Hosmer Lemeshow test : p =0.0041

AUC = 0.76

Abbreviations: AUC = Area Under the Curve; hosp = hospitalized; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer;
RA = rheumatoid arthritis; SERMs = selective estrogen receptor modulator; TNF = tumor necrosis factor; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

Table A.2. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), unmatched VTE cohort

	TNFi n = 10202	Baricitinib n = 3242
PS distribution		
Size (missing)	10202 (0)	3242 (0)
Mean (± SD)	0.20 (0.14)	0.37 (0.21)
Median	0.15	0.34
[p25% - p75%]	[0.11;0.23]	[0.18;0.53]
[Min - Max]	[0.02;0.96]	[0.02;0.97]
PS distribution, in categories, n (%)		
[0.00;0.05[	169 (1.7)	9 (0.3)
[0.05;0.10[	1754 (17.2)	130 (4.0)
[0.10;0.15[	2979 (29.2)	381 (11.8)
[0.15;0.20[	2087 (20.5)	436 (13.4)
[0.20;0.25[	987 (9.7)	308 (9.5)
[0.25;0.30[	501 (4.9)	215 (6.6)
[0.30;0.35[	357 (3.5)	186 (5.7)
[0.35;0.40[	293 (2.9)	192 (5.9)
[0.40;0.45[	259 (2.5)	211 (6.5)
[0.45;0.50[	241 (2.4)	217 (6.7)
[0.50;0.55[	183 (1.8)	238 (7.3)
[0.55;0.60[	133 (1.3)	201 (6.2)
[0.60;0.65[	82 (0.8)	139 (4.3)
[0.65;0.70[	49 (0.5)	109 (3.4)

	TNFi n = 10202		Baricitinib n = 3242	
[0.70;0.75[	49	(0.5)	71	(2.2)
[0.75;0.80[	36	(0.4)	79	(2.4)
[0.80;0.85[	22	(0.2)	67	(2.1)
[0.85;0.90[	14	(0.1)	35	(1.1)
[0.90;0.95[	5	(0.0)	12	(0.4)
[0.95;1.00]	2	(0.0)	6	(0.2)

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

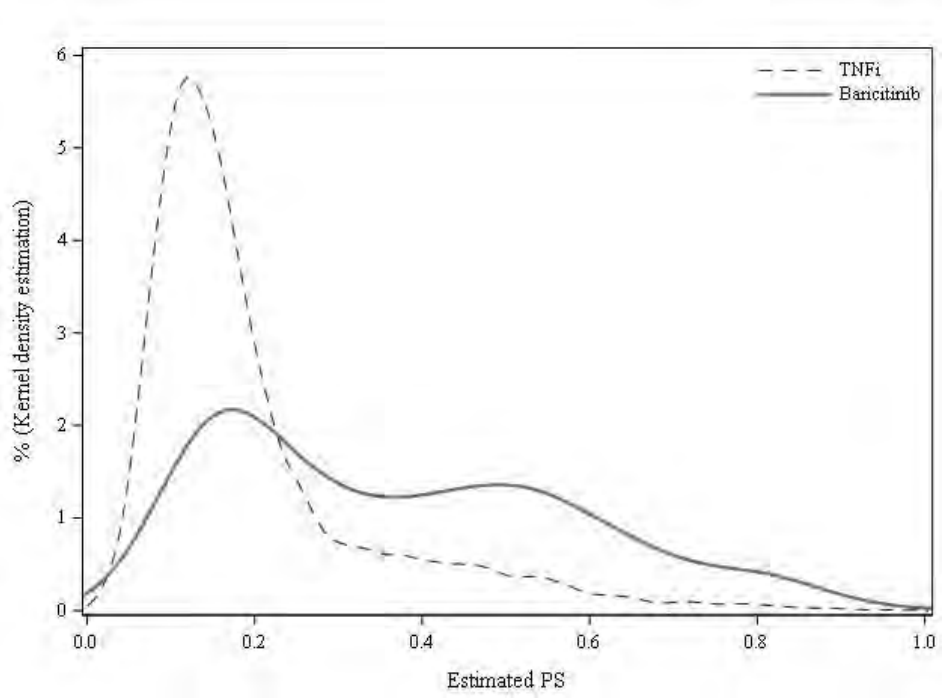

Figure A.1. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), unmatched VTE cohort

Table A.3. Number of matched TNFi by baricitinib, matched VTE cohort, *matching ratio 1:1 on PS ± 0.01* (pre-defined variables + variables with standardized difference ≥ 0.10)

	Baricitinib n = 2859
Number of matched TNFi by baricitinib, n (%)	
1	2859 (100.0)

Table A.4. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), matched VTE cohort, *matching ratio 1:1 on PS ± 0.01*

	TNFi n = 2859	Baricitinib n = 2859
PS distribution		
Size (missing)	2859 (0)	2859 (0)
Mean (± SD)	0.33 (0.19)	0.33 (0.19)
Median	0.29	0.29
[p25% - p75%]	[0.17;0.47]	[0.17;0.47]
[Min - Max]	[0.02;0.96]	[0.02;0.96]
PS distribution, in categories, n (%)		
[0.00;0.05[	9 (0.3)	9 (0.3)
[0.05;0.10[	130 (4.5)	130 (4.5)
[0.10;0.15[	381 (13.3)	381 (13.3)
[0.15;0.20[	435 (15.2)	436 (15.3)
[0.20;0.25[	309 (10.8)	308 (10.8)
[0.25;0.30[	212 (7.4)	215 (7.5)
[0.30;0.35[	189 (6.6)	186 (6.5)
[0.35;0.40[	192 (6.7)	192 (6.7)
[0.40;0.45[	209 (7.3)	211 (7.4)
[0.45;0.50[	219 (7.7)	214 (7.5)
[0.50;0.55[	183 (6.4)	183 (6.4)
[0.55;0.60[	133 (4.7)	141 (4.9)
[0.60;0.65[	82 (2.9)	77 (2.7)
[0.65;0.70[	49 (1.7)	49 (1.7)

	TNFi n = 2859		Baricitinib n = 2859	
[0.70;0.75[	49	(1.7)	46	(1.6)
[0.75;0.80[	36	(1.3)	35	(1.2)
[0.80;0.85[	22	(0.8)	26	(0.9)
[0.85;0.90[	14	(0.5)	13	(0.5)
[0.90;0.95[	4	(0.1)	5	(0.2)
[0.95;1.00]	2	(0.1)	2	(0.1)

AUC post matching = 0.53

Abbreviations: AUC = Area Under the Curve; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

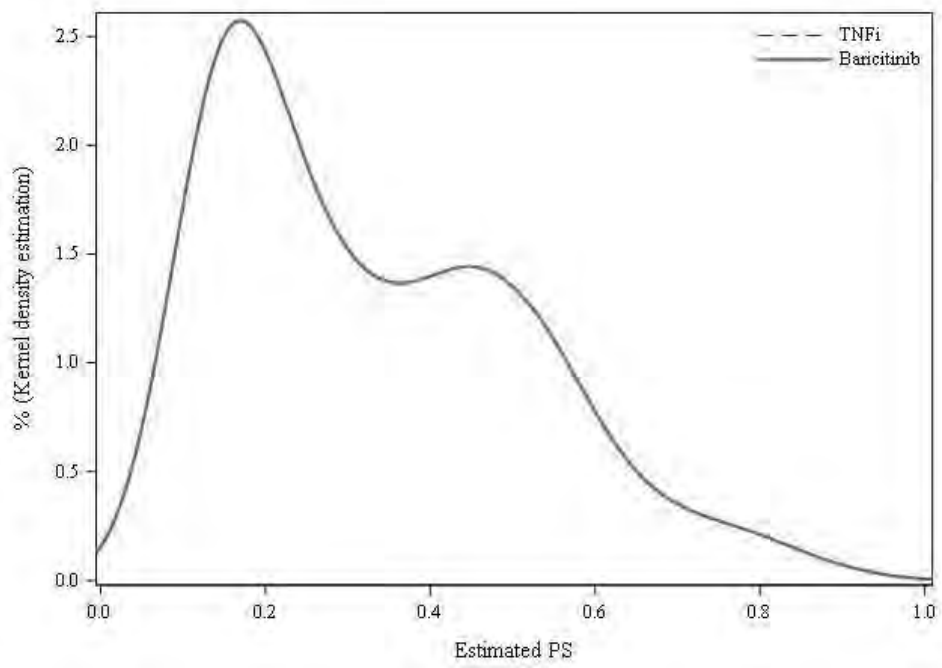

Figure A.2. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), matched VTE cohort, *matching ratio 1:1 on PS ± 0.01*

8.1.2 APPENDIX 2. PROPENSITY SCORE, MACE COHORT

Table A.5. Baricitinib vs TNFi PS model (pre-defined variables + variables with standardized difference ≥ 0.10), MACE cohort

	TNFi n=10175	Baricitinib n=3236	Total n=13411	Baricitinib vs TNFi OR [95%CI]	p
CIRAS score (during the year preceding index date)					0.0026
≤5.5	2110 (20.7)	819 (25.3)	2929 (21.8)	1	
]5.5-6.5]	2658 (26.1)	999 (30.9)	3657 (27.3)	0.98 [0.86 - 1.11]	
]6.5-7.5]	2193 (21.6)	747 (23.1)	2940 (21.9)	1.04 [0.90 - 1.20]	
>7.5	3214 (31.6)	671 (20.7)	3885 (29.0)	0.82 [0.70 - 0.95]	
Age (in years), in categories, n (%)					<0.0001
≥ 65	2748 (27.0)	1140 (35.2)	3888 (29.0)	1	
[18-30[	435 (4.3)	70 (2.2)	505 (3.8)	0.44 [0.32 - 0.60]	
[30-40[	1231 (12.1)	208 (6.4)	1439 (10.7)	0.47 [0.38 - 0.57]	
[40-50[	1742 (17.1)	461 (14.2)	2203 (16.4)	0.66 [0.57 - 0.78]	
[50-60[	2770 (27.2)	899 (27.8)	3669 (27.4)	0.82 [0.72 - 0.93]	
[60-65[	1249 (12.3)	458 (14.2)	1707 (12.7)	0.89 [0.77 - 1.03]	
Sex, n (%)					<0.0001
Female	7522 (73.9)	2593 (80.1)	10115 (75.4)	1	
Male	2653 (26.1)	643 (19.9)	3296 (24.6)	0.70 [0.63 - 0.78]	

	TNFi n=10175	Baricitinib n=3236	Total n=13411	Baricitinib vs TNFi OR [95%CI]	p
Unstable angina, Congestive Heart Failure, hospitalized, Ventricular arrhythmia, Cardiovascular revascularization procedure, CAD or TIA during baseline period, n (%)					0.2596
No	9778 (96.1)	3075 (95.0)	12853 (95.8)	1	
Yes	397 (3.9)	161 (5.0)	558 (4.2)	1.15 [0.90 - 1.45]	
Immune disorders during baseline period, n (%)					0.0788
No	9894 (97.2)	3113 (96.2)	13007 (97.0)	1	
Yes	281 (2.8)	123 (3.8)	404 (3.0)	1.24 [0.98 - 1.58]	
Diabete during the year preceding the year of index date, n (%)					0.4712
No	9300 (91.4)	2918 (90.2)	12218 (91.1)	1	
Yes	875 (8.6)	318 (9.8)	1193 (8.9)	0.94 [0.80 - 1.11]	
Current antihypertensives (during baseline period, index date excluded), n (%)					0.8046
No	7122 (70.0)	2051 (63.4)	9173 (68.4)	1	
Yes	3053 (30.0)	1185 (36.6)	4238 (31.6)	0.97 [0.78 - 1.21]	

	TNFi n=10175	Baricitinib n=3236	Total n=13411	Baricitinib vs TNFi OR [95%CI]	p
History antihypertensives 1 year before index date, baseline period excluded, n (%)					0.6497
0	7160 (70.4)	2060 (63.7)	9220 (68.7)	1	
1	307 (3.0)	100 (3.1)	407 (3.0)	0.99 [0.74 - 1.31]	
[2-4]	1438 (14.1)	568 (17.6)	2006 (15.0)	1.08 [0.85 - 1.36]	
≥ 5	1270 (12.5)	508 (15.7)	1778 (13.3)	0.98 [0.76 - 1.25]	
Lipid-lowering agents (during baseline period, index date excluded), n (%)					0.6747
No	8816 (86.6)	2686 (83.0)	11502 (85.8)	1	
Yes	1359 (13.4)	550 (17.0)	1909 (14.2)	1.03 [0.89 - 1.19]	
Aspirin (analgesic) (during baseline period, index date excluded), n (%)					0.7218
No	10059 (98.9)	3195 (98.7)	13254 (98.8)	1	
Yes	116 (1.1)	41 (1.3)	157 (1.2)	0.93 [0.63 - 1.38]	
Glucocorticosteroid (during baseline period index date excluded), n (%					<0.0001
0	3490 (34.3)	880 (27.2)	4370 (32.6)	1	
1	1578 (15.5)	434 (13.4)	2012 (15.0)	1.07 [0.93 - 1.23]	
[2-4]	2457 (24.1)	862 (26.6)	3319 (24.7)	1.38 [1.23 - 1.56]	
≥ 5	2650 (26.0)	1060 (32.8)	3710 (27.7)	1.65 [1.47 - 1.85]	

	TNFi n=10175	Baricitinib n=3236	Total n=13411	Baricitinib vs TNFi OR [95%CI]	p
Antiplatelet agents (during baseline period, index date excluded), n (%)					0.3620
No	9202 (90.4)	2846 (87.9)	12048 (89.8)	1	
Yes	973 (9.6)	390 (12.1)	1363 (10.2)	1.08 [0.91 - 1.28]	
Total hospital medical costs (in euros) per patient (during baseline period index date excluded), n (%)					0.2463
For an increase of one unit	10175 (100.0)	3236 (100.0)	13411 (100.0)	1.00 [1.00 - 1.00]	
Total non-hospital medical costs (in euros) per patient (during baseline period index date excluded), n (%)					0.5402
For an increase of one unit	10175 (100.0)	3236 (100.0)	13411 (100.0)	1.00 [1.00 - 1.00]	
Etanercept (during baseline period index date excluded), n (%)					<0.0001
No	9513 (93.5)	2878 (88.9)	12391 (92.4)	1	
Yes	662 (6.5)	358 (11.1)	1020 (7.6)	2.51 [2.16 - 2.92]	
Infliximab (during baseline period index date excluded), n (%)					<0.0001
No	9990 (98.2)	3144 (97.2)	13134 (97.9)	1	
Yes	185 (1.8)	92 (2.8)	277 (2.1)	2.40 [1.82 - 3.17]	

	TNFi n=10175	Baricitinib n=3236	Total n=13411	Baricitinib vs TNFi OR [95%CI]	p
Adalimumab (during baseline period index date excluded), n (%)					<0.0001
No	9767 (96.0)	2983 (92.2)	12750 (95.1)	1	
Yes	408 (4.0)	253 (7.8)	661 (4.9)	2.90 [2.42 - 3.47]	
Certolizumab pegol (during baseline period index date excluded), n (%)					<0.0001
No	10026 (98.5)	3079 (95.1)	13105 (97.7)	1	
Yes	149 (1.5)	157 (4.9)	306 (2.3)	5.06 [3.95 - 6.49]	
Golimumab (during baseline period index date excluded), n (%)					<0.0001
No	10029 (98.6)	3104 (95.9)	13133 (97.9)	1	
Yes	146 (1.4)	132 (4.1)	278 (2.1)	4.38 [3.38 - 5.68]	
Tocilizumab (during baseline period index date excluded), n (%)					<0.0001
No	9786 (96.2)	2733 (84.5)	12519 (93.3)	1	
Yes	389 (3.8)	503 (15.5)	892 (6.7)	5.73 [4.92 - 6.67]	
Abatacept (during baseline period index date excluded), n (%)					<0.0001
No	9685 (95.2)	2681 (82.8)	12366 (92.2)	1	

	TNFi n=10175	Baricitinib n=3236	Total n=13411	Baricitinib vs TNFi OR [95%CI]	p
Yes	490 (4.8)	555 (17.2)	1045 (7.8)	4.65 [4.03 - 5.36]	
Rituximab (during baseline period index date excluded), n (%)					<0.0001
No	10138 (99.6)	3114 (96.2)	13252 (98.8)	1	
Yes	37 (0.4)	122 (3.8)	159 (1.2)	15.71 [10.71 - 23.05]	
Anakinra (during baseline period index date excluded), n (%)					0.0009
No	10158 (99.8)	3220 (99.5)	13378 (99.8)	1	
Yes	17 (0.2)	16 (0.5)	33 (0.2)	3.50 [1.67 - 7.32]	
Sarilumab (during baseline period index date excluded), n (%)					<0.0001
No	10148 (99.7)	3189 (98.5)	13337 (99.4)	1	
Yes	27 (0.3)	47 (1.5)	74 (0.5)	5.87 [3.52 - 9.78]	
Methotrexate (during baseline period index date excluded), n (%)					0.0054
No	4092 (40.2)	1559 (48.2)	5651 (42.1)	1	
Yes	6083 (59.8)	1677 (51.8)	7760 (57.9)	0.87 [0.80 - 0.96]	
Leflunomid (during baseline period index date excluded), n (%)					0.0018

	TNFi n=10175	Baricitinib n=3236	Total n=13411	Baricitinib vs TNFi OR [95%CI]	p
No	9168 (90.1)	2827 (87.4)	11995 (89.4)	1	
Yes	1007 (9.9)	409 (12.6)	1416 (10.6)	1.26 [1.09 - 1.45]	
Vaccines (during baseline period index date excluded), n (%)					<0.0001
No	6393 (62.8)	2279 (70.4)	8672 (64.7)	1	
Yes	3782 (37.2)	957 (29.6)	4739 (35.3)	0.78 [0.71 - 0.86]	
Number of Physician Office Visits (rheumatologist visits excluded) during baseline period (Index date excluded), n (%)					<0.0001
0	3766 (37.0)	1256 (38.8)	5022 (37.4)	1	
1	2238 (22.0)	767 (23.7)	3005 (22.4)	1.03 [0.92 - 1.16]	
[2-3]	2328 (22.9)	719 (22.2)	3047 (22.7)	0.90 [0.80 - 1.01]	
[4-6]	1206 (11.9)	345 (10.7)	1551 (11.6)	0.77 [0.66 - 0.89]	
>6	637 (6.3)	149 (4.6)	786 (5.9)	0.68 [0.55 - 0.84]	
Hosmer Lemeshow test : p =0.0015					
AUC = 0.76					

Abbreviations: AUC = Area Under the Curve; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke;

Table A.6. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), unmatched MACE cohort

	TNFi n = 10175	Baricitinib n = 3236
PS distribution		
Size (missing)	10175 (0)	3236 (0)
Mean (± SD)	0.20 (0.14)	0.37 (0.21)
Median	0.15	0.34
[p25% - p75%]	[0.11;0.23]	[0.18;0.52]
[Min - Max]	[0.03;0.96]	[0.04;0.98]
PS distribution, in categories, n (%)		
[0.00;0.05[	69 (0.7)	5 (0.2)
[0.05;0.10[	1880 (18.5)	131 (4.0)
[0.10;0.15[	2893 (28.4)	384 (11.9)
[0.15;0.20[	2115 (20.8)	424 (13.1)
[0.20;0.25[	1008 (9.9)	314 (9.7)
[0.25;0.30[	510 (5.0)	218 (6.7)
[0.30;0.35[	353 (3.5)	187 (5.8)
[0.35;0.40[	281 (2.8)	179 (5.5)
[0.40;0.45[	235 (2.3)	236 (7.3)
[0.45;0.50[	261 (2.6)	230 (7.1)
[0.50;0.55[	193 (1.9)	225 (7.0)
[0.55;0.60[	123 (1.2)	201 (6.2)
[0.60;0.65[	80 (0.8)	151 (4.7)
[0.65;0.70[	60 (0.6)	79 (2.4)

	TNFi n = 10175		Baricitinib n = 3236	
[0.70;0.75[	29	(0.3)	67	(2.1)
[0.75;0.80[	36	(0.4)	78	(2.4)
[0.80;0.85[	27	(0.3)	74	(2.3)
[0.85;0.90[	14	(0.1)	36	(1.1)
[0.90;0.95[	5	(0.0)	13	(0.4)
[0.95;1.00]	3	(0.0)	4	(0.1)

Abbreviations: AUC = Area Under the Curve; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke;

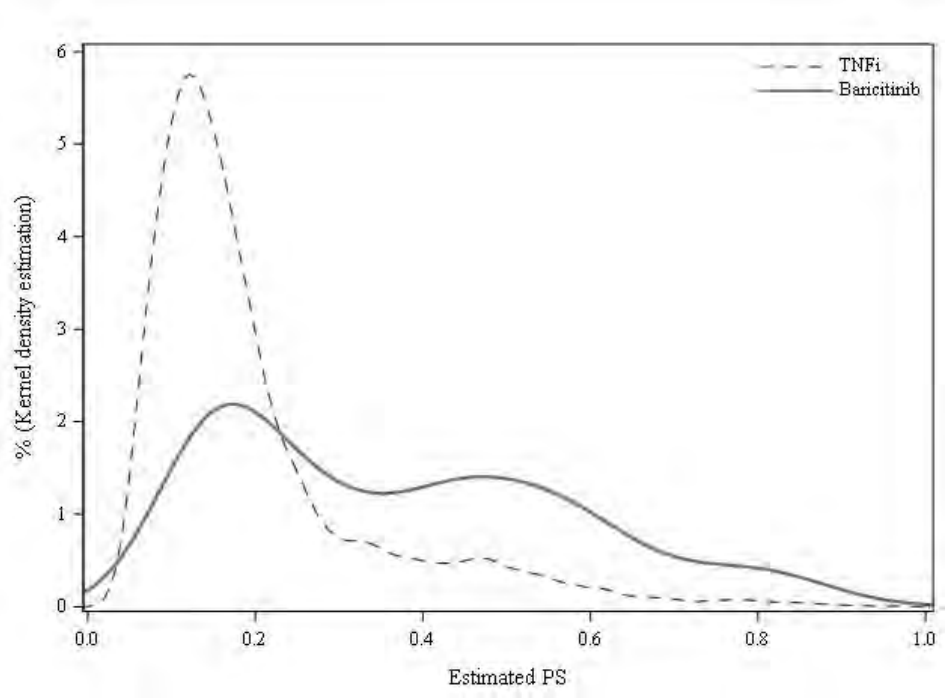

Figure A.3. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), unmatched MACE cohort

Table A.7. Number of matched TNFi by baricitinib, matched MACE cohort, matching ratio 1:1 on PS ± 0.01 (pre-defined variables + variables with standardized difference ≥ 0.10)

	Baricitinib n = 2864
Number of matched TNFi by baricitinib, n (%)	
1	2864 (100.0)

Table A.8. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), matched MACE cohort, *matching ratio 1:1 on PS ± 0.01*

	TNFi n = 2864	Baricitinib n = 2864
PS distribution		
Size (missing)	2864 (0)	2864 (0)
Mean (± SD)	0.33 (0.19)	0.33 (0.19)
Median	0.29	0.29
[p25% - p75%]	[0.17;0.47]	[0.17;0.47]
[Min - Max]	[0.04;0.96]	[0.04;0.97]
PS distribution, in categories, n (%)		
[0.00;0.05[	5 (0.2)	5 (0.2)
[0.05;0.10[	131 (4.6)	131 (4.6)
[0.10;0.15[	384 (13.4)	384 (13.4)
[0.15;0.20[	424 (14.8)	424 (14.8)
[0.20;0.25[	313 (10.9)	314 (11.0)
[0.25;0.30[	220 (7.7)	218 (7.6)
[0.30;0.35[	183 (6.4)	187 (6.5)
[0.35;0.40[	183 (6.4)	179 (6.3)
[0.40;0.45[	229 (8.0)	226 (7.9)
[0.45;0.50[	223 (7.8)	221 (7.7)
[0.50;0.55[	193 (6.7)	190 (6.6)
[0.55;0.60[	123 (4.3)	128 (4.5)
[0.60;0.65[	80 (2.8)	90 (3.1)
[0.65;0.70[	60 (2.1)	50 (1.7)
[0.70;0.75[	29 (1.0)	29 (1.0)

	TNFi n = 2864		Baricitinib n = 2864	
[0.75;0.80[	36	(1.3)	39	(1.4)
[0.80;0.85[	27	(0.9)	28	(1.0)
[0.85;0.90[	14	(0.5)	13	(0.5)
[0.90;0.95[	5	(0.2)	6	(0.2)
[0.95;1.00]	2	(0.1)	2	(0.1)

AUC post matching = 0.53

Abbreviations: AUC = Area Under the Curve; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke;

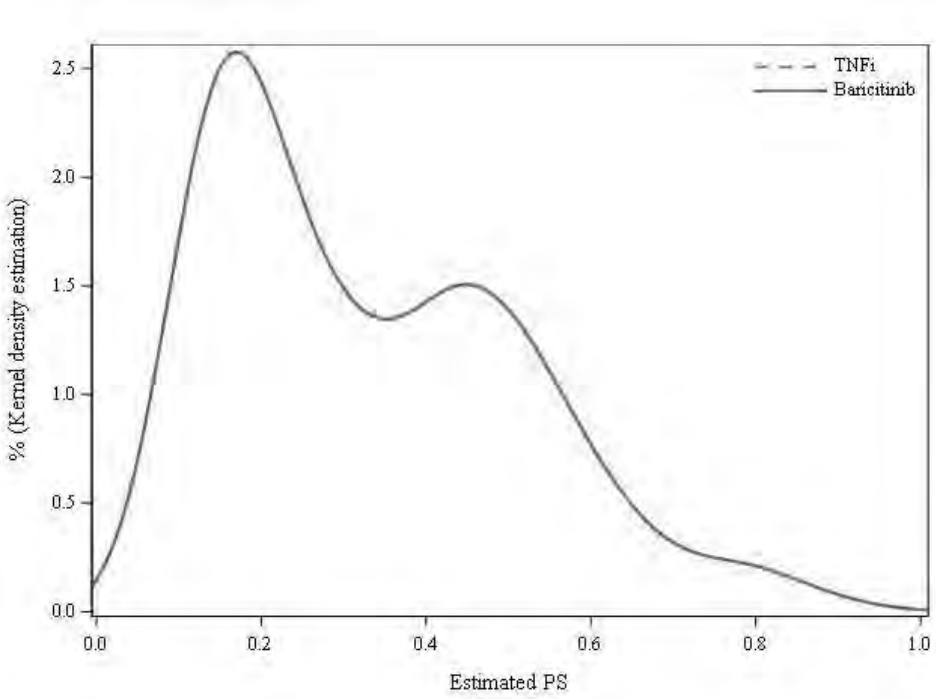

Figure A.4. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), matched MACE cohort, *matching ratio 1:1 on PS ± 0.01*

8.1.3 APPENDIX 3. PROPENSITY SCORE, SI COHORT

Table A.9. Baricitinib vs TNFi PS model (pre-defined variables + variables with standardized difference ≥ 0.10), SI cohort

	TNFi n=10451	Baricitinib n=3366	Total n=13817	Baricitinib vs TNFi OR [95%CI]	p
CIRAS score (during the year preceding index date)					0.0026
≤5.5	2220 (21.2)	892 (26.5)	3112 (22.5)	1	
]5.5-6.5]	2723 (26.1)	1031 (30.6)	3754 (27.2)	0.95 [0.84 - 1.07]	
]6.5-7.5]	2254 (21.6)	758 (22.5)	3012 (21.8)	0.99 [0.86 - 1.14]	
>7.5	3254 (31.1)	685 (20.4)	3939 (28.5)	0.79 [0.68 - 0.92]	
Sex, n (%)					<0.0001
Female	7672 (73.4)	2693 (80.0)	10365 (75.0)	1	
Male	2779 (26.6)	673 (20.0)	3452 (25.0)	0.70 [0.63 - 0.78]	
Age (in years), in categories, n (%)					<0.0001
≥ 65	2932 (28.1)	1238 (36.8)	4170 (30.2)	1	
[18-30[	436 (4.2)	70 (2.1)	506 (3.7)	0.43 [0.32 - 0.59]	
[30-40[	1234 (11.8)	208 (6.2)	1442 (10.4)	0.45 [0.37 - 0.55]	
[40-50[	1757 (16.8)	468 (13.9)	2225 (16.1)	0.65 [0.56 - 0.76]	
[50-60[	2813 (26.9)	911 (27.1)	3724 (27.0)	0.80 [0.71 - 0.90]	
[60-65[	1279 (12.2)	471 (14.0)	1750 (12.7)	0.88 [0.76 - 1.01]	
Immune disorders during baselin period, n (%)					0.0297

	TNFi n=10451	Baricitinib n=3366	Total n=13817	Baricitinib vs TNFi OR [95%CI]	p
No	10157 (97.2)	3232 (96.0)	13389 (96.9)	1	
Yes	294 (2.8)	134 (4.0)	428 (3.1)	1.29 [1.03 - 1.63]	
Diabete during the year preceding the year of index date, n (%)					0.7176
No	9519 (91.1)	3023 (89.8)	12542 (90.8)	1	
Yes	932 (8.9)	343 (10.2)	1275 (9.2)	0.97 [0.84 - 1.13]	
Treatment or hospitalisation for chronic lung disease during baseline period, n (%)					0.2369
No	8914 (85.3)	2774 (82.4)	11688 (84.6)	1	
Yes	1537 (14.7)	592 (17.6)	2129 (15.4)	1.07 [0.95 - 1.21]	
Treatment or hospitalisation for liver or pancreatic disease during baseline period, n (%)					0.9863
No	10393 (99.4)	3347 (99.4)	13740 (99.4)	1	
Yes	58 (0.5)	19 (0.6)	77 (0.6)	1.00 [0.57 - 1.77]	
TIA or Ischemic stroke during baseline period, n (%)					0.3169
No	10429 (99.8)	3354 (99.6)	13783 (99.8)	1	
Yes	22 (0.2)	12 (0.4)	34 (0.2)	1.49 [0.68 - 3.25]	

	TNFi n=10451	Baricitinib n=3366	Total n=13817	Baricitinib vs TNFi OR [95%CI]	p
Antibiotics (during baseline period, index date excluded), n (%)					0.1312
No	6471 (61.9)	1932 (57.4)	8403 (60.8)	1	
Yes	3980 (38.1)	1434 (42.6)	5414 (39.2)	1.07 [0.98 - 1.17]	
Glucocorticosteroid (during baseline period, index date excluded), n (%)					<0.0001
0	3562 (34.1)	903 (26.8)	4465 (32.3)	1	
1	1616 (15.5)	448 (13.3)	2064 (14.9)	1.06 [0.92 - 1.22]	
[2-4]	2516 (24.1)	898 (26.7)	3414 (24.7)	1.38 [1.23 - 1.56]	
≥ 5	2757 (26.4)	1117 (33.2)	3874 (28.0)	1.65 [1.47 - 1.85]	
Number of different cDMARD during baseline period (Index date excluded), n (%)					0.0233
0	2974 (28.5)	1129 (33.5)	4103 (29.7)	1	
1	6785 (64.9)	2043 (60.7)	8828 (63.9)	0.88 [0.79 - 0.97]	
[2-4]	692 (6.6)	194 (5.8)	886 (6.4)	0.96 [0.78 - 1.17]	
Total hospital medical costs (in euros) per patient (during baseline period index date excluded), n (%)					0.5255
For an increase of one unit	10451 (100.0)	3366 (100.0)	13817 (100.0)	1.00 [1.00 - 1.00]	

	TNFi n=10451	Baricitinib n=3366	Total n=13817	Baricitinib vs TNFi OR [95%CI]	p
Total non-hospital medical costs (in euros) per patient (during baseline period index date excluded), n (%)					0.3614
For an increase of one unit	10451 (100.0)	3366 (100.0)	13817 (100.0)	1.00 [1.00 - 1.00]	
Etanercept (during baseline period index date excluded), n (%)					<0.0001
No	9773 (93.5)	3002 (89.2)	12775 (92.5)	1	
Yes	678 (6.5)	364 (10.8)	1042 (7.5)	2.46 [2.11 - 2.85]	
Infliximab (during baseline period index date excluded), n (%)					<0.0001
No	10265 (98.2)	3269 (97.1)	13534 (98.0)	1	
Yes	186 (1.8)	97 (2.9)	283 (2.0)	2.49 [1.90 - 3.28]	
Adalimumab (during baseline period index date excluded), n (%)					<0.0001
No	10042 (96.1)	3104 (92.2)	13146 (95.1)	1	
Yes	409 (3.9)	262 (7.8)	671 (4.9)	2.95 [2.47 - 3.52]	
Certolizumab pegol (during baseline period index date excluded), n (%)					<0.0001
No	10298 (98.5)	3205 (95.2)	13503 (97.7)	1	

	TNFi n=10451	Baricitinib n=3366	Total n=13817	Baricitinib vs TNFi OR [95%CI]	p
Yes	153 (1.5)	161 (4.8)	314 (2.3)	4.96 [3.88 - 6.33]	
Golimumab baseline during period Index date excluded, n (%)					<0.0001
No	10300 (98.6)	3230 (96.0)	13530 (97.9)	1	
Yes	151 (1.4)	136 (4.0)	287 (2.1)	4.28 [3.32 - 5.53]	
Tocilizumab baseline during period Index date excluded, n (%)					<0.0001
No	10054 (96.2)	2846 (84.6)	12900 (93.4)	1	
Yes	397 (3.8)	520 (15.4)	917 (6.6)	5.72 [4.92 - 6.64]	
Abatacept (during baseline period index date excluded), n (%)					<0.0001
No	9936 (95.1)	2787 (82.8)	12723 (92.1)	1	
Yes	515 (4.9)	579 (17.2)	1094 (7.9)	4.55 [3.96 - 5.23]	
Rituximab (during baseline period index date excluded), n (%)					<0.0001
No	10414 (99.6)	3240 (96.3)	13654 (98.8)	1	
Yes	37 (0.3)	126 (3.7)	163 (1.2)	16.32 [11.14 - 23.89]	
Anakinra (during baseline period index date excluded), n (%)					0.0010

	TNFi n=10451	Baricitinib n=3366	Total n=13817	Baricitinib vs TNFi OR [95%CI]	p
No	10432 (99.8)	3349 (99.5)	13781 (99.7)	1	
Yes	19 (0.2)	17 (0.5)	36 (0.3)	3.27 [1.62 - 6.62]	
Sarilumab (during baseline period index date excluded), n (%)					<0.0001
No	10422 (99.7)	3317 (98.5)	13739 (99.4)	1	
Yes	29 (0.3)	49 (1.5)	78 (0.6)	5.76 [3.50 - 9.45]	
Leflunomid (during baseline period index date excluded), n (%)					<0.0001
No	9409 (90.0)	2941 (87.4)	12350 (89.4)	1	
Yes	1042 (9.97)	425 (12.6)	1467 (10.6)	1.38 [1.20 - 1.58]	
Vaccines (during baseline period index date excluded), n (%)					<0.0001
No	6534 (62.5)	2351 (69.8)	8885 (64.3)	1	
Yes	3917 (37.5)	1015 (30.2)	4932 (35.7)	0.78 [0.71 - 0.86]	
Number of Physician Office Visits (rheumatologist visits excluded) during baseline period (Index date excluded), n (%)					0.0001
0	3851 (36.8)	1296 (38.5)	5147 (37.3)	1	
1	2309 (22.1)	794 (23.6)	3103 (22.5)	1.02 [0.91 - 1.14]	

	TNFi n=10451	Baricitinib n=3366	Total n=13817	Baricitinib vs TNFi OR [95%CI]	p
[2-3]	2393 (22.9)	748 (22.2)	3141 (22.7)	0.90 [0.80 - 1.01]	
[4-6]	1244 (11.9)	366 (10.9)	1610 (11.7)	0.78 [0.67 - 0.90]	
>6	654 (6.3)	162 (4.8)	816 (5.9)	0.69 [0.56 - 0.85]	

Hosmer Lemeshow test : p =0.0013

AUC = 0.76

Abbreviations: AUC = Area Under the Curve; bDMARD = biologic disease-modifying antirheumatic drugs ; hosp = hospitalized; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer;
RA = rheumatoid arthritis; SERMs = selective estrogen receptor modulator; TNF = tumor necrosis factor; TNFi = tumor necrosis factor inhibitor; SI = Serious Infection.

Table A.10. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), unmatched SI cohort

	TNFi n = 10451	Baricitinib n = 3366
PS distribution		
Size (missing)	10451 (0)	3366 (0)
Mean (± SD)	0.20 (0.14)	0.37 (0.21)
Median	0.16	0.34
[p25% - p75%]	[0.11;0.23]	[0.19;0.53]
[Min - Max]	[0.03;0.96]	[0.04;0.98]
PS distribution, in categories, n (%)		
[0.00;0.05[	77 (0.7)	5 (0.1)
[0.05;0.10[	1876 (18.0)	144 (4.3)
[0.10;0.15[	2897 (27.7)	371 (11.0)
[0.15;0.20[	2151 (20.6)	435 (12.9)
[0.20;0.25[	1137 (10.9)	344 (10.2)
[0.25;0.30[	545 (5.2)	241 (7.2)
[0.30;0.35[	374 (3.6)	182 (5.4)
[0.35;0.40[	283 (2.7)	186 (5.5)
[0.40;0.45[	256 (2.4)	251 (7.5)
[0.45;0.50[	259 (2.5)	234 (7.0)
[0.50;0.55[	186 (1.8)	243 (7.2)
[0.55;0.60[	143 (1.4)	196 (5.8)
[0.60;0.65[	92 (0.9)	151 (4.5)
[0.65;0.70[	57 (0.5)	98 (2.9)
[0.70;0.75[	29 (0.3)	79 (2.3)

	TNFi n = 10451		Baricitinib n = 3366	
[0.75;0.80[	39	(0.4)	71	(2.1)
[0.80;0.85[	25	(0.2)	75	(2.2)
[0.85;0.90[	17	(0.2)	39	(1.2)
[0.90;0.95[	5	(0.0)	17	(0.5)
[0.95;1.00]	3	(0.0)	4	(0.1)

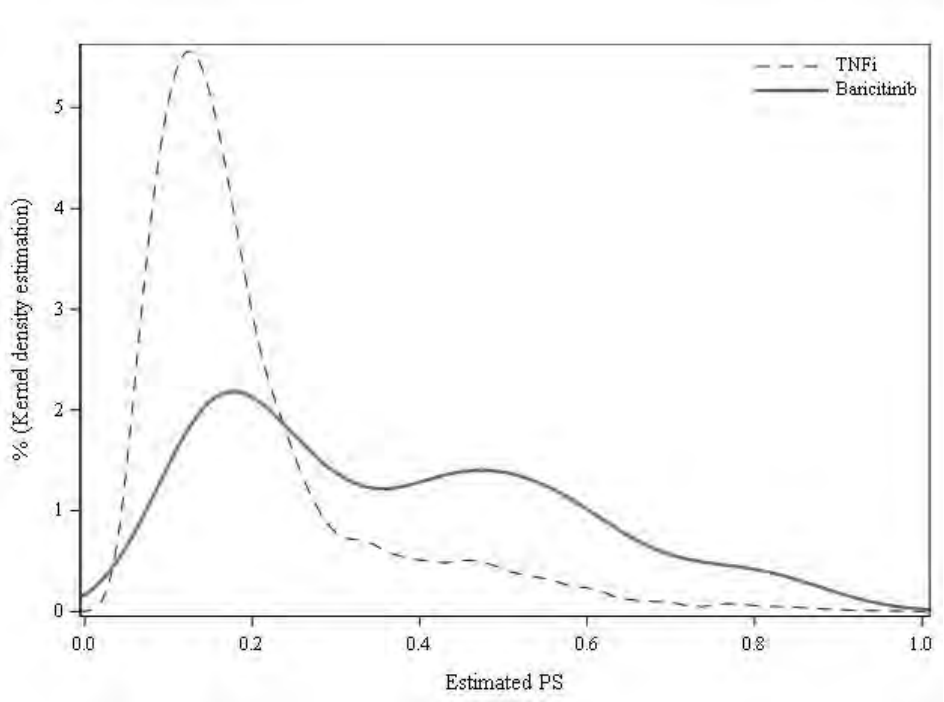

Figure A.5. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), unmatched SI cohort

Table A.11. Number of matched TNFi by baricitinib, matched SI cohort, *matching ratio 1:1 on PS ± 0.01* (pre-defined variables + variables with standardized difference ⩾ 0.10)

	Baricitinib n = 2979
Number of matched TNFi by baricitinib, n (%)	
1	2979 (100.0)

Table A.12. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), matched SI cohort, *matching ratio 1:1 on PS ± 0.01*

	TNFi n = 2979	Baricitinib n = 2979
PS distribution		
Size (missing)	2979 (0)	2979 (0)
Mean (± SD)	0.33 (0.19)	0.33 (0.19)
Median	0.29	0.29
[p25% - p75%]	[0.17;0.47]	[0.17;0.47]
[Min - Max]	[0.04;0.96]	[0.04;0.97]
PS distribution, in categories, n (%)		
[0.00;0.05[	5 (0.2)	5 (0.2)
[0.05;0.10[	144 (4.8)	144 (4.8)
[0.10;0.15[	371 (12.5)	371 (12.5)
[0.15;0.20[	435 (14.6)	435 (14.6)
[0.20;0.25[	344 (11.5)	344 (11.5)
[0.25;0.30[	241 (8.1)	241 (8.1)
[0.30;0.35[	182 (6.1)	182 (6.1)
[0.35;0.40[	184 (6.2)	186 (6.2)
[0.40;0.45[	242 (8.1)	240 (8.1)
[0.45;0.50[	236 (7.9)	234 (7.9)
[0.50;0.55[	186 (6.2)	189 (6.3)
[0.55;0.60[	143 (4.8)	139 (4.7)
[0.60;0.65[	92 (3.1)	97 (3.3)
[0.65;0.70[	57 (1.9)	54 (1.8)
[0.70;0.75[	29 (1.0)	30 (1.0)

	TNFi n = 2979		Baricitinib n = 2979	
[0.75;0.80[	39	(1.3)	39	(1.3)
[0.80;0.85[	25	(0.8)	26	(0.9)
[0.85;0.90[	17	(0.6)	14	(0.5)
[0.90;0.95[	5	(0.2)	7	(0.2)
[0.95;1.00]	2	(0.1)	2	(0.1)

AUC post matching = 0.53

Abbreviations: AUC = Area Under the Curve; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor; SI = Serious infections

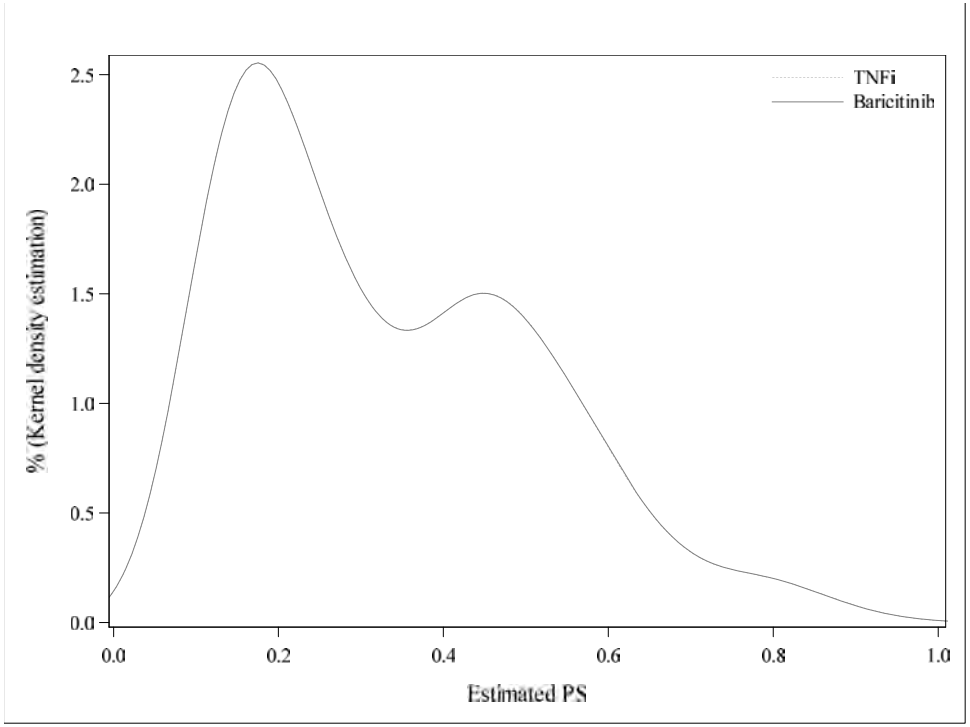

Figure A.6. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), matched VTE cohort, *matching ratio 1:1 on PS ± 0.01*

8.1.4 APPENDIX 4. PROPENSITY SCORE, TB COHORT

Table A.13. Baricitinib vs TNFi PS model (pre-defined variables + variables with standardized difference ≥ 0.10), TB cohort

	TNFi n=10512	Baricitinib n=3398	Total n=13910	Baricitinib vs TNFi OR [95%CI]	p
CIRAS score (during the year preceding index date)					0.0023
≤5.5	2240 (21.3)	905 (26.6)	3145 (22.6)	1	
]5.5-6.5]	2746 (26.1)	1041 (30.6)	3787 (27.2)	0.95 [0.84 - 1.07]	
]6.5-7.5]	2263 (21.5)	763 (22.5)	3026 (21.8)	0.99 [0.86 - 1.13]	
>7.5	3263 (31.0)	689 (20.3)	3952 (28.4)	0.79 [0.68 - 0.91]	
Sex, n (%)					<0.0001
Female	7717 (73.4)	2712 (79.8)	10429 (75.0)	1	
Male	2795 (26.6)	686 (20.2)	3481 (25.0)	0.71 [0.64 - 0.78]	
Age (in years), in categories, n (%)					<0.0001
≥ 65	2970 (28.3)	1259 (37.1)	4229 (30.4)	1	
[18-30[	436 (4.1)	70 (2.1)	506 (3.6)	0.43 [0.32 - 0.59]	
[30-40[	1235 (11.7)	208 (6.1)	1443 (10.4)	0.46 [0.37 - 0.55]	
[40-50[	1760 (16.7)	469 (13.8)	2229 (16.0)	0.65 [0.56 - 0.76]	
[50-60[	2822 (26.8)	919 (27.0)	3741 (26.9)	0.80 [0.71 - 0.91]	
[60-65[	1289 (12.3)	473 (13.9)	1762 (12.7)	0.87 [0.75 - 1.00]	
Immune disorders during baseline period, n (%)					0.0433

	TNFi n=10512	Baricitinib n=3398	Total n=13910	Baricitinib vs TNFi OR [95%CI]	p
No	10215 (97.2)	3263 (96.0)	13478 (96.9)	1	
Yes	297 (2.8)	135 (4.0)	432 (3.1)	1.27 [1.01 - 1.60]	
Diabete during the year preceding the year of index date, n (%)					0.6186
No	9567 (91.0)	3050 (89.8)	12617 (90.7)	1	
Yes	945 (9.0)	348 (10.2)	1293 (9.3)	0.96 [0.83 - 1.12]	
Treatment or hospitalisation for chronic lung disease during baseline period, n (%)					0.2710
No	8961 (85.2)	2797 (82.3)	11758 (84.5)	1	
Yes	1551 (14.8)	601 (17.7)	2152 (15.5)	1.07 [0.95 - 1.20]	
Treatment or hospitalisation for liver or pancreatic disease during baseline period, n (%)					0.9967
No	10454 (99.4)	3379 (99.4)	13833 (99.4)	1	
Yes	58 (0.5)	19 (0.6)	77 (0.5)	1.00 [0.57 - 1.76]	
TIA or Ischemic stroke during baseline period, n (%)					0.2439
No	10490 (99.8)	3385 (99.6)	13875 (99.7)	1	
Yes	22 (0.2)	13 (0.4)	35 (0.2)	1.57 [0.73 - 3.36]	

	TNFi n=10512	Baricitinib n=3398	Total n=13910	Baricitinib vs TNFi OR [95%CI]	p
Antibiotics (during baseline period, index date excluded), n (%)					0.1350
No	6482 (61.7)	1940 (57.1)	8422 (60.5)	1	
Yes	4030 (38.3)	1458 (42.9)	5488 (39.5)	1.07 [0.98 - 1.17]	
Glucocorticosteroid (during baseline period, index date excluded), n (%)					<0.0001
No	3579 (34.0)	908 (26.7)	4487 (32.3)	1	
Yes	1627 (15.5)	452 (13.3)	2079 (14.9)	1.06 [0.92 - 1.22]	
[2-4]	2529 (24.1)	902 (26.5)	3431 (24.7)	1.38 [1.23 - 1.55]	
≥ 5	2777 (26.4)	1136 (33.4)	3913 (28.1)	1.66 [1.48 - 1.86]	
Number of different cDMARD during baseline period (Index date excluded), n (%)					0.0191
0	2998 (28.5)	1144 (33.7)	4142 (29.8)	1	
1	6820 (64.9)	2060 (60.6)	8880 (63.8)	0.87 [0.79 - 0.96]	
[2-4]	694 (6.6)	194 (5.7)	888 (6.4)	0.95 [0.78 - 1.16]	
Total hospital medical costs (in euros) per patient (during baseline period, index date excluded), n (%)					0.2157
For an increase of one unit	10512 (100.0)	3398 (100.0)	13910 (100.0)	1.00 [1.00 - 1.00]	

	TNFi n=10512	Baricitinib n=3398	Total n=13910	Baricitinib vs TNFi OR [95%CI]	p
Total non-hospital medical costs (in euros) per patient (during baseline period index date excluded), n (%)					0.4506
For an increase of one unit	10512 (100.0)	3398 (100.0)	13910 (100.0)	1.00 [1.00 - 1.00]	
Etanercept (during baseline period index date excluded), n (%)					<0.0001
No	9834 (93.6)	3030 (89.2)	12864 (92.5)	1	
Yes	678 (6.4)	368 (10.8)	1046 (7.5)	2.50 [2.15 - 2.90]	
Infliximab (during baseline period index date excluded), n (%)					<0.0001
No	10322 (98.2)	3300 (97.1)	13622 (97.9)	1	
Yes	190 (1.8)	98 (2.9)	288 (2.1)	2.42 [1.85 - 3.17]	
Adalimumab (during baseline period index date excluded), n (%)					<0.0001
No	10100 (96.1)	3133 (92.2)	13233 (95.1)	1	
Yes	412 (3.9)	265 (7.8)	677 (4.9)	2.97 [2.49 - 3.54]	
Certolizumab pegol baseline during period Index date excluded, n (%)					<0.0001
No	10357 (98.5)	3237 (95.3)	13594 (97.7)	1	

	TNFi n=10512	Baricitinib n=3398	Total n=13910	Baricitinib vs TNFi OR [95%CI]	p
Yes	155 (1.5)	161 (4.7)	316 (2.3)	4.92 [3.85 - 6.28]	
Golimumab (during baseline period index date excluded), n (%)					<0.0001
No	10361 (98.6)	3262 (96.0)	13623 (97.9)	1	
Yes	151 (1.4)	136 (4.0)	287 (2.1)	4.31 [3.34 - 5.56]	
Tocilizumab (during baseline period index date excluded), n (%)					<0.0001
No	10112 (96.2)	2873 (84.5)	12985 (93.4)	1	
Yes	400 (3.8)	525 (15.5)	925 (6.6)	5.70 [4.91 - 6.62]	
Abatacept (during baseline period index date excluded), n (%)					<0.0001
No	9995 (95.1)	2810 (82.7)	12805 (92.1)	1	
Yes	517 (4.9)	588 (17.3)	1105 (7.9)	4.61 [4.01 - 5.29]	
Rituximab (during baseline period index date excluded), n (%)					<0.0001
No	10474 (99.6)	3270 (96.2)	13744 (98.8)	1	
Yes	38 (0.4)	128 (3.8)	166 (1.2)	15.91 [10.92 - 23.19]	
Anakinra (during baseline period index date excluded), n (%)					0.0010

	TNFi n=10512	Baricitinib n=3398	Total n=13910	Baricitinib vs TNFi OR [95%CI]	p
No	10493 (99.8)	3381 (99.5)	13874 (99.7)	1	
Yes	19 (0.2)	17 (0.5)	36 (0.3)	3.27 [1.62 - 6.61]	
Sarilumab (during baseline period index date excluded), n (%)					<0.0001
No	10483 (99.7)	3349 (98.6)	13832 (99.4)	1	
Yes	29 (0.3)	49 (1.4)	78 (0.6)	5.76 [3.51 - 9.45]	
Leflunomid (during baseline period index date excluded), n (%)					<0.0001
No	9465 (90.0)	2968 (87.3)	12433 (89.4)	1	
Yes	1047 (9.96)	430 (12.7)	1477 (10.6)	1.39 [1.21 - 1.59]	
Vaccines (during baseline period index date excluded), n (%)					<0.0001
No	6572 (62.5)	2373 (69.8)	8945 (64.3)	1	
Yes	3940 (37.5)	1025 (30.2)	4965 (35.7)	0.79 [0.72 - 0.86]	
Number of Physician Office Visits (rheumatologist visits excluded) during baseline period (Index date excluded), n (%)					<0.0001
0	3861 (36.7)	1301 (38.3)	5162 (37.1)	1	
1	2316 (22.0)	801 (23.6)	3117 (22.4)	1.03 [0.92 - 1.15]	

	TNFi n=10512	Baricitinib n=3398	Total n=13910	Baricitinib vs TNFi OR [95%CI]	p
[2-3]	2411 (22.9)	762 (22.4)	3173 (22.8)	0.90 [0.81 - 1.01]	
[4-6]	1257 (12.0)	371 (10.9)	1628 (11.7)	0.78 [0.67 - 0.90]	
>6	667 (6.3)	163 (4.8)	830 (6.0)	0.68 [0.55 - 0.83]	

Hosmer Lemeshow test : p =0.0009

AUC = 0.76

Abbreviations: AUC = Area Under the Curve; bDMARD = biologic disease-modifying antirheumatic drugs ; hosp = hospitalized; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer;
RA = rheumatoid arthritis; SERMs = selective estrogen receptor modulator; TNF = tumor necrosis factor; TNFi = tumor necrosis factor inhibitor; TB = Tuberculosis

Table A.14. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), unmatched TB cohort

	TNFi n = 10512	Baricitinib n = 3398
PS distribution		
Size (missing)	10512 (0)	3398 (0)
Mean (± SD)	0.20 (0.14)	0.37 (0.21)
Median	0.16	0.34
[p25% - p75%]	[0.11;0.23]	[0.19;0.53]
[Min - Max]	[0.03;0.96]	[0.04;0.98]
PS distribution, in categories, n (%)		
[0.00;0.05[	72 (0.7)	6 (0.2)
[0.05;0.10[	1880 (17.9)	143 (4.2)
[0.10;0.15[	2924 (27.8)	373 (11.0)
[0.15;0.20[	2174 (20.7)	445 (13.1)
[0.20;0.25[	1121 (10.7)	338 (9.9)
[0.25;0.30[	551 (5.2)	236 (6.9)
[0.30;0.35[	381 (3.6)	189 (5.6)
[0.35;0.40[	290 (2.8)	181 (5.3)
[0.40;0.45[	257 (2.4)	262 (7.7)
[0.45;0.50[	258 (2.5)	242 (7.1)
[0.50;0.55[	191 (1.8)	238 (7.0)
[0.55;0.60[	142 (1.4)	197 (5.8)
[0.60;0.65[	92 (0.9)	160 (4.7)

	TNFi n = 10512		Baricitinib n = 3398	
[0.65;0.70[	58	(0.6)	98	(2.9)
[0.70;0.75[	28	(0.3)	80	(2.4)
[0.75;0.80[	43	(0.4)	81	(2.4)
[0.80;0.85[	25	(0.2)	71	(2.1)
[0.85;0.90[	17	(0.2)	36	(1.1)
[0.90;0.95[	5	(0.0)	18	(0.5)
[0.95;1.00]	3	(0.0)	4	(0.1)

Abbreviations: AUC = Area Under the Curve; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor; TB = Tuberculosis

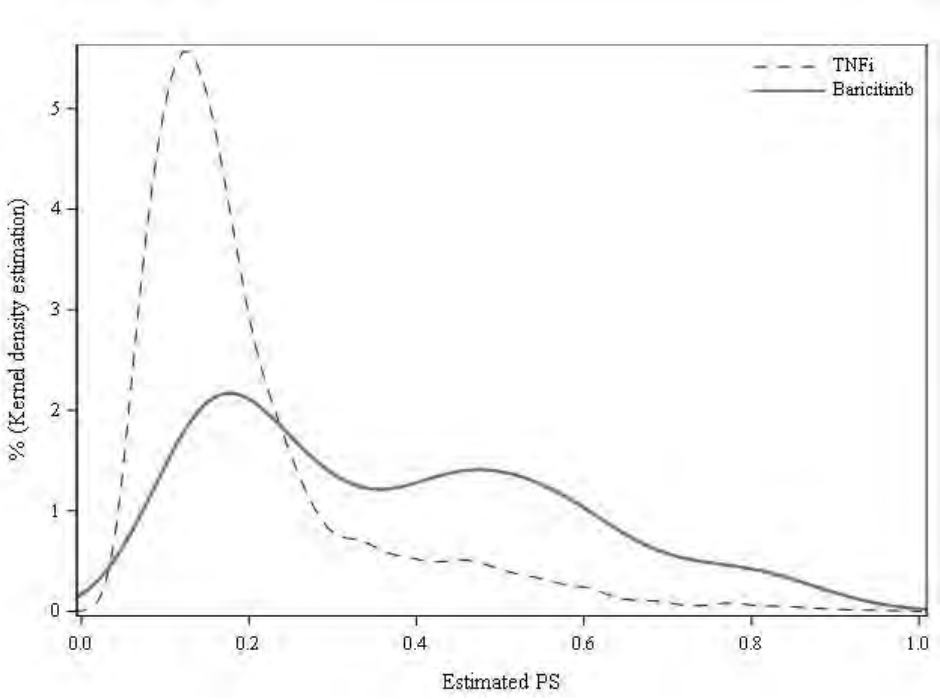

Figure A.7. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), unmatched TB cohort

Table A.15. Number of matched TNFi by baricitinib, matched TB cohort, *matching ratio 1:1 on PS ± 0.01* (pre-defined variables + variables with standardized difference ≥ 0.10)

	Baricitinib n = 3005
Number of matched TNFi by baricitinib, n (%)	
1	3005 (100.0)

Table A.16. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), matched TB cohort, *matching ratio 1:1 on PS ± 0.01*

	TNFi n = 3005	Baricitinib n = 3005
PS distribution		
Size (missing)	3005 (0)	3005 (0)
Mean (± SD)	0.33 (0.19)	0.33 (0.19)
Median	0.29	0.29
[p25% - p75%]	[0.17;0.47]	[0.17;0.47]
[Min - Max]	[0.04;0.96]	[0.04;0.97]
PS distribution, in categories, n (%)		
[0.00;0.05[	6 (0.2)	6 (0.2)
[0.05;0.10[	143 (4.8)	143 (4.8)
[0.10;0.15[	372 (12.4)	373 (12.4)
[0.15;0.20[	446 (14.8)	445 (14.8)
[0.20;0.25[	338 (11.2)	338 (11.2)
[0.25;0.30[	235 (7.8)	236 (7.9)
[0.30;0.35[	190 (6.3)	189 (6.3)
[0.35;0.40[	181 (6.0)	181 (6.0)
[0.40;0.45[	251 (8.4)	254 (8.5)
[0.45;0.50[	240 (8.0)	239 (8.0)
[0.50;0.55[	191 (6.4)	187 (6.2)
[0.55;0.60[	142 (4.7)	139 (4.6)
[0.60;0.65[	92 (3.1)	99 (3.3)
[0.65;0.70[	58 (1.9)	56 (1.9)
[0.70;0.75[	28 (0.9)	30 (1.0)

	TNFi n = 3005		Baricitinib n = 3005	
[0.75;0.80[	43	(1.4)	40	(1.3)
[0.80;0.85[	25	(0.8)	26	(0.9)
[0.85;0.90[	17	(0.6)	16	(0.5)
[0.90;0.95[	5	(0.2)	6	(0.2)
[0.95;1.00]	2	(0.1)	2	(0.1)

AUC post matching = 0.53

Abbreviations: AUC = Area Under the Curve; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor; TB = Tuberculosis

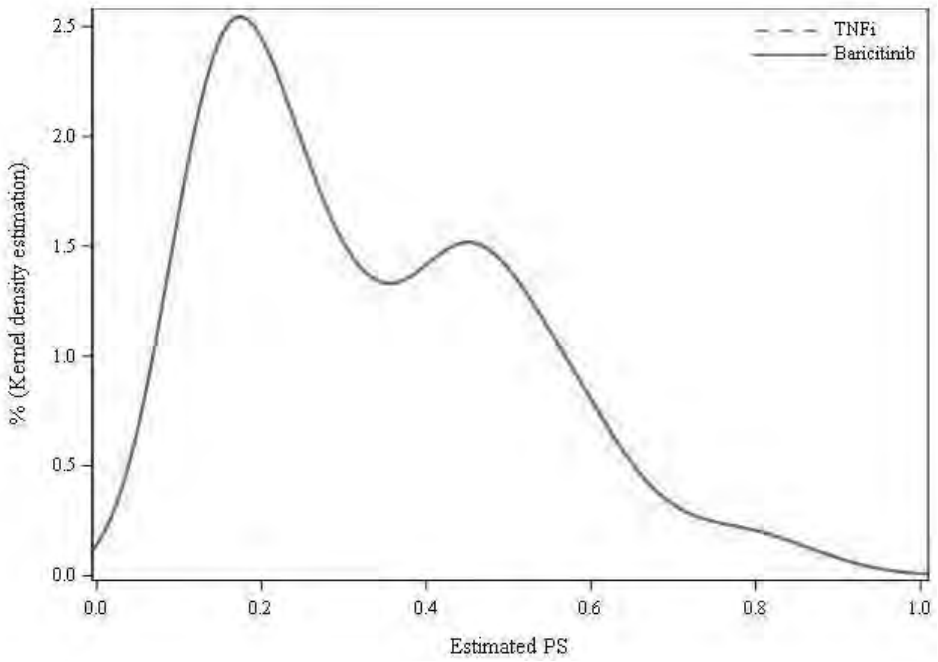

Figure A.8. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), matched TB cohort, *matching ratio 1:1 on PS ± 0.01*

8.2 PROPENSITY SCORE, SENSITIVE ANALYSES: ANALYSIS BY BDMARD STATUS

8.2.1 APPENDIX 5. PROPENSITY SCORE, VTE COHORT

Table A.17. Baricitinib vs TNFi PS model (pre-defined variables + variables with standardized difference ≥ 0.10), bDMARD in details, VTE cohort

	TNFi n=10202		Baricitinib n=3242		Total n=13444		Baricitinib vs TNFi OR [95%CI]		p
CIRAS score (during the year preceding index date)									0.0045
≤5.5	2122	(20.8)	823	(25.4)	2945	(21.9)	1		
]5.5-6.5]	2663	(26.1)	1002	(30.9)	3665	(27.3)	0.99	[0.87 - 1.13]	
]6.5-7.5]	2201	(21.6)	746	(23.0)	2947	(21.9)	1.05	[0.90 - 1.22]	
>7.5	3216	(31.5)	671	(20.7)	3887	(28.9)	0.83	[0.71 - 0.97]	
Age (in years), in categories, n (%)									<0.0001
≥ 65	2766	(27.1)	1142	(35.2)	3908	(29.1)	1		
[18-30[	435	(4.3)	70	(2.2)	505	(3.8)	0.47	[0.34 - 0.64]	
[30-40[	1231	(12.1)	208	(6.4)	1439	(10.7)	0.48	[0.39 - 0.59]	
[40-50[	1743	(17.1)	462	(14.3)	2205	(16.4)	0.67	[0.57 - 0.79]	
[50-60[	2776	(27.2)	899	(27.7)	3675	(27.3)	0.82	[0.72 - 0.93]	
[60-65[	1251	(12.3)	461	(14.2)	1712	(12.7)	0.91	[0.79 - 1.06]	
Sex, n (%)									<0.0001
Female	7534	(73.8)	2597	(80.1)	10131	(75.4)	1		

	TNFi n=10202	Baricitinib n=3242	Total n=13444	Baricitinib vs TNFi OR [95%CI]	p
Male	2668 (26.2)	645 (19.9)	3313 (24.6)	0.72 [0.65 - 0.81]	
Cancer during baseline period, n (%)					0.5230
No	9883 (96.9)	3142 (96.9)	13025 (96.9)	1	
Yes	319 (3.1)	100 (3.1)	419 (3.1)	0.92 [0.72 - 1.18]	
Atrial arrhythmia/fibrillation, Ventricular arrhythmia or Congestive Heart Failure, hospitalized during baseline period, n (%)					0.3859
No	10064 (98.6)	3179 (98.1)	13243 (98.5)	1	
Yes	138 (1.4)	63 (1.9)	201 (1.5)	1.16 [0.83 - 1.64]	
Immune disorders during baseline period, n (%)					0.1853
No	9920 (97.2)	3119 (96.2)	13039 (97.0)	1	
Yes	282 (2.8)	123 (3.8)	405 (3.0)	1.18 [0.92 - 1.51]	
Diabete during the year preceding the year of index date, n (%)					0.5767
No	9318 (91.3)	2921 (90.1)	12239 (91.0)	1	
Yes	884 (8.7)	321 (9.9)	1205 (9.0)	0.96 [0.82 - 1.12]	

	TNFi n=10202		Baricitinib n=3242		Total n=13444		Baricitinib vs TNFi OR [95%CI]		p
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date), n (%)									0.0267
No	10058	(98.6)	3234	(99.8)	13292	(98.9)	1		
Yes	144	(1.4)	8	(0.3)	152	(1.1)	0.43	[0.20 - 0.91]	
≥1 recent surgery, n (%)									0.3721
No	9762	(95.7)	3118	(96.2)	12880	(95.8)	1		
Yes	440	(4.3)	124	(3.8)	564	(4.2)	1.12	[0.88 - 1.42]	
≥1 recent Trauma, n (%)									0.8110
No	10135	(99.3)	3221	(99.4)	13356	(99.3)	1		
Yes	67	(0.7)	21	(0.7)	88	(0.7)	0.94	[0.54 - 1.61]	
Aspirin (analgesic) (during baseline period, index date excluded), n (%)									0.7816
No	10085	(98.9)	3201	(98.7)	13286	(98.8)	1		
Yes	117	(1.1)	41	(1.3)	158	(1.2)	0.95	[0.64 - 1.41]	
Anticoagulant (during baseline period, index date excluded), n (%)									0.9829
No	9737	(95.4)	3100	(95.6)	12837	(95.5)	1		
Yes	465	(4.6)	142	(4.4)	607	(4.5)	1.00	[0.80 - 1.25]	

	TNFi n=10202	Baricitinib n=3242	Total n=13444	Baricitinib vs TNFi OR [95%CI]	p
Glucocorticosteroid (during baseline period, index date excluded), n (%)					<0.0001
0	3493 (34.2)	883 (27.2)	4376 (32.5)	1	
1	1585 (15.5)	435 (13.4)	2020 (15.0)	1.07 [0.93 - 1.23]	
[2-4]	2466 (24.2)	865 (26.7)	3331 (24.8)	1.38 [1.22 - 1.56]	
≥ 5	2658 (26.1)	1059 (32.7)	3717 (27.6)	1.67 [1.49 - 1.88]	
Methotrexate (during baseline period, index date excluded), n (%)					<0.0001
0	4108 (40.3)	1563 (48.2)	5671 (42.2)	1	
1	506 (5.0)	155 (4.8)	661 (4.9)	0.93 [0.75 - 1.15]	
[2-4]	2200 (21.6)	685 (21.1)	2885 (21.5)	0.93 [0.83 - 1.05]	
≥ 5	3388 (33.2)	839 (25.9)	4227 (31.4)	0.75 [0.67 - 0.83]	
Oral Contraceptives (during baseline period, index date excluded), n (%)					0.3231
No	9429 (92.4)	3085 (95.2)	12514 (93.1)	1	
Yes	773 (7.6)	157 (4.8)	930 (6.9)	0.90 [0.73 - 1.11]	
HRT (during baseline period, index date excluded), n (%)					0.6852

	TNFi n=10202	Baricitinib n=3242	Total n=13444	Baricitinib vs TNFi OR [95%CI]	p
No	9518 (93.3)	2997 (92.4)	12515 (93.1)	1	
Yes	684 (6.7)	245 (7.6)	929 (6.9)	0.97 [0.81 - 1.15]	
SERMs (during baseline period, index date excluded), n (%)					0.4382
No	10168 (99.7)	3233 (99.7)	13401 (99.7)	1	
Yes	34 (0.3)	9 (0.3)	43 (0.3)	0.73 [0.33 - 1.61]	
Total hospital medical costs (in euros) per patient (during baseline period, index date excluded), n (%)					0.4679
For an increase of one unit	10202 (100.0)	3242 (100.0)	13444 (100.0)	1.00 [1.00 - 1.00]	
Total non-hospital medical costs (in euros) per patient (during baseline period, index date excluded), n (%)					0.7968
For an increase of one unit	10202 (100.0)	3242 (100.0)	13444 (100.0)	1.00 [1.00 - 1.00]	
Etanercept (during baseline period index date excluded), n (%)					<0.0001
No	9538 (93.5)	2883 (88.9)	12421 (92.4)	1	
Yes	664 (6.5)	359 (11.1)	1023 (7.6)	2.46 [2.12 - 2.87]	

	TNFi n=10202		Baricitinib n=3242		Total n=13444		Baricitinib vs TNFi OR [95%CI]		p
Infliximab (during baseline period index date excluded), n (%)									<0.0001
No	10017	(98.2)	3150	(97.2)	13167	(97.9)	1		
Yes	185	(1.8)	92	(2.8)	277	(2.1)	1.97	[1.46 - 2.67]	
Adalimumab (during baseline period index date excluded), n (%)									<0.0001
No	9794	(96.0)	2989	(92.2)	12783	(95.1)	1		
Yes	408	(4.0)	253	(7.8)	661	(4.9)	2.88	[2.40 - 3.45]	
Certolizumab pegol (during baseline period index date excluded), n (%)									<0.0001
No	10052	(98.5)	3085	(95.2)	13137	(97.7)	1		
Yes	150	(1.5)	157	(4.8)	307	(2.3)	4.90	[3.82 - 6.29]	
Golimumab (during baseline period index date excluded), n (%)									<0.0001
No	10056	(98.6)	3110	(95.9)	13166	(97.9)	1		
Yes	146	(1.4)	132	(4.1)	278	(2.1)	4.32	[3.33 - 5.61]	
Tocilizumab (during baseline period index date excluded), n (%)									<0.0001

	TNFi n=10202		Baricitinib n=3242		Total n=13444		Baricitinib vs TNFi OR [95%CI]		p
No	9813	(96.2)	2736	(84.4)	12549	(93.3)	1		
Yes	389	(3.8)	506	(15.6)	895	(6.7)	5.24	[4.47 - 6.15]	
Abatacept (during baseline period index date excluded), n (%)									<0.0001
No	9712	(95.2)	2686	(82.9)	12398	(92.2)	1		
Yes	490	(4.8)	556	(17.1)	1046	(7.8)	4.41	[3.81 - 5.12]	
Rituximab (during baseline period index date excluded), n (%)									<0.0001
No	10164	(99.6)	3120	(96.2)	13284	(98.8)	1		
Yes	38	(0.4)	122	(3.8)	160	(1.2)	15.65	[10.62 - 23.05]	
Anakinra (during baseline period index date excluded), n (%)									0.0011
No	10185	(99.8)	3226	(99.5)	13411	(99.8)	1		
Yes	17	(0.2)	16	(0.5)	33	(0.3)	3.42	[1.64 - 7.12]	
Sarilumab (during baseline period index date excluded), n (%)									<0.0001
No	10175	(99.7)	3195	(98.6)	13370	(99.4)	1		
Yes	27	(0.3)	47	(1.4)	74	(0.6)	5.84	[3.49 - 9.77]	

	TNFi n=10202	Baricitinib n=3242	Total n=13444	Baricitinib vs TNFi OR [95%CI]	p
Hydroxychloroquine (during baseline period index date excluded), n (%)excluded					0.0009
No	9713 (95.2)	3064 (94.5)	12777 (95.0)	1	
Yes	489 (4.8)	178 (5.5)	667 (5.0)	1.39 [1.15 - 1.69]	
Vaccines (during baseline period index date excluded), n (%)					<0.0001
No	6406 (62.8)	2284 (70.5)	8690 (64.6)	1	
Yes	3796 (37.2)	958 (29.5)	4754 (35.4)	0.80 [0.72 - 0.88]	
Number of hospitalisations (during baseline period index date excluded), n (%)					0.0002
0	5400 (52.9)	1649 (50.9)	7049 (52.4)	1	
1	3187 (31.2)	755 (23.3)	3942 (29.3)	0.86 [0.77 - 0.96]	
2	899 (8.8)	302 (9.3)	1201 (8.9)	0.93 [0.77 - 1.11]	
≥3	716 (7.0)	536 (16.5)	1252 (9.3)	1.28 [1.03 - 1.60]	
Number of Physician Office Visits (rheumatologist visits excluded) (during baseline period index date excluded), n (%)					0.0001
0	3777 (37.0)	1259 (38.8)	5036 (37.5)	1	

	TNFi n=10202	Baricitinib n=3242	Total n=13444	Baricitinib vs TNFi OR [95%CI]	p
1	2244 (22.0)	768 (23.7)	3012 (22.4)	1.03 [0.92 - 1.16]	
[2-3]	2336 (22.9)	721 (22.2)	3057 (22.7)	0.90 [0.80 - 1.01]	
[4-6]	1205 (11.8)	345 (10.6)	1550 (11.5)	0.77 [0.66 - 0.90]	
>6	640 (6.3)	149 (4.6)	789 (5.9)	0.68 [0.55 - 0.85]	
Number of rheumatologist office Visits (during baseline period index date excluded),					0.2035
0	3683 (36.1)	1190 (36.7)	4873 (36.2)	1	
1	2239 (21.9)	755 (23.3)	2994 (22.3)	1.06 [0.94 - 1.20]	
≥2	4280 (42.0)	1297 (40.0)	5577 (41.5)	0.96 [0.86 - 1.07]	
Number of Other Outpatient Visits (during baseline period index date excluded),					0.0141
0	891 (8.7)	218 (6.7)	1109 (8.2)	1	
□ 3	2509 (24.6)	707 (21.8)	3216 (23.9)	1.13 [0.94 - 1.36]	
[4-7]	2082 (20.4)	639 (19.7)	2721 (20.2)	1.16 [0.96 - 1.41]	
[8-20]	2402 (23.5)	751 (23.2)	3153 (23.5)	1.13 [0.94 - 1.37]	
>20	2318 (22.7)	927 (28.6)	3245 (24.1)	1.35 [1.11 - 1.63]	

Hosmer Lemeshow test : p =0.0066

AUC = 0.76

Abbreviations: AUC = Area Under the Curve; bDMARD = biologic disease-modifying antirheumatic drugs ; hosp = hospitalized; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer;
RA = rheumatoid arthritis; SERMs = selective estrogen receptor modulator; TNF = tumor necrosis factor; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

Table A.18. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), unmatched VTE cohort

	TNFi n = 10202	Baricitinib n = 3242
PS distribution		
Size (missing)	10202 (0)	3242 (0)
Mean (± SD)	0.20 (0.14)	0.37 (0.21)
Median	0.15	0.34
[p25% - p75%]	[0.11;0.23]	[0.19;0.53]
[Min - Max]	[0.02;0.96]	[0.02;0.98]
PS distribution, in categories, n (%)		
[0.00;0.05[	194 (1.9)	8 (0.2)
[0.05;0.10[	1849 (18.1)	135 (4.2)
[0.10;0.15[	2889 (28.3)	376 (11.6)
[0.15;0.20[	2035 (19.9)	416 (12.8)
[0.20;0.25[	1023 (10.0)	316 (9.7)
[0.25;0.30[	474 (4.6)	229 (7.1)
[0.30;0.35[	363 (3.6)	206 (6.4)
[0.35;0.40[	301 (3.0)	174 (5.4)
[0.40;0.45[	260 (2.5)	193 (6.0)
[0.45;0.50[	231 (2.3)	224 (6.9)
[0.50;0.55[	178 (1.7)	243 (7.5)
[0.55;0.60[	143 (1.4)	203 (6.3)
[0.60;0.65[	81 (0.8)	134 (4.1)
[0.65;0.70[	57 (0.6)	108 (3.3)

	TNFi		Baricitinib	
	n = 10202		n = 3242	
[0.70;0.75[	38	(0.4)	78	(2.4)
[0.75;0.80[	44	(0.4)	76	(2.3)
[0.80;0.85[	23	(0.2)	70	(2.2)
[0.85;0.90[	12	(0.1)	35	(1.1)
[0.90;0.95[	5	(0.0)	11	(0.3)
[0.95;1.00]	2	(0.0)	7	(0.2)

Abbreviations: AUC = Area Under the Curve; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

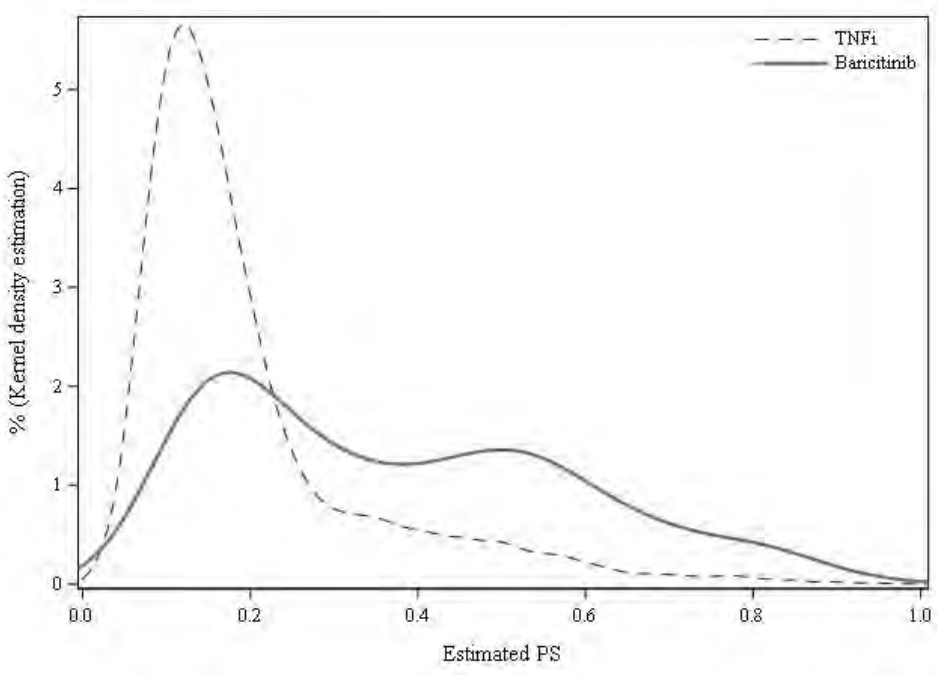

Figure A.9. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), unmatched VTE cohort

Table A.19. Number of matched TNFi by baricitinib, matched VTE cohort, *matching ratio 1:1 on PS ± 0.01* (pre-defined variables + variables with standardized difference ≥ 0.10)

	Baricitinib n = 2860
Number of matched TNFi by baricitinib, n (%)	
1	2860 (100.0)

Table A.20. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), matched VTE cohort, *matching ratio 1:1 on PS ± 0.01*

	TNFi n = 2860	Baricitinib n = 2860
PS distribution		
Size (missing)	2860 (0)	2860 (0)
Mean (± SD)	0.33 (0.19)	0.33 (0.19)
Median	0.29	0.29
[p25% - p75%]	[0.17;0.47]	[0.17;0.47]
[Min - Max]	[0.02;0.96]	[0.02;0.96]
PS distribution, in categories, n (%)		
[0.00;0.05[	8 (0.3)	8 (0.3)
[0.05;0.10[	135 (4.7)	135 (4.7)
[0.10;0.15[	377 (13.2)	376 (13.1)
[0.15;0.20[	414 (14.5)	416 (14.5)
[0.20;0.25[	317 (11.1)	316 (11.0)
[0.25;0.30[	229 (8.0)	229 (8.0)
[0.30;0.35[	202 (7.1)	206 (7.2)
[0.35;0.40[	178 (6.2)	174 (6.1)
[0.40;0.45[	192 (6.7)	191 (6.7)
[0.45;0.50[	225 (7.9)	223 (7.8)
[0.50;0.55[	178 (6.2)	180 (6.3)
[0.55;0.60[	143 (5.0)	147 (5.1)
[0.60;0.65[	81 (2.8)	85 (3.0)
[0.65;0.70[	57 (2.0)	46 (1.6)

	TNFi n = 2860		Baricitinib n = 2860	
[0.70;0.75[	38	(1.3)	43	(1.5)
[0.75;0.80[	44	(1.5)	42	(1.5)
[0.80;0.85[	23	(0.8)	24	(0.8)
[0.85;0.90[	12	(0.4)	10	(0.3)
[0.90;0.95[	5	(0.2)	6	(0.2)
[0.95;1.00]	2	(0.1)	3	(0.1)

AUC post matching = 0.54

Abbreviations: AUC = Area Under the Curve; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

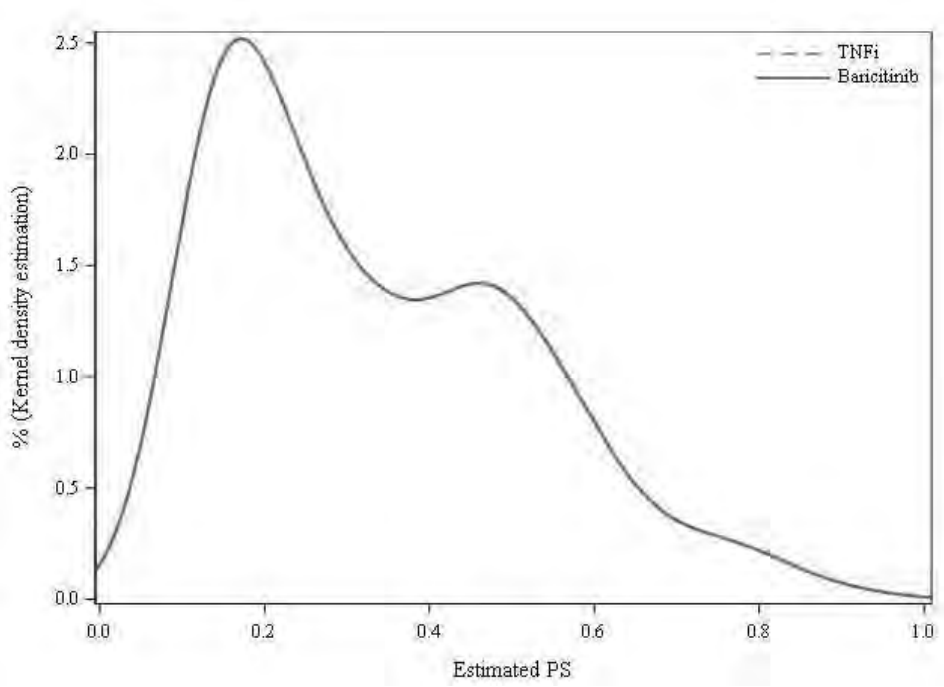

Figure A.10. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), matched VTE cohort, *matching ratio 1:1 on PS ± 0.01*

8.2.2 APPENDIX 6. PROPENSITY SCORE, MACE COHORT

Table A.21. Baricitinib vs TNFi PS model (pre-defined variables + variables with standardized difference ≥ 0.10), MACE cohort

	TNFi n=10175	Baricitinib n=3236	Total n=13411	Baricitinib vs TNFi OR [95%CI]	p
CIRAS score (during the year preceding index date)					0.0045
≤5.5	2110 (20.7)	819 (25.3)	2929 (21.8)	1	
]5.5-6.5]	2658 (26.1)	999 (30.9)	3657 (27.3)	0.98 [0.86 - 1.12]	
]6.5-7.5]	2193 (21.6)	747 (23.1)	2940 (21.9)	1.07 [0.92 - 1.24]	
>7.5	3214 (31.6)	671 (20.7)	3885 (29.0)	0.84 [0.72 - 0.98]	
Age (in years), in categories, n (%)					<0.0001
≥ 65	2748 (27.0)	1140 (35.2)	3888 (29.0)	1	
[18-30[	435 (4.3)	70 (2.2)	505 (3.8)	0.43 [0.32 - 0.59]	
[30-40[	1231 (12.1)	208 (6.4)	1439 (10.7)	0.45 [0.37 - 0.56]	
[40-50[	1742 (17.1)	461 (14.2)	2203 (16.4)	0.65 [0.55 - 0.76]	
[50-60[	2770 (27.2)	899 (27.8)	3669 (27.4)	0.80 [0.71 - 0.91]	
[60-65[	1249 (12.3)	458 (14.2)	1707 (12.7)	0.89 [0.76 - 1.03]	
Sex, n (%)					<0.0001
Female	7522 (73.9)	2593 (80.1)	10115 (75.4)	1	
Male	2653 (26.1)	643 (19.9)	3296 (24.6)	0.71 [0.63 - 0.79]	

	TNFi n=10175	Baricitinib n=3236	Total n=13411	Baricitinib vs TNFi OR [95%CI]	p
Unstable angina, Congestive Heart Failure, hospitalized, Ventricular arrhythmia, Cardiovascular revascularization procedure, CAD or TIA during baseline period, n (%)					0.2192
No	9778 (96.1)	3075 (95.0)	12853 (95.8)	1	
Yes	397 (3.9)	161 (5.0)	558 (4.2)	1.16 [0.91 - 1.47]	
Immune disorders during baseline period, n (%)					0.1623
No	9894 (97.2)	3113 (96.2)	13007 (97.0)	1	
Yes	281 (2.8)	123 (3.8)	404 (3.0)	1.19 [0.93 - 1.52]	
Diabete during the year preceding the year of index date, n (%)					0.4299
No	9300 (91.4)	2918 (90.2)	12218 (91.1)	1	
Yes	875 (8.6)	318 (9.8)	1193 (8.9)	0.94 [0.80 - 1.10]	
Current antihypertensives (during baseline period, index date excluded), n (%)					0.7820
No	7122 (70.0)	2051 (63.4)	9173 (68.4)	1	
Yes	3053 (30.0)	1185 (36.6)	4238 (31.6)	0.97 [0.78 - 1.21]	
History antihypertensives 1 year before index date, baseline period excluded, n (%)					0.6464
0	7160 (70.4)	2060 (63.7)	9220 (68.7)	1	

	TNFi n=10175	Baricitinib n=3236	Total n=13411	Baricitinib vs TNFi OR [95%CI]	p
1	307 (3.0)	100 (3.1)	407 (3.0)	0.99 [0.74 - 1.31]	
[2-4]	1438 (14.1)	568 (17.6)	2006 (15.0)	1.08 [0.85 - 1.36]	
≥ 5	1270 (12.5)	508 (15.7)	1778 (13.3)	0.98 [0.76 - 1.25]	
Lipid-lowering agents (during baseline period, index date excluded), n (%)					0.6757
No	8816 (86.6)	2686 (83.0)	11502 (85.8)	1	
Yes	1359 (13.4)	550 (17.0)	1909 (14.2)	1.03 [0.89 - 1.19]	
Aspirin (analgesic) (during baseline period, index date excluded), n (%)					0.6941
No	10059 (98.9)	3195 (98.7)	13254 (98.8)	1	
Yes	116 (1.1)	41 (1.3)	157 (1.2)	0.92 [0.62 - 1.37]	
Glucocorticosteroid (during baseline period index date excluded), n (%					<0.0001
0	3490 (34.3)	880 (27.2)	4370 (32.6)	1	
1	1578 (15.5)	434 (13.4)	2012 (15.0)	1.08 [0.94 - 1.24]	
[2-4]	2457 (24.1)	862 (26.6)	3319 (24.7)	1.39 [1.23 - 1.56]	
≥ 5	2650 (26.0)	1060 (32.8)	3710 (27.7)	1.65 [1.47 - 1.85]	
Antiplatelet agents (during baseline period, index date excluded), n (%)					0.4124
No	9202 (90.4)	2846 (87.9)	12048 (89.8)	1	

	TNFi n=10175	Baricitinib n=3236	Total n=13411	Baricitinib vs TNFi OR [95%CI]	p
Yes	973 (9.6)	390 (12.1)	1363 (10.2)	1.07 [0.91 - 1.27]	
Total hospital medical costs (in euros) per patient (during baseline period index date excluded), n (%)					0.6418
For an increase of one unit	10175 (100.0)	3236 (100.0)	13411 (100.0)	1.00 [1.00 - 1.00]	
Total non-hospital medical costs (in euros) per patient (during baseline period index date excluded), n (%)					0.2283
For an increase of one unit	10175 (100.0)	3236 (100.0)	13411 (100.0)	1.00 [1.00 - 1.00]	
Etanercept (during baseline period index date excluded), n (%)					<0.0001
No	9513 (93.5)	2878 (88.9)	12391 (92.4)	1	
Yes	662 (6.5)	358 (11.1)	1020 (7.6)	2.50 [2.14 - 2.90]	
Infliximab (during baseline period index date excluded), n (%)					<0.0001
No	9990 (98.2)	3144 (97.2)	13134 (97.9)	1	
Yes	185 (1.8)	92 (2.8)	277 (2.1)	1.95 [1.44 - 2.64]	
Adalimumab (during baseline period index date excluded), n (%)					<0.0001
No	9767 (96.0)	2983 (92.2)	12750 (95.1)	1	

	TNFi n=10175	Baricitinib n=3236	Total n=13411	Baricitinib vs TNFi OR [95%CI]	p
Yes	408 (4.0)	253 (7.8)	661 (4.9)	2.87 [2.40 - 3.44]	
Certolizumab pegol (during baseline period index date excluded), n (%)					<0.0001
No	10026 (98.5)	3079 (95.1)	13105 (97.7)	1	
Yes	149 (1.5)	157 (4.9)	306 (2.3)	4.98 [3.89 - 6.38]	
Golimumab (during baseline period index date excluded), n (%)					<0.0001
No	10029 (98.6)	3104 (95.9)	13133 (97.9)	1	
Yes	146 (1.4)	132 (4.1)	278 (2.1)	4.32 [3.33 - 5.60]	
Tocilizumab (during baseline period index date excluded), n (%)					<0.0001
No	9786 (96.2)	2733 (84.5)	12519 (93.3)	1	
Yes	389 (3.8)	503 (15.5)	892 (6.7)	5.27 [4.49 - 6.19]	
Abatacept (during baseline period index date excluded), n (%)					<0.0001
No	9685 (95.2)	2681 (82.8)	12366 (92.2)	1	
Yes	490 (4.8)	555 (17.2)	1045 (7.8)	4.37 [3.77 - 5.06]	
Rituximab (during baseline period index date excluded), n (%)					<0.0001

	TNFi n=10175	Baricitinib n=3236	Total n=13411	Baricitinib vs TNFi OR [95%CI]	p
No	10138 (99.6)	3114 (96.2)	13252 (98.8)	1	
Yes	37 (0.4)	122 (3.8)	159 (1.2)	16.03 [10.86 - 23.67]	
Anakinra (during baseline period index date excluded), n (%)					0.0009
No	10158 (99.8)	3220 (99.5)	13378 (99.8)	1	
Yes	17 (0.2)	16 (0.5)	33 (0.3)	3.46 [1.66 - 7.22]	
Sarilumab (during baseline period index date excluded), n (%)					<0.0001
No	10148 (99.7)	3189 (98.5)	13337 (99.4)	1	
Yes	27 (0.3)	47 (1.5)	74 (0.6)	5.96 [3.57 - 9.96]	
Methotrexate (during baseline period index date excluded), n (%)					0.0091
No	4092 (40.2)	1559 (48.2)	5651 (42.1)	1	
Yes	6083 (59.8)	1677 (51.8)	7760 (57.9)	0.88 [0.80 - 0.97]	
Hydroxychloroquine (during baseline period index date excluded), n (%)					0.0006
No	9690 (95.2)	3058 (94.5)	12748 (95.1)	1	
Yes	485 (4.8)	178 (5.5)	663 (4.9)	1.41 [1.16 - 1.71]	

	TNFi n=10175	Baricitinib n=3236	Total n=13411	Baricitinib vs TNFi OR [95%CI]	p
Leflunomid (during baseline period index date excluded), n (%)					0.0011
No	9168 (90.1)	2827 (87.4)	11995 (89.4)	1	
Yes	1007 (9.9)	409 (12.6)	1416 (10.6)	1.27 [1.10 - 1.47]	
Vaccines (during baseline period index date excluded), n (%)					<0.0001
No	6393 (62.8)	2279 (70.4)	8672 (64.7)	1	
Yes	3782 (37.2)	957 (29.6)	4739 (35.3)	0.79 [0.72 - 0.87]	
Antineoplastic agent (during baseline period index date excluded), n (%)					0.8851
No	10150 (99.8)	3224 (99.6)	13374 (99.7)	1	
Yes	25 (0.3)	12 (0.4)	37 (0.3)	0.94 [0.43 - 2.08]	
Number of Physician Office Visits (rheumatologist visits excluded) during baseline period (Index date excluded), n (%)					<0.0001
0	3766 (37.0)	1256 (38.8)	5022 (37.4)	1	
1	2238 (22.0)	767 (23.7)	3005 (22.4)	1.04 [0.93 - 1.16]	
[2-3]	2328 (22.9)	719 (22.2)	3047 (22.7)	0.90 [0.80 - 1.02]	
[4-6]	1206 (11.9)	345 (10.7)	1551 (11.6)	0.78 [0.67 - 0.91]	
>6	637 (6.3)	149 (4.6)	786 (5.9)	0.68 [0.55 - 0.84]	

	TNFi n=10175	Baricitinib n=3236	Total n=13411	Baricitinib vs TNFi OR [95%CI]	p
Number of hospitalisations during baseline period (Index date excluded), n (%)					<0.0001
0	5399 (53.1)	1649 (51.0)	7048 (52.6)	1	
1	3174 (31.2)	753 (23.3)	3927 (29.3)	0.86 [0.77 - 0.96]	
2	892 (8.8)	301 (9.3)	1193 (8.9)	0.95 [0.79 - 1.13]	
≥3	710 (7.0)	533 (16.5)	1243 (9.3)	1.31 [1.06 - 1.63]	
Number of rheumatologist office Visits during baseline period (Index date excluded), n (%)					0.1919
0	3680 (36.2)	1186 (36.7)	4866 (36.3)	1	
1	2235 (22.0)	753 (23.3)	2988 (22.3)	1.05 [0.93 - 1.18]	
≥2	4260 (41.9)	1297 (40.1)	5557 (41.4)	0.94 [0.85 - 1.05]	

Hosmer Lemeshow test : p =0.0095

AUC = 0.76

Abbreviations: AUC = Area Under the Curve; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke;

Table A.22. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), unmatched MACE cohort

	TNFi n = 10175	Baricitinib n = 3236
PS distribution		
Size (missing)	10175 (0)	3236 (0)
Mean (± SD)	0.20 (0.14)	0.37 (0.21)
Median	0.15	0.33
[p25% - p75%]	[0.11;0.23]	[0.18;0.53]
[Min - Max]	[0.03;0.97]	[0.04;0.98]
PS distribution, in categories, n (%)		
[0.00;0.05[	106 (1.0)	7 (0.2)
[0.05;0.10[	1968 (19.3)	141 (4.4)
[0.10;0.15[	2827 (27.8)	366 (11.3)
[0.15;0.20[	2035 (20.0)	414 (12.8)
[0.20;0.25[	1002 (9.8)	313 (9.7)
[0.25;0.30[	521 (5.1)	245 (7.6)
[0.30;0.35[	356 (3.5)	174 (5.4)
[0.35;0.40[	279 (2.7)	190 (5.9)
[0.40;0.45[	251 (2.5)	210 (6.5)
[0.45;0.50[	262 (2.6)	248 (7.7)
[0.50;0.55[	179 (1.8)	204 (6.3)
[0.55;0.60[	135 (1.3)	191 (5.9)
[0.60;0.65[	82 (0.8)	148 (4.6)
[0.65;0.70[	49 (0.5)	110 (3.4)
[0.70;0.75[	36 (0.4)	75 (2.3)

	TNFi		Baricitinib	
	n = 10175		n = 3236	
[0.75;0.80[	38	(0.4)	76	(2.3)
[0.80;0.85[	29	(0.3)	66	(2.0)
[0.85;0.90[	11	(0.1)	44	(1.4)
[0.90;0.95[	6	(0.1)	7	(0.2)
[0.95;1.00]	3	(0.0)	7	(0.2)

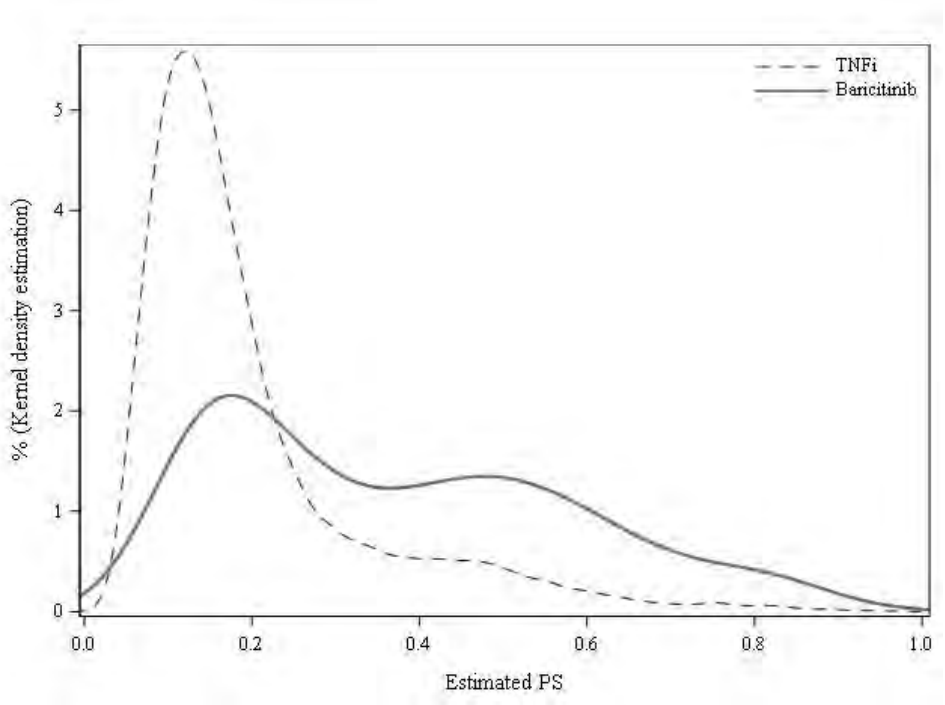

Figure A.11. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), unmatched MACE cohort

Table A.23. Number of matched TNFi by baricitinib, matched MACE cohort, matching ratio 1:1 *on PS ± 0.01* (pre-defined variables + variables with standardized difference ≥ 0.10)

	Baricitinib n = 2863
Number of matched TNFi by baricitinib, n (%)	
1	2863 (100.0)

Table A.24. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), matched MACE cohort, matching ratio 1:1 on PS ± 0.01

	TNFi n = 2863	Baricitinib n = 2863
PS distribution		
Size (missing)	2863 (0)	2863 (0)
Mean (± SD)	0.33 (0.19)	0.33 (0.19)
Median	0.29	0.29
[p25% - p75%]	[0.17;0.47]	[0.17;0.47]
[Min - Max]	[0.04;0.97]	[0.04;0.97]
PS distribution, in categories, n (%)		
[0.00;0.05[	7 (0.2)	7 (0.2)
[0.05;0.10[	140 (4.9)	141 (4.9)
[0.10;0.15[	367 (12.8)	366 (12.8)
[0.15;0.20[	413 (14.4)	414 (14.5)
[0.20;0.25[	317 (11.1)	313 (10.9)
[0.25;0.30[	241 (8.4)	245 (8.6)
[0.30;0.35[	177 (6.2)	174 (6.1)
[0.35;0.40[	190 (6.6)	188 (6.6)
[0.40;0.45[	199 (7.0)	210 (7.3)
[0.45;0.50[	245 (8.6)	243 (8.5)
[0.50;0.55[	179 (6.3)	174 (6.1)
[0.55;0.60[	135 (4.7)	130 (4.5)
[0.60;0.65[	82 (2.9)	87 (3.0)
[0.65;0.70[	49 (1.7)	49 (1.7)

	TNFi n = 2863		Baricitinib n = 2863	
[0.70;0.75[	36	(1.3)	37	(1.3)
[0.75;0.80[	38	(1.3)	39	(1.4)
[0.80;0.85[	29	(1.0)	27	(0.9)
[0.85;0.90[	11	(0.4)	12	(0.4)
[0.90;0.95[	5	(0.2)	4	(0.1)
[0.95;1.00]	3	(0.1)	3	(0.1)

AUC post matching = 0.54

Abbreviations: AUC = Area Under the Curve; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke;

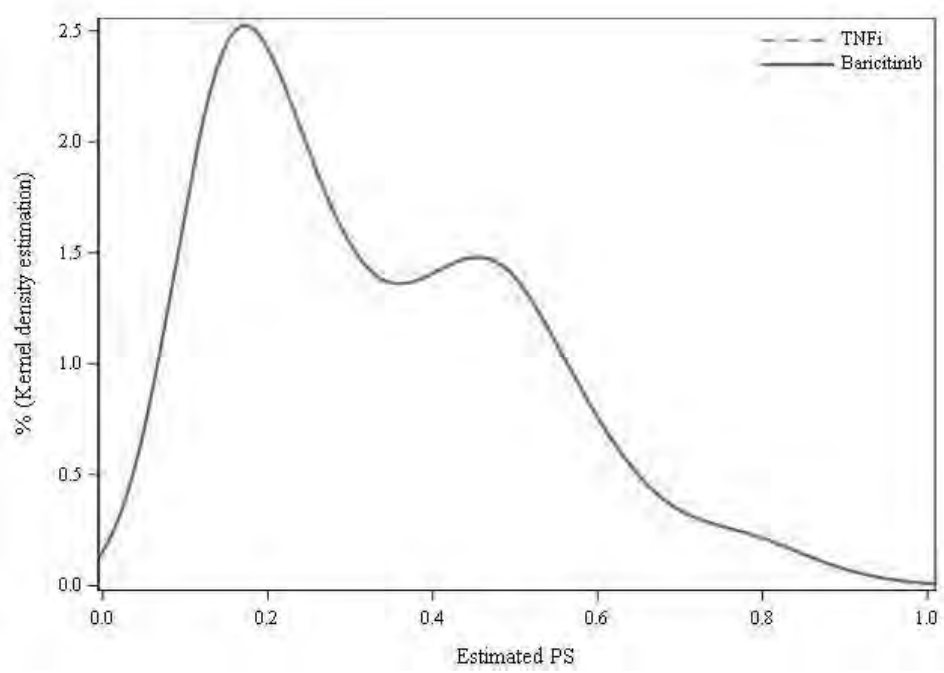

Figure A.12. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), matched MACE cohort, *matching ratio 1:1 on PS ± 0.01*

8.2.3 APPENDIX 7. PROPENSITY SCORE, SI COHORT

Table A.25. Baricitinib vs TNFi PS model (pre-defined variables + variables with standardized difference ≥ 0.10), SI cohort

	TNFi n=10451	Baricitinib n=3366	Total n=13817	Baricitinib vs TNFi OR [95%CI]	p
CIRAS score (during the year preceding index date)					0.0050
≤5.5	2220 (21.2)	892 (26.5)	3112 (22.5)	1	
]5.5-6.5]	2723 (26.1)	1031 (30.6)	3754 (27.2)	0.95 [0.84 - 1.08]	
]6.5-7.5]	2254 (21.6)	758 (22.5)	3012 (21.8)	1.00 [0.86 - 1.16]	
>7.5	3254 (31.1)	685 (20.4)	3939 (28.5)	0.80 [0.68 - 0.94]	
Sex, n (%)					<0.0001
Female	7672 (73.4)	2693 (80.0)	10365 (75.0)	1	
Male	2779 (26.6)	673 (20.0)	3452 (25.0)	0.70 [0.63 - 0.78]	
Age (in years), in categories, n (%)					<0.0001
≥ 65	2932 (28.1)	1238 (36.8)	4170 (30.2)	1	
[18-30[	436 (4.2)	70 (2.1)	506 (3.7)	0.45 [0.33 - 0.61]	
[30-40[	1234 (11.8)	208 (6.2)	1442 (10.4)	0.47 [0.39 - 0.58]	
[40-50[	1757 (16.8)	468 (13.9)	2225 (16.1)	0.67 [0.57 - 0.79]	
[50-60[	2813 (26.9)	911 (27.1)	3724 (27.0)	0.82 [0.72 - 0.93]	
[60-65[	1279 (12.2)	471 (14.0)	1750 (12.7)	0.90 [0.78 - 1.05]	
Immune disorders during baseline period, n (%)					0.0929
No	10157 (97.2)	3232 (96.0)	13389 (96.9)	1	
Yes	294 (2.8)	134 (4.0)	428 (3.1)	1.22 [0.97 - 1.55]	
Diabete during the year preceding the year of index date, n (%)					0.6376
No	9519 (91.1)	3023 (89.8)	12542 (90.8)	1	
Yes	932 (8.9)	343 (10.2)	1275 (9.2)	0.96 [0.83 - 1.12]	
Treatment or hospitalisation for chronic lung disease during baseline period, n (%)					0.3371

	TNFi n=10451	Baricitinib n=3366	Total n=13817	Baricitinib vs TNFi OR [95%CI]	p
No	8914 (85.3)	2774 (82.4)	11688 (84.6)	1	
Yes	1537 (14.7)	592 (17.6)	2129 (15.4)	1.06 [0.94 - 1.19]	
Treatment or hospitalisation for liver or pancreatic disease during baseline period, n (%)					0.9233
No	10393 (99.4)	3347 (99.4)	13740 (99.4)	1	
Yes	58 (0.6)	19 (0.6)	77 (0.6)	0.97 [0.55 - 1.72]	
TIA or Ischemic stroke during baseline period, n (%)					0.4708
No	10429 (99.8)	3354 (99.6)	13783 (99.8)	1	
Yes	22 (0.2)	12 (0.4)	34 (0.3)	1.34 [0.61 - 2.97]	
Antibiotics (during baseline period, index date excluded), n (%)					0.1813
No	6471 (61.9)	1932 (57.4)	8403 (60.8)	1	
Yes	3980 (38.1)	1434 (42.6)	5414 (39.2)	1.06 [0.97 - 1.17]	
Glucocorticosteroid (during baseline period, index date excluded), n (%)					<0.0001
0	3562 (34.1)	903 (26.8)	4465 (32.3)	1	
1	1616 (15.5)	448 (13.3)	2064 (14.9)	1.06 [0.92 - 1.22]	
[2-4]	2516 (24.1)	898 (26.7)	3414 (24.7)	1.39 [1.24 - 1.57]	
≥ 5	2757 (26.4)	1117 (33.2)	3874 (28.0)	1.64 [1.46 - 1.84]	
Number of different cDMARD during baseline period (Index date excluded), n (%)					0.1239
0	2974 (28.5)	1129 (33.5)	4103 (29.7)	1	
1	6785 (64.9)	2043 (60.7)	8828 (63.9)	0.79 [0.60 - 1.03]	
[2-4]	692 (6.6)	194 (5.8)	886 (6.4)	0.59 [0.36 - 0.98]	
Total hospital medical costs (in euros) per patient (during baseline period index date excluded), n (%)					0.1563
For an increase of one unit	10451 (100.0)	3366 (100.0)	13817 (100.0)	1.00 [1.00 - 1.00]	

	TNFi n=10451	Baricitinib n=3366	Total n=13817	Baricitinib vs TNFi OR [95%CI]	p
Total non-hospital medical costs (in euros) per patient (during baseline period index date excluded), n (%)					0.5422
For an increase of one unit	10451 (100.0)	3366 (100.0)	13817 (100.0)	1.00 [1.00 - 1.00]	
Etanercept (during baseline period index date excluded), n (%)					<0.0001
No	9773 (93.5)	3002 (89.2)	12775 (92.5)	1	
Yes	678 (6.5)	364 (10.8)	1042 (7.5)	2.45 [2.11 - 2.85]	
Infliximab (during baseline period index date excluded), n (%)					<0.0001
No	10265 (98.2)	3269 (97.1)	13534 (98.0)	1	
Yes	186 (1.8)	97 (2.9)	283 (2.0)	2.03 [1.51 - 2.73]	
Adalimumab (during baseline period index date excluded), n (%)					<0.0001
No	10042 (96.1)	3104 (92.2)	13146 (95.1)	1	
Yes	409 (3.9)	262 (7.8)	671 (4.9)	2.98 [2.49 - 3.56]	
Certolizumab pegol (during baseline period index date excluded), n (%)					<0.0001
No	10298 (98.5)	3205 (95.2)	13503 (97.7)	1	
Yes	153 (1.5)	161 (4.8)	314 (2.3)	4.86 [3.80 - 6.21]	
Golimumab baseline during period Index date excluded, n (%)					<0.0001
No	10300 (98.6)	3230 (96.0)	13530 (97.9)	1	
Yes	151 (1.4)	136 (4.0)	287 (2.1)	4.27 [3.30 - 5.52]	
Tocilizumab baseline during period Index date excluded, n (%)					<0.0001
No	10054 (96.2)	2846 (84.6)	12900 (93.4)	1	
Yes	397 (3.8)	520 (15.4)	917 (6.6)	5.22 [4.46 - 6.12]	

	TNFi n=10451	Baricitinib n=3366	Total n=13817	Baricitinib vs TNFi OR [95%CI]	p
Abatacept (during baseline period index date excluded), n (%)					<0.0001
No	9936 (95.1)	2787 (82.8)	12723 (92.1)	1	
Yes	515 (4.9)	579 (17.2)	1094 (7.9)	4.24 [3.66 - 4.90]	
Rituximab (during baseline period index date excluded), n (%)					<0.0001
No	10414 (99.6)	3240 (96.3)	13654 (98.8)	1	
Yes	37 (0.4)	126 (3.7)	163 (1.2)	16.98 [11.52 - 25.02]	
Anakinra (during baseline period index date excluded), n (%)					0.0012
No	10432 (99.8)	3349 (99.5)	13781 (99.7)	1	
Yes	19 (0.2)	17 (0.5)	36 (0.3)	3.21 [1.59 - 6.47]	
Sarilumab (during baseline period index date excluded), n (%)					<0.0001
No	10422 (99.7)	3317 (98.5)	13739 (99.4)	1	
Yes	29 (0.3)	49 (1.5)	78 (0.6)	5.81 [3.53 - 9.57]	
Methotrexate (during baseline period index date excluded), n (%)					0.4773
No	4217 (40.4)	1634 (48.5)	5851 (42.3)	1	
Yes	6234 (59.6)	1732 (51.5)	7966 (57.7)	1.10 [0.85 - 1.42]	
Hydroxychloroquine (during baseline period index date excluded), n (%)					0.0002
No	9954 (95.2)	3177 (94.4)	13131 (95.0)	1	
Yes	497 (4.8)	189 (5.6)	686 (5.0)	1.83 [1.33 - 2.52]	
Leflunomid (during baseline period index date excluded), n (%)					0.0008
No	9409 (90.0)	2941 (87.4)	12350 (89.4)	1	
Yes	1042 (9.97)	425 (12.6)	1467 (10.6)	1.61 [1.22 - 2.12]	
Vaccines (during baseline period index date excluded), n (%)					<0.0001

	TNFi n=10451	Baricitinib n=3366	Total n=13817	Baricitinib vs TNFi OR [95%CI]	p
No	6534 (62.5)	2351 (69.8)	8885 (64.3)	1	
Yes	3917 (37.5)	1015 (30.2)	4932 (35.7)	0.79 [0.72 - 0.87]	
Number of Physician Office Visits (rheumatologist visits excluded) during baseline period (Index date excluded), n (%)					<0.0001
0	3851 (36.8)	1296 (38.5)	5147 (37.3)	1	
1	2309 (22.1)	794 (23.6)	3103 (22.5)	1.02 [0.91 - 1.14]	
[2-3]	2393 (22.9)	748 (22.2)	3141 (22.7)	0.89 [0.79 - 1.00]	
[4-6]	1244 (11.9)	366 (10.9)	1610 (11.7)	0.78 [0.67 - 0.91]	
>6	654 (6.3)	162 (4.8)	816 (5.9)	0.68 [0.55 - 0.84]	
Number of hospitalisations during baseline period (Index date excluded), n (%)					<0.0001
0	5501 (52.6)	1688 (50.1)	7189 (52.0)	1	
1	3282 (31.4)	801 (23.8)	4083 (29.6)	0.87 [0.78 - 0.97]	
2	929 (8.9)	320 (9.5)	1249 (9.0)	0.94 [0.78 - 1.12]	
≥3	739 (7.1)	557 (16.5)	1296 (9.4)	1.36 [1.09 - 1.69]	
Number of rheumatologist office Visits during baseline period (Index date excluded), n (%)					0.3078
0	3785 (36.2)	1252 (37.2)	5037 (36.5)	1	
1	2294 (22.0)	770 (22.9)	3064 (22.2)	1.04 [0.93 - 1.17]	
≥2	4372 (41.8)	1344 (39.9)	5716 (41.4)	0.95 [0.86 - 1.06]	
Number of Other Outpatient Visits during baseline period (Index date excluded), n (%)					0.0237
0	895 (8.6)	222 (6.6)	1117 (8.1)	1	
≤ 3	2539 (24.3)	715 (21.2)	3254 (23.6)	1.10 [0.92 - 1.33]	
[4-7]	2118 (20.3)	666 (19.8)	2784 (20.1)	1.15 [0.96 - 1.40]	
[8-20]	2471 (23.6)	775 (23.0)	3246 (23.5)	1.08 [0.90 - 1.31]	
>20	2428 (23.2)	988 (29.4)	3416 (24.7)	1.29 [1.07 - 1.57]	

	TNFi n=10451	Baricitinib n=3366	Total n=13817	Baricitinib vs TNFi OR [95%CI]	p
Anticoagulant (during baseline period index date excluded), n (%)					0.5411
No	9698 (92.8)	3082 (91.6)	12780 (92.5)	1	
Yes	753 (7.2)	284 (8.4)	1037 (7.5)	1.06 [0.89 - 1.26]	
Atrial fibrillation during baseline period, n (%)					0.0068
No	10323 (98.8)	3287 (97.7)	13610 (98.5)	1	
Yes	128 (1.2)	79 (2.3)	207 (1.5)	1.60 [1.14 - 2.24]	
Hosmer Lemeshow test : p =0.0010					
AUC = 0.76					

Abbreviations: AUC = Area Under the Curve; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor; SI = Serious Infections.

Table A.26. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ⩾ 0.10), unmatched SI cohort

	TNFi n = 10451	Baricitinib n = 3366
PS distribution		
Size (missing)	10451 (0)	3366 (0)
Mean (± SD)	0.20 (0.14)	0.38 (0.21)
Median	0.16	0.34
[p25% - p75%]	[0.11;0.23]	[0.19;0.53]
[Min - Max]	[0.03;0.97]	[0.03;0.98]
PS distribution, in categories, n (%)		
[0.00;0.05[	127 (1.2)	9 (0.3)
[0.05;0.10[	2011 (19.2)	140 (4.2)
[0.10;0.15[	2847 (27.2)	377 (11.2)
[0.15;0.20[	2050 (19.6)	423 (12.6)
[0.20;0.25[	1047 (10.0)	324 (9.6)
[0.25;0.30[	550 (5.3)	239 (7.1)
[0.30;0.35[	411 (3.9)	206 (6.1)
[0.35;0.40[	296 (2.8)	195 (5.8)
[0.40;0.45[	252 (2.4)	237 (7.0)
[0.45;0.50[	260 (2.5)	231 (6.9)
[0.50;0.55[	184 (1.8)	220 (6.5)
[0.55;0.60[	147 (1.4)	200 (5.9)
[0.60;0.65[	89 (0.9)	153 (4.5)
[0.65;0.70[	56 (0.5)	107 (3.2)
[0.70;0.75[	40 (0.4)	86 (2.6)
[0.75;0.80[	34 (0.3)	89 (2.6)
[0.80;0.85[	31 (0.3)	72 (2.1)
[0.85;0.90[	10 (0.1)	42 (1.2)
[0.90;0.95[	6 (0.1)	9 (0.3)
[0.95;1.00]	3 (0.0)	7 (0.2)

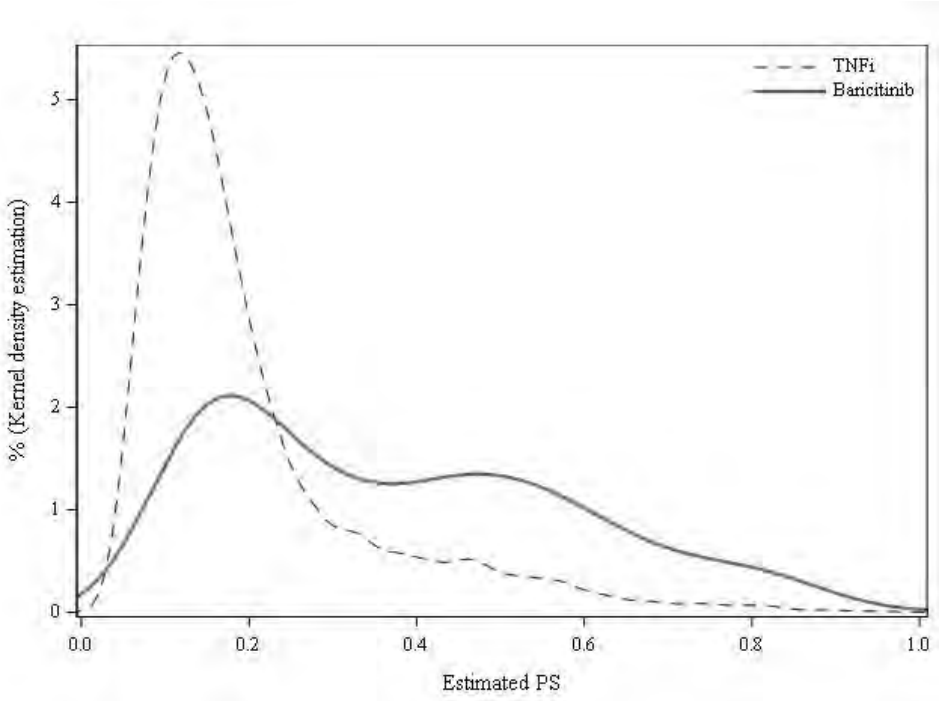

Figure A.13. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), unmatched SI cohort

Table A.27. Number of matched TNFi by baricitinib, matched SI cohort, matching ratio 1:1 *on PS ± 0.01* (pre-defined variables + variables with standardized difference ≥ 0.10)

	Baricitinib n = 2962
Number of matched TNFi by baricitinib, n (%)	
1	2962 (100.0)

Table A.28. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), matched SI cohort, *matching ratio 1:1 on PS ± 0.01*

	TNFi n = 2962	Baricitinib n = 2962
PS distribution		
Size (missing)	2962 (0)	2962 (0)
Mean (± SD)	0.33 (0.19)	0.33 (0.19)
Median	0.29	0.29
[p25% - p75%]	[0.18;0.47]	[0.18;0.47]
[Min - Max]	[0.03;0.97]	[0.03;0.97]
PS distribution, in categories, n (%)		
[0.00;0.05[	9 (0.3)	9 (0.3)
[0.05;0.10[	140 (4.7)	140 (4.7)
[0.10;0.15[	377 (12.7)	377 (12.7)
[0.15;0.20[	423 (14.3)	423 (14.3)
[0.20;0.25[	322 (10.9)	324 (10.9)
[0.25;0.30[	239 (8.1)	239 (8.1)
[0.30;0.35[	214 (7.2)	206 (7.0)
[0.35;0.40[	189 (6.4)	195 (6.6)
[0.40;0.45[	228 (7.7)	232 (7.8)
[0.45;0.50[	222 (7.5)	216 (7.3)
[0.50;0.55[	183 (6.2)	180 (6.1)
[0.55;0.60[	147 (5.0)	152 (5.1)
[0.60;0.65[	89 (3.0)	86 (2.9)
[0.65;0.70[	56 (1.9)	58 (2.0)
[0.70;0.75[	40 (1.4)	40 (1.4)
[0.75;0.80[	34 (1.1)	37 (1.2)
[0.80;0.85[	31 (1.0)	30 (1.0)
[0.85;0.90[	10 (0.3)	9 (0.3)
[0.90;0.95[	6 (0.2)	6 (0.2)
[0.95;1.00]	3 (0.1)	3 (0.1)
AUC post matching = 0.53		

Abbreviations: AUC = Area Under the Curve; Max = maximum; Min = minimum; N = number of patients in the specified category; SD = standard deviation; TNFi = tumor necrosis factor inhibitor; SI = Serious Infections;

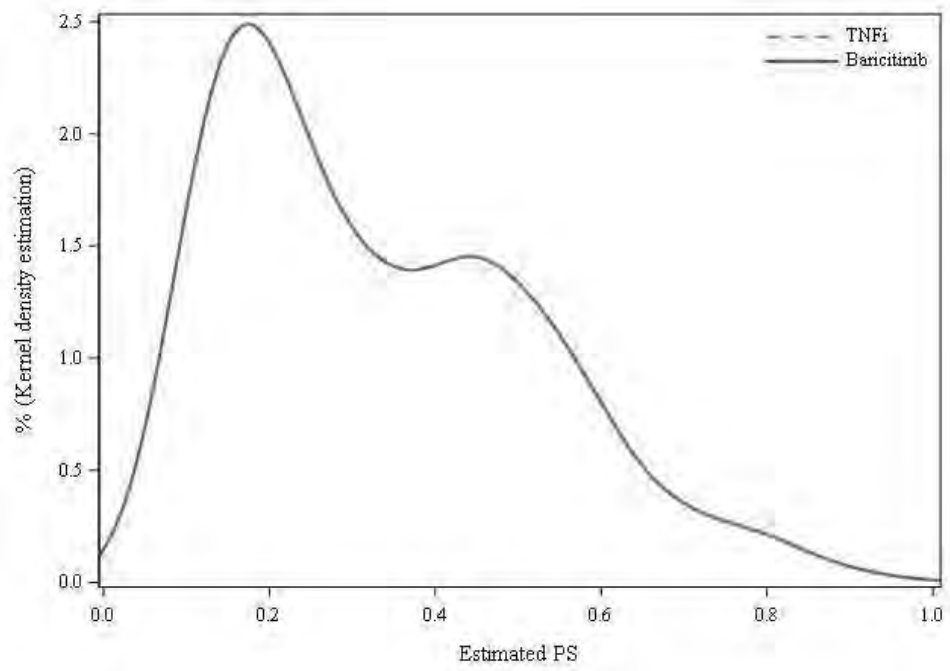

Figure A.14. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), matched VTE cohort, *matching ratio 1:1 on PS ± 0.01*

8.3 PROPENSITY SCORE, SENSITIVE ANALYSES: POTENTIAL CLASS EFFECTS OF JAK MEDICATIONS

8.3.1 APPENDIX 8. PROPENSITY SCORE, VTE COHORT

Table A.29. Baricitinib vs TNFi PS model (pre-defined variables + variables with standardized difference ≥ 0.10), VTE cohort

	TNFi n=9747	JAK n=5663	Total n=15410	JAK vs TNFi OR [95%CI]	p
Age (in years), in categories, n (%)					<0.0001
≥ 65	2643 (27.1)	1965 (34.7)	4608 (29.9)	1	
[18-30[	417 (4.3)	109 (1.9)	526 (3.4)	0.38 [0.29 - 0.49]	
[30-40[	1192 (12.2)	365 (6.4)	1557 (10.1)	0.44 [0.37 - 0.52]	
[40-50[	1663 (17.1)	797 (14.1)	2460 (16.0)	0.64 [0.56 - 0.73]	
[50-60[	2641 (27.1)	1599 (28.2)	4240 (27.5)	0.83 [0.74 - 0.92]	
[60-65[	1191 (12.2)	828 (14.6)	2019 (13.1)	0.93 [0.83 - 1.06]	
Sex, n (%)					<0.0001
Female	7180 (73.7)	4492 (79.3)	11672 (75.7)	1	
Male	2567 (26.3)	1171 (20.7)	3738 (24.3)	0.73 [0.67 - 0.80]	
Cancer during baseline period, n (%)					0.5644
No	9438 (96.8)	5485 (96.9)	14923 (96.8)	1	
Yes	309 (3.2)	178 (3.1)	487 (3.2)	0.94 [0.76 - 1.16]	
Atrial arrhythmia/fibrillation, Ventricular arrhythmia or Congestive Heart Failure, hospitalized during baseline period, n (%)					0.4968
No	9617 (98.7)	5561 (98.2)	15178 (98.5)	1	
Yes	130 (1.3)	102 (1.8)	232 (1.5)	1.11 [0.82 - 1.50]	
Immune disorders during baseline period, n (%)					0.0762
No	9478 (97.2)	5454 (96.3)	14932 (96.9)	1	
Yes	269 (2.8)	209 (3.7)	478 (3.1)	1.21 [0.98 - 1.49]	
Diabete during the year preceding the year of index date, n (%)					0.2445

	TNFi n=9747	JAK n=5663	Total n=15410	JAK vs TNFi OR [95%CI]	p
No	8917 (91.5)	5064 (89.4)	13981 (90.7)	1	
Yes	830 (8.5)	599 (10.6)	1429 (9.3)	1.08 [0.95 - 1.23]	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date), n (%)					0.0039
No	9609 (98.6)	5649 (99.8)	15258 (99.0)	1	
Yes	138 (1.4)	14 (0.3)	152 (1.0)	0.42 [0.23 - 0.76]	
≥1 recent surgery, n (%)					0.2885
No	9327 (95.7)	5447 (96.2)	14774 (95.9)	1	
Yes	420 (4.3)	216 (3.8)	636 (4.1)	1.12 [0.91 - 1.37]	
≥1 recent Trauma, n (%)					0.4753
No	9686 (99.4)	5619 (99.2)	15305 (99.3)	1	
Yes	61 (0.6)	44 (0.8)	105 (0.7)	1.18 [0.75 - 1.83]	
Aspirin (analgesic) (during baseline period, index date excluded), n (%)					0.5676
No	9634 (98.8)	5586 (98.6)	15220 (98.8)	1	
Yes	113 (1.2)	77 (1.4)	190 (1.2)	1.10 [0.79 - 1.53]	
Anticoagulant (during baseline period, index date excluded), n (%)					0.4053
No	9303 (95.4)	5401 (95.4)	14704 (95.4)	1	
Yes	444 (4.6)	262 (4.6)	706 (4.6)	1.08 [0.90 - 1.30]	
Glucocorticosteroid (during baseline period, index date excluded), n (%)					<0.0001
0	3364 (34.5)	1548 (27.3)	4912 (31.9)	1	
1	1521 (15.6)	809 (14.3)	2330 (15.1)	1.16 [1.03 - 1.31]	
[2-4]	2332 (23.9)	1520 (26.8)	3852 (25.0)	1.47 [1.33 - 1.62]	
□ 5	2530 (26.0)	1786 (31.5)	4316 (28.0)	1.69 [1.53 - 1.87]	
Methotrexate (during baseline period, index date excluded), n (%)					<0.0001

	TNFi n=9747	JAK n=5663	Total n=15410	JAK vs TNFi OR [95%CI]	p
0	3904 (40.1)	2701 (47.7)	6605 (42.9)	1	
1	490 (5.0)	276 (4.9)	766 (5.0)	0.95 [0.80 - 1.13]	
[2-4]	2099 (21.5)	1229 (21.7)	3328 (21.6)	0.95 [0.86 - 1.04]	
□ 5	3254 (33.4)	1457 (25.7)	4711 (30.6)	0.74 [0.68 - 0.81]	
Oral Contraceptives (during baseline period, index date excluded), n (%)					0.8363
No	9008 (92.4)	5376 (94.9)	14384 (93.3)	1	
Yes	739 (7.6)	287 (5.1)	1026 (6.7)	0.98 [0.82 - 1.17]	
HRT (during baseline period, index date excluded), n (%)					0.8442
No	9099 (93.4)	5235 (92.4)	14334 (93.0)	1	
Yes	648 (6.6)	428 (7.6)	1076 (7.0)	1.01 [0.88 - 1.17]	
SERMs (during baseline period, index date excluded), n (%)					0.5741
No	9714 (99.7)	5642 (99.6)	15356 (99.6)	1	
Yes	33 (0.3)	21 (0.4)	54 (0.4)	0.84 [0.46 - 1.54]	
Total hospital medical costs (in euros) per patient (during baseline period, index date excluded), n (%)					0.2266
For an increase of one unit	9747 (100.0)	5663 (100.0)	15410 (100.0)	1.00 [1.00 - 1.00]	
Total non-hospital medical costs (in euros) per patient (during baseline period, index date excluded), n (%)					0.1194
For an increase of one unit	9747 (100.0)	5663 (100.0)	15410 (100.0)	1.00 [1.00 - 1.00]	
Etanercept (during baseline period index date excluded), n (%)					<0.0001
No	9138 (93.8)	4985 (88.0)	14123 (91.6)	1	
Yes	609 (6.2)	678 (12.0)	1287 (8.4)	2.78 [2.45 - 3.17]	
Infliximab (during baseline period index date excluded), n (%)					<0.0001

	TNFi n=9747	JAK n=5663	Total n=15410	JAK vs TNFi OR [95%CI]	p
No	9569 (98.2)	5521 (97.5)	15090 (97.9)	1	
Yes	178 (1.8)	142 (2.5)	320 (2.1)	1.79 [1.37 - 2.34]	
Adalimumab (during baseline period index date excluded), n (%)					<0.0001
No	9357 (96.0)	5244 (92.6)	14601 (94.8)	1	
Yes	390 (4.0)	419 (7.4)	809 (5.2)	2.63 [2.25 - 3.07]	
Certolizumab pegol (during baseline period index date excluded), n (%)					<0.0001
No	9611 (98.6)	5375 (94.9)	14986 (97.2)	1	
Yes	136 (1.4)	288 (5.1)	424 (2.8)	5.69 [4.56 - 7.11]	
Golimumab (during baseline period index date excluded), n (%)					<0.0001
No	9609 (98.6)	5412 (95.6)	15021 (97.5)	1	
Yes	138 (1.4)	251 (4.4)	389 (2.5)	4.66 [3.71 - 5.84]	
Tocilizumab (during baseline period index date excluded), n (%)					<0.0001
No	9422 (96.7)	4793 (84.6)	14215 (92.2)	1	
Yes	325 (3.3)	870 (15.4)	1195 (7.8)	6.04 [5.21 - 7.00]	
Abatacept (during baseline period index date excluded), n (%)					<0.0001
No	9323 (95.6)	4750 (83.9)	14073 (91.3)	1	
Yes	424 (4.4)	913 (16.1)	1337 (8.7)	4.68 [4.09 - 5.36]	
Rituximab (during baseline period index date excluded), n (%)					<0.0001
No	9714 (99.7)	5470 (96.6)	15184 (98.5)	1	
Yes	33 (0.3)	193 (3.4)	226 (1.5)	16.47 [11.21 - 24.21]	
Anakinra (during baseline period index date excluded), n (%)					0.0005
No	9730 (99.8)	5637 (99.5)	15367 (99.7)	1	

	TNFi n=9747	JAK n=5663	Total n=15410	JAK vs TNFi OR [95%CI]	p
Yes	17 (0.2)	26 (0.5)	43 (0.3)	3.21 [1.67 - 6.17]	
Sarilumab (during baseline period index date excluded), n (%)					<0.0001
No	9721 (99.7)	5595 (98.8)	15316 (99.4)	1	
Yes	26 (0.3)	68 (1.2)	94 (0.6)	4.75 [2.92 - 7.71]	
Vaccines (during baseline period index date excluded), n (%)					<0.0001
No	6102 (62.6)	3974 (70.2)	10076 (65.4)	1	
Yes	3645 (37.4)	1689 (29.8)	5334 (34.6)	0.80 [0.74 - 0.87]	
Number of hospitalisations (during baseline period index date excluded), n (%)					<0.0001
0	5173 (53.1)	2947 (52.0)	8120 (52.7)	1	
1	3060 (31.4)	1318 (23.3)	4378 (28.4)	0.85 [0.77 - 0.93]	
2	860 (8.8)	498 (8.8)	1358 (8.8)	0.88 [0.76 - 1.03]	
≥3	654 (6.7)	900 (15.9)	1554 (10.1)	1.33 [1.10 - 1.61]	
Number of Physician Office Visits (rheumatologist visits excluded) (during baseline period index date excluded), n (%)					<0.0001
0	3619 (37.1)	2238 (39.5)	5857 (38.0)	1	
1	2148 (22.0)	1308 (23.1)	3456 (22.4)	0.99 [0.90 - 1.09]	
[2-3]	2232 (22.9)	1274 (22.5)	3506 (22.8)	0.89 [0.81 - 0.98]	
[4-6]	1146 (11.8)	589 (10.4)	1735 (11.3)	0.75 [0.66 - 0.86]	
>6	602 (6.2)	254 (4.5)	856 (5.6)	0.71 [0.59 - 0.85]	
CIRAS score (during the year preceding index date)					0.0371
≤5.5	2039 (20.9)	1435 (25.3)	3474 (22.5)	1	
]5.5-6.5]	2541 (26.1)	1736 (30.7)	4277 (27.8)	1.00 [0.90 - 1.11]	
]6.5-7.5]	2090 (21.4)	1279 (22.6)	3369 (21.9)	1.08 [0.96 - 1.22]	
>7.5	3077 (31.6)	1213 (21.4)	4290 (27.8)	0.92 [0.81 - 1.04]	

	TNFi n=9747	JAK n=5663	Total n=15410	JAK vs TNFi OR [95%CI]	p
Hosmer Lemeshow test : p =0.0012					
AUC = 0.76					

Abbreviations: AUC = Area Under the Curve; hosp = hospitalized; HRT = hormone replacement therapy; N = number of patients in the specified category; NMSC = non-melanoma skin cancer;
RA = rheumatoid arthritis; SERMs = selective estrogen receptor modulator; TNF = tumor necrosis factor; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

Table A.30. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), unmatched VTE cohort

	TNFi n = 9747	JAK n = 5663
PS distribution		
Size (missing)	9747 (0)	5663 (0)
Mean (± SD)	0.29 (0.17)	0.49 (0.23)
Median	0.25	0.49
[p25% - p75%]	[0.18;0.34]	[0.28;0.69]
[Min - Max]	[0.03;0.98]	[0.04;0.99]
PS distribution, in categories, n (%)		
[0.00;0.05[	53 (0.5)	2 (0.0)
[0.05;0.10[	261 (2.7)	27 (0.5)
[0.10;0.15[	1037 (10.6)	138 (2.4)
[0.15;0.20[	1707 (17.5)	322 (5.7)
[0.20;0.25[	1891 (19.4)	553 (9.8)
[0.25;0.30[	1544 (15.8)	521 (9.2)
[0.30;0.35[	926 (9.5)	465 (8.2)
[0.35;0.40[	476 (4.9)	343 (6.1)
[0.40;0.45[	316 (3.2)	258 (4.6)
[0.45;0.50[	259 (2.7)	260 (4.6)
[0.50;0.55[	240 (2.5)	295 (5.2)
[0.55;0.60[	219 (2.2)	346 (6.1)
[0.60;0.65[	237 (2.4)	391 (6.9)
[0.65;0.70[	200 (2.1)	439 (7.8)
[0.70;0.75[	163 (1.7)	417 (7.4)
[0.75;0.80[	84 (0.9)	325 (5.7)
[0.80;0.85[	62 (0.6)	212 (3.7)
[0.85;0.90[	43 (0.4)	183 (3.2)
[0.90;0.95[	25 (0.3)	135 (2.4)
[0.95;1.00]	4 (0.0)	31 (0.5)

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

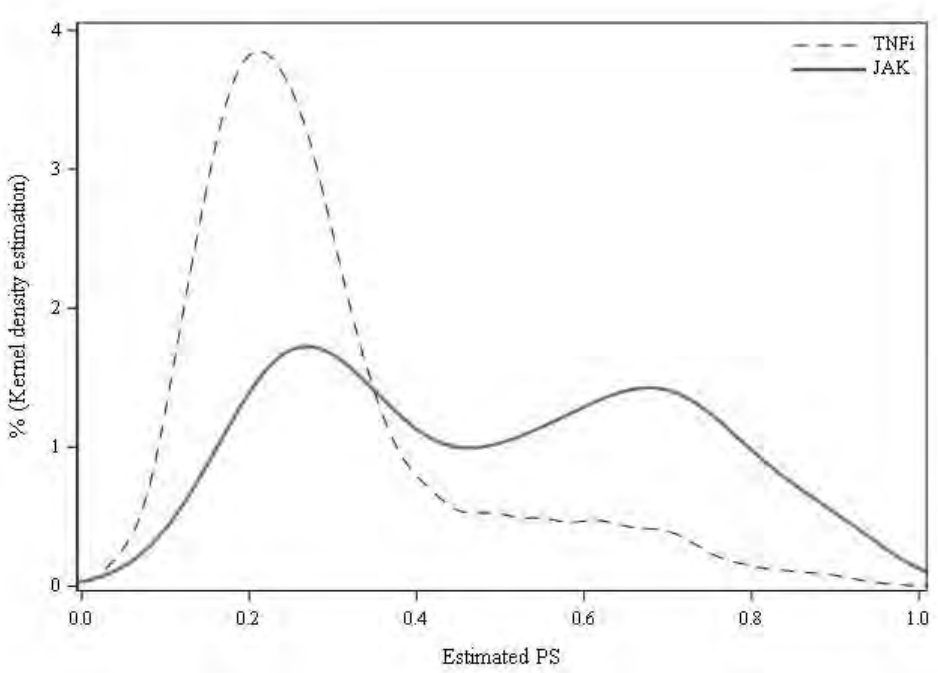

Figure A.15. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), unmatched VTE cohort

Table A.31. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), matched VTE cohort, *matching ratio 1:1 on PS ± 0.01*

	TNFi n = 4153	JAK n = 4153
PS distribution		
Size (missing)	4153 (0)	4153 (0)
Mean (± SD)	0.41 (0.19)	0.41 (0.19)
Median	0.35	0.35
[p25% - p75%]	[0.25;0.55]	[0.25;0.55]
[Min - Max]	[0.04;0.98]	[0.04;0.98]
PS distribution, in categories, n (%)		
[0.00;0.05[	2 (0.0)	2 (0.0)
[0.05;0.10[	27 (0.7)	27 (0.7)
[0.10;0.15[	138 (3.3)	138 (3.3)
[0.15;0.20[	322 (7.8)	322 (7.8)
[0.20;0.25[	551 (13.3)	553 (13.3)
[0.25;0.30[	523 (12.6)	521 (12.5)
[0.30;0.35[	466 (11.2)	465 (11.2)
[0.35;0.40[	344 (8.3)	343 (8.3)
[0.40;0.45[	248 (6.0)	257 (6.2)
[0.45;0.50[	255 (6.1)	244 (5.9)
[0.50;0.55[	240 (5.8)	244 (5.9)
[0.55;0.60[	219 (5.3)	225 (5.4)
[0.60;0.65[	237 (5.7)	231 (5.6)
[0.65;0.70[	200 (4.8)	199 (4.8)
[0.70;0.75[	163 (3.9)	165 (4.0)
[0.75;0.80[	84 (2.0)	85 (2.0)
[0.80;0.85[	62 (1.5)	60 (1.4)
[0.85;0.90[	43 (1.0)	44 (1.1)
[0.90;0.95[	25 (0.6)	23 (0.6)
[0.95;1.00]	4 (0.1)	5 (0.1)
AUC post matching = 0.52		

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

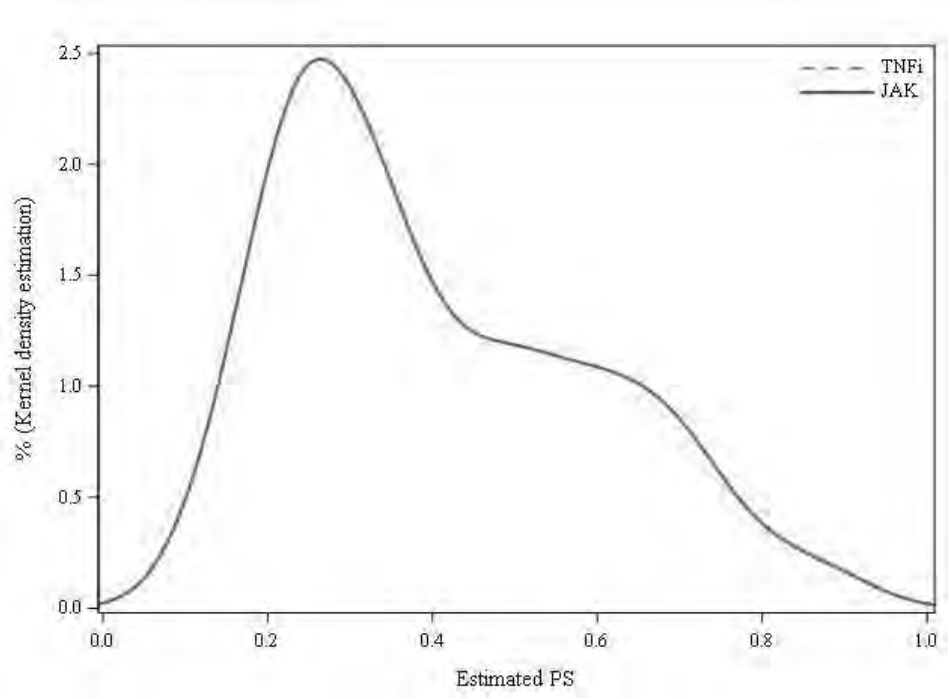

Figure A.16. Baricitinib vs TNFi PS distribution (pre-defined variables + variables with standardized difference ≥ 0.10), *matching ratio 1:1 on PS ± 0.01*

II. Supplemental Analyses

The following tables are from a sensitivity analysis with a 2-year baseline period. These tables are included to allow a comparison between patient characteristics based on using a 6-month baseline (main analysis, Section 10.3.2.7) and a 2-year baseline. Patient characteristics (Tables 1S – 4S and 6S - 9S) are reported below. No comparative analyses were executed using this baseline.

Table 1S_SNDS. Baseline Demographics, Unmatched Cohort (with 2-year Baseline Period) [SNDS]

	Baricitinib Any[a] N=3203	Baricitinib 4 mg n=2600	Baricitinib 2 mg n=599	TNFi N=8707	Std. Diff. (Any vs TNFi)
Age at Index Date [in Years]					0.298
n (missing)	3203 (0)	2600 (0)	599 (0)	8707 (0)	
Mean (SD)	58.8 (13.2)	56.4 (12.0)	69.3 (12.8)	54.8 (14.0)	
Median	59.0	57.0	72.0	56.0	
Min; Max	[18.0;92.0]	[18.0;90.0]	[20.0;92.0]	[18.0;94.0]	
Age (in Years), in Categories, n (%)					
[18-30[	68 (2.1)	62 (2.4)	≤ 10	360 (4.1)	
[30-40[	208 (6.5)	195 (7.5)	13 (2.2)	1053 (12.1)	
[40-50[	461 (14.4)	423 (16.3)	38 (6.3)	1511 (17.4)	
[50-60[	889 (27.8)	825 (31.7)	62 (10.4)	2422 (27.8)	
[60-65[	455 (14.2)	404 (15.5)	50 (8.3)	1068 (12.3)	
≥65	1122 (35.0)	691 (26.6)	430 (71.8)	2293 (26.3)	
Sex, n (%)					-0.151
Male	642 (20.0)	535 (20.6)	107 (17.9)	2299 (26.4)	
Female	2561 (80.0)	2065 (79.4)	492 (82.1)	6408 (73.6)	

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

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

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Table 2S_SNDS. Baseline Demographics - VTE Cohort, Matched (with 2-year Baseline Period) [SNDS]

	Baricitinib Any[b] n=2490	Baricitinib 4 mg n=2035	Baricitinib 2 mg n=454	TNFi[a] n=2490	Std. Diff. (Any vs TNFi)	Total n=4980
Age at Index Date [in Years]					0.005	
N (missing)	2490 (0)	2035 (0)	454 (0)	2490 (0)		4980 (0)
Mean (SD)	58.2 (13.2)	55.8 (12.1)	68.5 (13.1)	58.1 (13.4)		58.1 (13.3)
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]	55 (2.2)	49 (2.4)	≤ 10	62 (2.5)		117 (2.3)
[30-40]	180 (7.2)	169 (8.3)	11 (2.4)	171 (6.9)		351 (7.0)
[40-50]	375 (15.1)	345 (17.0)	30 (6.6)	360 (14.5)		735 (14.8)
[50-60]	711 (28.6)	659 (32.4)	51 (11.2)	706 (28.4)		1417 (28.5)
[60-65]	356 (14.3)	313 (15.4)	43 (9.5)	346 (13.9)		702 (14.1)
≥65	813 (32.7)	500 (24.6)	313 (68.9)	845 (33.9)		1658 (33.3)
Sex, n (%)					0.028	
Male	511 (20.5)	428 (21.0)	83 (18.3)	483 (19.4)		994 (20.0)
Female	1979 (79.5)	1607 (79.0)	371 (81.7)	2007 (80.6)		3986 (80.0)

Abbreviations: N = number of patients in the specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus; VTE = venous thromboembolism.

[a] Matching ratio 1:1 is applied.

[b] n=1 subject was dispensed both baricitinib 4 mg and 2 mg at index date, is included in the overall « Baricitinib Any » group but not in the strata according to the dosage.

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Table 3S_SNDS. Baseline demographics - MACE cohort, Matched (with 2-year baseline period) [SNDS]

	Baricitinib Any n = 2490	Baricitinib 4 mg n = 2039	Baricitinib 2 mg n = 451	TNFi[a] n = 2490	Std. Diff. (Any vs TNFi)	Total n = 4980
Age at index date [in years]					-0.016	
N (missing)	2490 (0)	2039 (0)	451 (0)	2490 (0)		4980 (0)
Mean (SD)	58.2 (13.3)	55.9 (12.3)	68.8 (12.7)	58.4 (13.1)		58.3 (13.2)
Median	59.0	57.0	71.0	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[	59 (2.4)	54 (2.6)	≤ 10	51 (2.0)		110 (2.2)
[30-40[	181 (7.3)	170 (8.3)	11 (2.4)	167 (6.7)		348 (7.0)
[40-50[	374 (15.0)	346 (17.0)	28 (6.2)	356 (14.3)		730 (14.7)
[50-60[	699 (28.1)	649 (31.8)	50 (11.1)	687 (27.6)		1386 (27.8)
[60-65[	339 (13.6)	298 (14.6)	41 (9.1)	353 (14.2)		692 (13.9)
≥65	838 (33.7)	522 (25.6)	316 (70.1)	876 (35.2)		1714 (34.4)
Sex, n (%)					0.043	
Male	518 (20.8)	438 (21.5)	80 (17.7)	475 (19.1)		993 (19.9)
Female	1972 (79.2)	1601 (78.5)	371 (82.3)	2015 (80.9)		3987 (80.1)

Abbreviations: 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; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

a Matching ratio 1:1 is applied

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Table 4S_SNDS. Baseline demographics - Incident Serious Infections cohort, Matched (with 2-year baseline period) [SNDS]

	Baricitinib Any[b] n = 2556	Baricitinib 4 mg n = 2083	Baricitinib 2 mg n = 470	TNFi[a] n = 2556	Std. Diff. (Any vs TNFi)	Total n = 5112
Age at index date [in years]					-0.007	
N (missing)	2556 (0)	2083 (0)	470 (0)	2556 (0)		5112 (0)
Mean (SD)	58.4 (13.3)	55.9 (12.2)	69.2 (12.9)	58.5 (13.3)		58.4 (13.3)
Median	59.0	57.0	72.0	59.0		59.0
Min; Max	[18.0;91.0]	[18.0;90.0]	[20.0;91.0]	[18.0;91.0]		[18.0;91.0]
Age (in years), in categories, n (%)						

	Baricitinib Any[b] n = 2556	**Baricitinib 4 mg n = 2083**	**Baricitinib 2 mg n = 470**	**TNFi[a] n = 2556**	**Std. Diff. (Any vs TNFi)**	**Total n = 5112**
[18-30[	58 (2.3)	52 (2.5)	≤ 10	53 (2.1)		111 (2.2)
[30-40[	180 (7.0)	169 (8.1)	11 (2.3)	169 (6.6)		349 (6.8)
[40-50[	384 (15.0)	356 (17.1)	28 (6.0)	388 (15.2)		772 (15.1)
[50-60[	714 (27.9)	666 (32.0)	46 (9.8)	710 (27.8)		1424 (27.9)
[60-65[	359 (14.0)	313 (15.0)	45 (9.6)	340 (13.3)		699 (13.7)
≥65	861 (33.7)	527 (25.3)	334 (71.1)	896 (35.1)		1757 (34.4)
Sex, n (%)					0.046	
Male	537 (21.0)	447 (21.5)	90 (19.1)	490 (19.2)		1027 (20.1)
Female	2019 (79.0)	1636 (78.5)	380 (80.9)	2066 (80.8)		4085 (79.9)

Abbreviations: N = number of patients in the specified category; Std. Diff = standardised difference; TNFi = tumour necrosis factor inhibitor; vs = versus.

a Matching ratio 1:1 is applied

b n=3 subjects were dispensed both baricitinib 4mg and 2mg at index date, are included in the overall « Baricitinib Any » group but not in the strata according to the dosage

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Table 6S_ SNDS Clinical history at baseline - Unmatched cohort (with 2-year baseline period) [SNDS]

Characteristics[a]	Baricitinib Any[d] n = 3203	Baricitinib 4 mg n = 2600	Baricitinib 2 mg n = 599	TNFi n = 8707	Std. Diff. (Any vs TNFi)
Clinical conditions during baseline period, n (%)					
Cancer, excluding NMSC	117 (3.7)	83 (3.2)	33 (5.5)	300 (3.4)	0.011
NMSC	15 (0.5)	≤ 10	≤ 10	35 (0.4)	0.010
Chronic lung disease, excluding cystic fibrosis[c]	537 (16.8)	393 (15.1)	143 (23.9)	1057 (12.1)	0.132
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	54 (1.7)	25 (1.0)	29 (4.8)	65 (0.7)	0.086
Cardiovascular revascularization procedure	35 (1.1)	20 (0.8)	15 (2.5)	66 (0.8)	0.035
Congestive Heart Failure, hospitalized	41 (1.3)	14 (0.5)	27 (4.5)	53 (0.6)	0.070
Coronary artery disease	174 (5.4)	112 (4.3)	62 (10.4)	341 (3.9)	0.072
Unstable angina	≤ 10	≤ 10	≤ 10	27 (0.3)	-0.011
Ventricular arrhythmia	65 (2.0)	32 (1.2)	33 (5.5)	119 (1.4)	0.051
Stroke	36 (1.1)	24 (0.9)	12 (2.0)	67 (0.8)	0.037
Haemorrhagic	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.011
Ischemic	19 (0.6)	11 (0.4)	≤ 10	35 (0.4)	0.027
Unknown	26 (0.8)	19 (0.7)	≤ 10	37 (0.4)	0.049
TIA	≤ 10	≤ 10	≤ 10	15 (0.2)	0.004
Diabetes Mellitus[c]	325 (10.1)	241 (9.3)	83 (13.9)	751 (8.6)	0.052
Treated insulin dependent	N/A	N/A	N/A	N/A	
Treated non insulin dependent	N/A	N/A	N/A	N/A	
Dyslipidaemia (not available in SNDS)	N/A	N/A	N/A	N/A	
Hypertension (not available in SNDS)	N/A	N/A	N/A	N/A	
History of hypertension	N/A	N/A	N/A	N/A	
Current hypertension	N/A	N/A	N/A	N/A	
Immune disorders	174 (5.4)	121 (4.7)	53 (8.8)	357 (4.1)	0.063
AIDS/HIV	≤ 10	≤ 10	0 (0.0)	11 (0.1)	-0.034
Antiphospholipid syndrome	N/A	N/A	N/A	N/A	
SLE	39 (1.2)	31 (1.2)	≤ 10	58 (0.7)	0.057

Characteristics[a]	Baricitinib Any[d] n = 3203	Baricitinib 4 mg n = 2600	Baricitinib 2 mg n = 599	TNFi n = 8707	Std. Diff. (Any vs TNFi)
Primary Sjogren Syndrome	146 (4.6)	98 (3.8)	48 (8.0)	303 (3.5)	0.055
Liver or pancreatic disorder[c]	127 (4.0)	94 (3.6)	32 (5.3)	246 (2.8)	0.063
Obesity (not available in SNDS)	N/A	N/A	N/A	N/A	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date)	≤ 10	≤ 10	0 (0.0)	60 (0.7)	-0.07
RA Severity (CIRAS Index)					-0.337
Mean (SD)	6.4 (1.4)	6.6 (1.3)	5.8 (1.4)	6.9 (1.5)	
Smoking (not available in SNDS)	N/A	N/A	N/A	N/A	
DMARDs, n (%)					
cDMARDs, during baseline period					
n, total (%)	2556 (79.8)	2111 (81.2)	441 (73.6)	7412 (85.1)	-0.14
Mean (SD)	1.0 (0.7)	1.0 (0.7)	0.9 (0.8)	1.1 (0.7)	-0.112
Median	1.0	1.0	1.0	1.0	
Min; Max	[0.0;4.0]	[0.0;4.0]	[0.0;4.0]	[0.0;4.0]	
>1 cDMARD concomitantly	369 (11.5)	296 (11.4)	72 (12.0)	1099 (12.6)	-0.034
Hydroxychloroquine	300 (9.4)	241 (9.3)	58 (9.7)	791 (9.1)	0.010
Chloroquine	≤ 10	≤ 10	≤ 10	≤ 10	-0.003
Azathioprine	27 (0.8)	18 (0.7)	≤ 10	53 (0.6)	0.028
Leflunomide	582 (18.2)	482 (18.5)	99 (16.5)	1299 (14.9)	0.088
Methotrexate	2082 (65.0)	1722 (66.2)	357 (59.6)	6567 (75.4)	-0.229
Mycophenolate mofetil	≤ 10	≤ 10	≤ 10	≤ 10	0.029
Sulfasalazine	213 (6.7)	171 (6.6)	41 (6.8)	681 (7.8)	-0.045
Cyclosporin	≤ 10	≤ 10	≤ 10	≤ 10	0.029
Penicillamine	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.030
bDMARDs, during baseline period					
n, total (%)	2390 (74.6)	1975 (76.0)	411 (68.6)	2830 (32.5)	0.932
Mean (SD)	1.2 (1.0)	1.2 (1.0)	1.1 (1.0)	0.4 (0.7)	0.945
Median	1.0	1.0	1.0	0.0	
Min; Max	[0.0;6.0]	[0.0;6.0]	[0.0;6.0]	[0.0;5.0]	
cDMARDs, concomitant	1591 (49.7)	1350 (51.9)	238 (39.7)	1778 (20.4)	0.644
Adalimumab[b]	456 (14.2)	389 (15.0)	67 (11.2)	604 (6.9)	0.239

Characteristics[a]	Baricitinib Any[d] n = 3203	Baricitinib 4 mg n = 2600	Baricitinib 2 mg n = 599	TNFi n = 8707	Std. Diff. (Any vs TNFi)
Certolizumab pegol[b]	281 (8.8)	240 (9.2)	40 (6.7)	232 (2.7)	0.265
Etanercept[b]	628 (19.6)	527 (20.3)	99 (16.5)	952 (10.9)	0.243
Golimumab[b]	229 (7.1)	202 (7.8)	26 (4.3)	211 (2.4)	0.223
Infliximab[b]	160 (5.0)	141 (5.4)	18 (3.0)	306 (3.5)	0.073
Rituximab	326 (10.2)	252 (9.7)	73 (12.2)	120 (1.4)	0.384
Sarilumab	49 (1.5)	39 (1.5)	≤ 10	25 (0.3)	0.131
Abatacept	865 (27.0)	684 (26.3)	178 (29.7)	580 (6.7)	0.565
Tocilizumab	846 (26.4)	720 (27.7)	126 (21.0)	496 (5.7)	0.588
Anakinra	28 (0.9)	19 (0.7)	≤ 10	24 (0.3)	0.079
TNFi naïve at baseline	1803 (56.3)	1401 (53.9)	401 (66.9)	6636 (76.2)	-0.431
Other prescription medications during baseline period, n (%)					
Antibiotics	2571 (80.3)	2074 (79.8)	493 (82.3)	6594 (75.7)	0.110
Antidiabetic agents	322 (10.1)	242 (9.3)	79 (13.2)	764 (8.8)	0.044
Insulins	137 (4.3)	103 (4.0)	34 (5.7)	274 (3.1)	0.06
Non-insulins	270 (8.4)	205 (7.9)	64 (10.7)	661 (7.6)	0.031
Cardiovascular					
Antithrombotic agents	821 (25.6)	594 (22.8)	224 (37.4)	1890 (21.7)	0.093
Anticoagulant	457 (14.3)	334 (12.8)	121 (20.2)	1059 (12.2)	0.062
Antiplatelet	446 (13.9)	309 (11.9)	136 (22.7)	987 (11.3)	0.078
Antihypertensives	1226 (38.3)	866 (33.3)	358 (59.8)	2749 (31.6)	0.141
Angiotensin converting enzyme inhibitors (ACE)	359 (11.2)	247 (9.5)	111 (18.5)	858 (9.9)	0.044
Angiotensin receptor blockers (ARB)	477 (14.9)	327 (12.6)	150 (25.0)	1105 (12.7)	0.064
Beta blocker	564 (17.6)	389 (15.0)	174 (29.0)	1185 (13.6)	0.110
Calcium channel blocker	450 (14.0)	302 (11.6)	146 (24.4)	918 (10.5)	0.107
Nitrates	79 (2.5)	48 (1.8)	31 (5.2)	168 (1.9)	0.037
Acyclovir	56 (1.7)	42 (1.6)	14 (2.3)	135 (1.6)	0.016
Valacyclovir	294 (9.2)	228 (8.8)	66 (11.0)	614 (7.1)	0.078
Hormonal	711 (22.2)	616 (23.7)	94 (15.7)	2158 (24.8)	-0.061
HRT	463 (14.5)	387 (14.9)	75 (12.5)	1183 (13.6)	0.025

Characteristics[a]	Baricitinib Any[d] n = 3203	Baricitinib 4 mg n = 2600	Baricitinib 2 mg n = 599	TNFi n = 8707	Std. Diff. (Any vs TNFi)
Oral Contraceptives	249 (7.8)	229 (8.8)	20 (3.3)	1007 (11.6)	-0.129
SERMs	17 (0.5)	15 (0.6)	≤ 10	38 (0.4)	0.014
Topic with progestogens and/or estrogens	39 (1.2)	38 (1.5)	≤ 10	171 (2.0)	-0.06
Lipid-lowering agents	679 (21.2)	491 (18.9)	187 (31.2)	1432 (16.4)	0.122
HMG CoA reductase inhibitors	550 (17.2)	393 (15.1)	156 (26.0)	1169 (13.4)	0.104
Fibrates	73 (2.3)	53 (2.0)	20 (3.3)	148 (1.7)	0.042
Bile acid sequestrants	32 (1.0)	26 (1.0)	≤ 10	71 (0.8)	0.019
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Other lipid modifying agents	50 (1.6)	35 (1.3)	15 (2.5)	96 (1.1)	0.04
Lipid modifying agents, combinations	55 (1.7)	42 (1.6)	13 (2.2)	101 (1.2)	0.047
Rheumatoid arthritis-related					
Aspirin	103 (3.2)	80 (3.1)	22 (3.7)	308 (3.5)	-0.018
Cox-2 Inhibitor	377 (11.8)	331 (12.7)	44 (7.3)	1244 (14.3)	-0.075
NSAIDs	2129 (66.5)	1806 (69.5)	320 (53.4)	6554 (75.3)	-0.195
Glucocorticosteroid	2902 (90.6)	2348 (90.3)	550 (91.8)	7675 (88.1)	0.08
Vaccines	1902 (59.4)	1465 (56.3)	437 (73.0)	5611 (64.4)	-0.104
Antineoplastic agents	24 (0.7)	14 (0.5)	≤ 10	57 (0.7)	0.011

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; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or haemorrhagic stroke; Max = maximum; MI = myocardial infarction; 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; TB = tuberculosis; TIA = transient ischemic attack; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

a All conditions and characteristics are measured during the 2 years 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 TNF inhibitors

c CNAM algorithm based on the year preceding the year of inclusion

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

Source:lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\french snds_SNDS\BARICITINIB - Supplemental SNDS analyses Points I to VI V1.0 20220328.docx – Table 22 page(s) 49 - 54

Table 7S_SNDS Clinical characteristics at baseline - VTE cohort, Matched (with 2-year baseline period) [SNDS]

Characteristics[b]	Baricitinib Any[e] n = 2490	Baricitinib 4 mg n = 2035	Baricitinib 2 mg n = 454	TNFi[a] n = 2490	Std. Diff. (Any vs TNFi)
Clinical conditions during baseline period, n (%)					
Cancer, excluding NMSC	92 (3.7)	68 (3.3)	24 (5.3)	99 (4.0)	-0.015
NMSC	≤ 10	≤ 10	≤ 10	15 (0.6)	-0.028
Chronic lung disease, excluding cystic fibrosis[d]	398 (16.0)	294 (14.4)	104 (22.9)	349 (14.0)	0.055
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	37 (1.5)	19 (0.9)	18 (4.0)	27 (1.1)	0.036
Cardiovascular revascularization procedure	20 (0.8)	≤ 10	11 (2.4)	21 (0.8)	-0.004
Congestive Heart Failure, hospitalized	31 (1.2)	13 (0.6)	18 (4.0)	25 (1.0)	0.023
Coronary artery disease	126 (5.1)	85 (4.2)	41 (9.0)	122 (4.9)	0.007
Unstable angina	≤ 10	≤ 10	≤ 10	≤ 10	-0.021
Ventricular arrhythmia	42 (1.7)	22 (1.1)	20 (4.4)	52 (2.1)	-0.030
Stroke	21 (0.8)	14 (0.7)	≤ 10	28 (1.1)	-0.029
Hemorrhagic	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.057

Characteristics[b]	Baricitinib Any[e] n = 2490	Baricitinib 4 mg n = 2035	Baricitinib 2 mg n = 454	TNFi[a] n = 2490	Std. Diff. (Any vs TNFi)
Ischemic	≤ 10	≤ 10	≤ 10	13 (0.5)	-0.024
Unknown	18 (0.7)	13 (0.6)	≤ 10	16 (0.6)	0.01
TIA	≤ 10	0 (0.0)	≤ 10	≤ 10	-0.032
Diabetes Mellitus[d]	232 (9.3)	174 (8.6)	58 (12.8)	235 (9.4)	-0.004
Treated insulin dependent	N/A	N/A	N/A	N/A	
Treated non insulin dependent	N/A	N/A	N/A	N/A	
Dyslipidaemia (not available in SNDS)	N/A	N/A	N/A	N/A	
Hypertension (not available in SNDS)					
History of hypertension	N/A	N/A	N/A	N/A	
Current hypertension	N/A	N/A	N/A	N/A	
Immune disorders	126 (5.1)	90 (4.4)	36 (7.9)	119 (4.8)	0.013
AIDS/HIV	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.046
Antiphospholipid syndrome	N/A	N/A	N/A	N/A	
SLE	31 (1.2)	26 (1.3)	≤ 10	≤ 10	0.093
Primary Sjogren Syndrome	101 (4.1)	69 (3.4)	32 (7.0)	108 (4.3)	-0.014
Liver or pancreatic disorder[d]	87 (3.5)	65 (3.2)	21 (4.6)	88 (3.5)	-0.002
Obesity (not available in SNDS)	N/A	N/A	N/A	N/A	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date)	≤ 10	≤ 10	0 (0.0)	≤ 10	0.036
RA Severity (CIRAS Index)					0.025
Mean (± SD)	6.5 (1.4)	6.7 (1.3)	5.8 (1.4)	6.5 (1.4)	
Smoking (not available in SNDS)	N/A	N/A	N/A	N/A	
DMARDs, n (%)					
cDMARDs, during baseline period					
n, total (%)	2016 (81.0)	1666 (81.9)	349 (76.9)	1980 (79.5)	0.036
Mean (SD)	1.0 (0.7)	1.0 (0.7)	1.0 (0.8)	1.0 (0.7)	0.031
Median	1.0	1.0	1.0	1.0	
Min; Max	[0.0;4.0]	[0.0;4.0]	[0.0;4.0]	[0.0;4.0]	
>1 cDMARD concomitantly	308 (12.4)	243 (11.9)	65 (14.3)	275 (11.0)	0.041
Hydroxychloroquine	242 (9.7)	193 (9.5)	49 (10.8)	215 (8.6)	0.038
Chloroquine	≤ 10	≤ 10	≤ 10	≤ 10	-0.013

Characteristics[b]	Baricitinib Any[e] n = 2490	Baricitinib 4 mg n = 2035	Baricitinib 2 mg n = 454	TNFi[a] n = 2490	Std. Diff. (Any vs TNFi)
Azathioprin	18 (0.7)	13 (0.6)	≤ 10	16 (0.6)	0.010
Leflunomid	445 (17.9)	366 (18.0)	79 (17.4)	413 (16.6)	0.034
Methotrexate	1666 (66.9)	1376 (67.6)	290 (63.9)	1683 (67.6)	-0.015
Mycophenolate mofetil	≤ 10	≤ 10	≤ 10	≤ 10	0.016
Sulfasalazin	171 (6.9)	134 (6.6)	37 (8.1)	160 (6.4)	0.018
Cyclosporin	≤ 10	≤ 10	≤ 10	≤ 10	0.028
Penicillamin	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.04
bDMARDs, during baseline period					
n, total (%)	1677 (67.3)	1410 (69.3)	266 (58.6)	1638 (65.8)	0.033
Mean (SD)	0.9 (0.8)	1.0 (0.8)	0.8 (0.8)	0.9 (0.8)	0.003
Median	1.0	1.0	1.0	1.0	
Min; Max	[0.0;5.0]	[0.0;5.0]	[0.0;4.0]	[0.0;5.0]	
cDMARDs, concomitant	1127 (45.3)	965 (47.4)	161 (35.5)	1011 (40.6)	0.094
Adalimumab[c]	301 (12.1)	259 (12.7)	42 (9.3)	333 (13.4)	-0.039
Certolizumab pegol[c]	170 (6.8)	144 (7.1)	26 (5.7)	168 (6.7)	0.003
Etanercept[c]	467 (18.8)	399 (19.6)	68 (15.0)	460 (18.5)	0.007
Golimumab[c]	130 (5.2)	118 (5.8)	12 (2.6)	144 (5.8)	-0.025
Infliximab[c]	111 (4.5)	100 (4.9)	≤ 10	117 (4.7)	-0.012
Rituximab	131 (5.3)	102 (5.0)	29 (6.4)	118 (4.7)	0.024
Sarilumab	22 (0.9)	16 (0.8)	≤ 10	22 (0.9)	0.000
Abatacept	500 (20.1)	405 (19.9)	94 (20.7)	476 (19.1)	0.024
Tocilizumab	457 (18.4)	398 (19.6)	59 (13.0)	448 (18.0)	0.009
Anakinra	19 (0.8)	13 (0.6)	≤ 10	16 (0.6)	0.014
TNFi naïve at baseline	1509 (60.6)	1183 (58.1)	326 (71.8)	1459 (58.6)	0.041
Other prescription medications during baseline period, n (%)					
Antibiotics	1976 (79.4)	1608 (79.0)	367 (80.8)	1941 (78.0)	0.034
Antidiabetic agents	231 (9.3)	175 (8.6)	56 (12.3)	237 (9.5)	-0.008
Insulins	94 (3.8)	71 (3.5)	23 (5.1)	88 (3.5)	0.013
Non-insulins	194 (7.8)	148 (7.3)	46 (10.1)	207 (8.3)	-0.019

Characteristics[b]	Baricitinib Any[e] n = 2490	Baricitinib 4 mg n = 2035	Baricitinib 2 mg n = 454	TNFi[a] n = 2490	Std. Diff. (Any vs TNFi)
Cardiovascular					
Antithrombotic agents	609 (24.5)	449 (22.1)	159 (35.0)	599 (24.1)	0.009
Anticoagulant	335 (13.5)	255 (12.5)	79 (17.4)	350 (14.1)	-0.018
Antiplatelet	331 (13.3)	231 (11.4)	100 (22.0)	319 (12.8)	0.014
Antihypertensives	923 (37.1)	661 (32.5)	262 (57.7)	912 (36.6)	0.009
Angiotensin converting enzyme inhibitors (ACE)	267 (10.7)	191 (9.4)	76 (16.7)	270 (10.8)	-0.004
Angiotensin receptor blockers (ARB)	364 (14.6)	252 (12.4)	112 (24.7)	368 (14.8)	-0.005
Beta blocker	426 (17.1)	299 (14.7)	127 (28.0)	397 (15.9)	0.031
Calcium channel blocker	315 (12.7)	212 (10.4)	103 (22.7)	314 (12.6)	0.001
Nitrates	51 (2.0)	30 (1.5)	21 (4.6)	66 (2.7)	-0.04
Acyclovir	38 (1.5)	27 (1.3)	11 (2.4)	47 (1.9)	-0.028
Valacyclovir	222 (8.9)	176 (8.6)	46 (10.1)	226 (9.1)	-0.006
Hormonal	552 (22.2)	477 (23.4)	74 (16.3)	547 (22.0)	0.005
HRT	350 (14.1)	292 (14.3)	57 (12.6)	345 (13.9)	0.006
Oral Contraceptives	203 (8.2)	185 (9.1)	18 (4.0)	199 (8.0)	0.006
SERMs	14 (0.6)	12 (0.6)	≤ 10	12 (0.5)	0.011
Topic with progestogens and/or estrogens	33 (1.3)	32 (1.6)	≤ 10	36 (1.4)	-0.010
Lipid-lowering agents	492 (19.8)	358 (17.6)	134 (29.5)	462 (18.6)	0.031
HMG CoA reductase inhibitors	393 (15.8)	281 (13.8)	112 (24.7)	376 (15.1)	0.019
Fibrates	50 (2.0)	33 (1.6)	17 (3.7)	42 (1.7)	0.024
Bile acid sequestrants	25 (1.0)	22 (1.1)	≤ 10	27 (1.1)	-0.008
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Other lipid modifying agents	38 (1.5)	27 (1.3)	11 (2.4)	33 (1.3)	0.017
Lipid modifying agents, combinations	47 (1.9)	38 (1.9)	≤ 10	34 (1.4)	0.041
Rheumatoid arthritis-related					
Aspirin	77 (3.1)	59 (2.9)	18 (4.0)	90 (3.6)	-0.029
Cox-2 Inhibitor	285 (11.4)	250 (12.3)	35 (7.7)	340 (13.7)	-0.067
NSAIDs	1670 (67.1)	1420 (69.8)	250 (55.1)	1736 (69.7)	-0.057
Glucocorticosteroid	2235 (89.8)	1822 (89.5)	412 (90.7)	2234 (89.7)	0.001
Vaccines	1503 (60.4)	1164 (57.2)	339 (74.7)	1500 (60.2)	0.003
Antineoplastic agents	21 (0.8)	13 (0.6)	≤ 10	25 (1.0)	-0.017

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; CNAM = Caisse Nationale de l'Assurance Maladie; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; HMG-CoA = β-Hydroxy β-methylglutaryl-CoA; Max = maximum; Min = minimum; N = number of patients in the specified category; NSAID = non-steroidal anti-inflammatory medication; N/A = not applicable; 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 Matching ratio 1:1 is applied

b All conditions and characteristics are measured during the 2 years 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 TNF inhibitors.

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

e n=1 subject was dispensed both baricitinib 4mg and 2mg at index date, is included in the overall « Baricitinib Any » group but not in the strata according to the dosage

Source:lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\french snds_SNDS\BARICITINIB - Supplemental SNDS analyses Points I to VI V1.0 20220328.docx – Table 23 page(s) 55 - 59

Table 8S_ SNDS Clinical characteristics at baseline - MACE cohort, Matched (with 2-year baseline period) [SNDS]

Characteristics[b]	Baricitinib Any n = 2490	Baricitinib 4 mg n = 2039	Baricitinib 2 mg n = 451	TNFi[a] n = 2490	Std. Diff. (Any vs TNFi)
Clinical conditions during baseline period, n (%)					
Cancer, excluding NMSC	95 (3.8)	70 (3.4)	25 (5.5)	118 (4.7)	-0.046
NMSC	13 (0.5)	≤ 10	≤ 10	≤ 10	0.018
Chronic lung disease, excluding cystic fibrosis[d]	409 (16.4)	306 (15.0)	103 (22.8)	364 (14.6)	0.05
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	40 (1.6)	18 (0.9)	22 (4.9)	24 (1.0)	0.057
Cardiovascular revascularization procedure	12 (0.5)	≤ 10	≤ 10	≤ 10	0.012
Congestive Heart Failure, hospitalized	24 (1.0)	≤ 10	16 (3.5)	13 (0.5)	0.052
Coronary artery disease	112 (4.5)	73 (3.6)	39 (8.6)	115 (4.6)	-0.006
Unstable angina	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.057
Ventricular arrhythmia	38 (1.5)	18 (0.9)	20 (4.4)	39 (1.6)	-0.003
Stroke (LTD or associated diagnosis)	15 (0.6)	11 (0.5)	≤ 10	18 (0.7)	-0.015

Characteristics[b]	Baricitinib Any n = 2490	Baricitinib 4 mg n = 2039	Baricitinib 2 mg n = 451	TNFi[a] n = 2490	Std. Diff. (Any vs TNFi)
Hemorrhagic	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.049
Ischemic	≤ 10	≤ 10	≤ 10	≤ 10	-0.023
Unknown	14 (0.6)	≤ 10	≤ 10	12 (0.5)	0.011
TIA	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.049
Diabetes Mellitus[d]	226 (9.1)	171 (8.4)	55 (12.2)	227 (9.1)	-0.001
Treated insulin dependent	N/A	N/A	N/A	N/A	
Treated non insulin dependent	N/A	N/A	N/A	N/A	
Dyslipidaemia (not available in SNDS)	N/A	N/A	N/A	N/A	
Hypertension (not available in SNDS)					
History of hypertension	N/A	N/A	N/A	N/A	
Current hypertension	N/A	N/A	N/A	N/A	
Immune disorders	128 (5.1)	93 (4.6)	35 (7.8)	117 (4.7)	0.02
AIDS/HIV	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.028
Antiphospholipid syndrome	N/A	N/A	N/A	N/A	
SLE	32 (1.3)	25 (1.2)	≤ 10	13 (0.5)	0.081
Primary Sjogren Syndrome	105 (4.2)	74 (3.6)	31 (6.9)	106 (4.3)	-0.002
Liver or pancreatic disorder[d]	78 (3.1)	59 (2.9)	19 (4.2)	91 (3.7)	-0.029
Obesity (not available in SNDS)	N/A	N/A	N/A	N/A	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date)	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.021
RA Severity (CIRAS Index)					0.05
Mean (± SD)	6.5 (1.4)	6.7 (1.4)	5.8 (1.4)	6.4 (1.4)	
Smoking (not available in SNDS)	N/A	N/A	N/A	N/A	
DMARDs, n (%)					
cDMARDs, during baseline period					
n, total (%)	2014 (80.9)	1673 (82.1)	341 (75.6)	1990 (79.9)	0.024
Mean (SD)	1.0 (0.7)	1.0 (0.7)	1.0 (0.8)	1.0 (0.7)	0.012
Median	1.0	1.0	1.0	1.0	
Min; Max	[0.0;4.0]	[0.0;4.0]	[0.0;4.0]	[0.0;4.0]	
>1 cDMARD concomitantly	302 (12.1)	241 (11.8)	61 (13.5)	270 (10.8)	0.04

Characteristics[b]	Baricitinib Any n = 2490	Baricitinib 4 mg n = 2039	Baricitinib 2 mg n = 451	TNFi[a] n = 2490	Std. Diff. (Any vs TNFi)
Hydroxychloroquine	240 (9.6)	192 (9.4)	48 (10.6)	210 (8.4)	0.042
Chloroquine	≤ 10	≤ 10	≤ 10	≤ 10	-0.023
Azathioprin	14 (0.6)	11 (0.5)	≤ 10	16 (0.6)	-0.01
Leflunomid	428 (17.2)	355 (17.4)	73 (16.2)	443 (17.8)	-0.016
Methotrexate	1670 (67.1)	1389 (68.1)	281 (62.3)	1670 (67.1)	0.000
Mycophenolate mofetil	≤ 10	≤ 10	0 (0.0)	≤ 10	0.000
Sulfasalazin	170 (6.8)	132 (6.5)	38 (8.4)	160 (6.4)	0.016
Cyclosporin	≤ 10	≤ 10	≤ 10	≤ 10	0.028
Penicillamin	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.040
bDMARDs, during baseline period					
n, total (%)	1679 (67.4)	1415 (69.4)	264 (58.5)	1646 (66.1)	0.028
Mean (SD)	0.9 (0.8)	1.0 (0.8)	0.8 (0.9)	0.9 (0.8)	0.005
Median	1.0	1.0	1.0	1.0	
Min; Max	[0.0;6.0]	[0.0;5.0]	[0.0;6.0]	[0.0;5.0]	
cDMARDs, concomitant	1129 (45.3)	970 (47.6)	159 (35.3)	1015 (40.8)	0.093
Adalimumab[c]	317 (12.7)	277 (13.6)	40 (8.9)	321 (12.9)	-0.005
Certolizumab pegol[c]	164 (6.6)	141 (6.9)	23 (5.1)	169 (6.8)	-0.008
Etanercept[c]	432 (17.3)	371 (18.2)	61 (13.5)	479 (19.2)	-0.049
Golimumab[c]	131 (5.3)	121 (5.9)	≤ 10	138 (5.5)	-0.012
Infliximab[c]	102 (4.1)	93 (4.6)	≤ 10	108 (4.3)	-0.012
Rituximab	145 (5.8)	109 (5.3)	36 (8.0)	117 (4.7)	0.050
Sarilumab	23 (0.9)	19 (0.9)	≤ 10	24 (1.0)	-0.004
Abatacept	498 (20.0)	396 (19.4)	102 (22.6)	473 (19.0)	0.025
Tocilizumab	466 (18.7)	402 (19.7)	64 (14.2)	439 (17.6)	0.028
Anakinra	20 (0.8)	12 (0.6)	≤ 10	20 (0.8)	0.000
TNFi naïve at baseline	1533 (61.6)	1204 (59.0)	329 (72.9)	1448 (58.2)	0.07
Other prescription medications during baseline period, n (%)					
Antibiotics	1985 (79.7)	1613 (79.1)	372 (82.5)	1937 (77.8)	0.047
Antidiabetic agents	228 (9.2)	173 (8.5)	55 (12.2)	226 (9.1)	0.003

Characteristics[b]	Baricitinib Any n = 2490	Baricitinib 4 mg n = 2039	Baricitinib 2 mg n = 451	TNFi[a] n = 2490	Std. Diff. (Any vs TNFi)
Insulins	98 (3.9)	76 (3.7)	22 (4.9)	90 (3.6)	0.017
Non-insulins	189 (7.6)	144 (7.1)	45 (10.0)	193 (7.8)	-0.006
Cardiovascular					
Antithrombotic agents	606 (24.3)	448 (22.0)	158 (35.0)	594 (23.9)	0.011
Anticoagulant	350 (14.1)	261 (12.8)	89 (19.7)	337 (13.5)	0.015
Antiplatelet	313 (12.6)	221 (10.8)	92 (20.4)	318 (12.8)	-0.006
Antihypertensives	916 (36.8)	646 (31.7)	270 (59.9)	933 (37.5)	-0.014
Angiotensin converting enzyme inhibitors (ACE)	273 (11.0)	189 (9.3)	84 (18.6)	289 (11.6)	-0.020
Angiotensin receptor blockers (ARB)	361 (14.5)	243 (11.9)	118 (26.2)	391 (15.7)	-0.034
Beta blocker	405 (16.3)	279 (13.7)	126 (27.9)	402 (16.1)	0.003
Calcium channel blocker	326 (13.1)	217 (10.6)	109 (24.2)	306 (12.3)	0.024
Nitrates	44 (1.8)	28 (1.4)	16 (3.5)	62 (2.5)	-0.05
Acyclovir	39 (1.6)	28 (1.4)	11 (2.4)	43 (1.7)	-0.013
Valacyclovir	217 (8.7)	167 (8.2)	50 (11.1)	228 (9.2)	-0.016
Hormonal	551 (22.1)	476 (23.3)	75 (16.6)	560 (22.5)	-0.009
HRT	353 (14.2)	295 (14.5)	58 (12.9)	364 (14.6)	-0.013
Oral Contraceptives	203 (8.2)	185 (9.1)	18 (4.0)	196 (7.9)	0.010
SERMs	12 (0.5)	11 (0.5)	≤ 10	13 (0.5)	-0.006
Topic with progestogens and/or estrogens	30 (1.2)	29 (1.4)	≤ 10	32 (1.3)	-0.007
Lipid-lowering agents	480 (19.3)	343 (16.8)	137 (30.4)	488 (19.6)	-0.008
HMG CoA reductase inhibitors	378 (15.2)	267 (13.1)	111 (24.6)	406 (16.3)	-0.031
Fibrates	50 (2.0)	33 (1.6)	17 (3.8)	49 (2.0)	0.003
Bile acid sequestrants	24 (1.0)	21 (1.0)	≤ 10	23 (0.9)	0.004
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Other lipid modifying agents	38 (1.5)	26 (1.3)	12 (2.7)	31 (1.2)	0.024
Lipid modifying agents, combinations	46 (1.8)	36 (1.8)	≤ 10	31 (1.2)	0.049
Rheumatoid arthritis-related					
Aspirin	77 (3.1)	60 (2.9)	17 (3.8)	69 (2.8)	0.019
Cox-2 Inhibitor	288 (11.6)	254 (12.5)	34 (7.5)	347 (13.9)	-0.071
NSAIDs	1668 (67.0)	1421 (69.7)	247 (54.8)	1724 (69.2)	-0.048
Glucocorticosteroid	2230 (89.6)	1822 (89.4)	408 (90.5)	2241 (90.0)	-0.015

Characteristics[b]	Baricitinib Any n = 2490	Baricitinib 4 mg n = 2039	Baricitinib 2 mg n = 451	TNFi[a] n = 2490	Std. Diff. (Any vs TNFi)
Vaccines	1512 (60.7)	1174 (57.6)	338 (74.9)	1466 (58.9)	0.038
Antineoplastic agents	24 (1.0)	14 (0.7)	≤ 10	26 (1.0)	-0.008

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; CNAM = Caisse Nationale de l'Assurance Maladie; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; HMG-CoA = β-Hydroxy β-methylglutaryl-CoA; 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; NSAID = non-steroidal anti-inflammatory drug; 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 Matching ratio 1:1 is applied

b All conditions and characteristics are measured during the 2 years 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 TNF inhibitors.

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

e n=1 subject was dispensed both baricitinib 4mg and 2mg at index date, is included in the overall « Baricitinib Any » group but not in the strata according to the dosage

a Matching ratio 1:1 is applied

b All conditions and characteristics are measured during the 2 years 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 TNF inhibitors.

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

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Table 9S_SNDS [SNDS] Clinical Characteristics at baseline - Incident Serious Infection cohort, Matched (with 2-year baseline period)

Characteristics[b]	Baricitinib Any[e] n = 2556	Baricitinib 4 mg n = 2083	Baricitinib 2 mg n = 470	TNFi[a] n = 2556	Std. Diff. (Any vs TNFi)
Clinical conditions during baseline period, n (%)					
Cancer, excluding NMSC	100 (3.9)	73 (3.5)	26 (5.5)	111 (4.3)	-0.022
NMSC	12 (0.5)	≤ 10	≤ 10	15 (0.6)	-0.016
Chronic lung disease, excluding cystic fibrosis[d]	412 (16.1)	309 (14.8)	102 (21.7)	381 (14.9)	0.034
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	68 (2.7)	33 (1.6)	35 (7.4)	78 (3.1)	-0.024
Cardiovascular revascularization procedure	29 (1.1)	16 (0.8)	13 (2.8)	22 (0.9)	0.028
Congestive Heart Failure, hospitalized	34 (1.3)	14 (0.7)	20 (4.3)	32 (1.3)	0.007
Coronary artery disease	147 (5.8)	105 (5.0)	42 (8.9)	129 (5.0)	0.031
Unstable angina	≤ 10	≤ 10	≤ 10	≤ 10	-0.008
Ventricular arrhythmia	54 (2.1)	29 (1.4)	25 (5.3)	51 (2.0)	0.008
Stroke	30 (1.2)	20 (1.0)	≤ 10	36 (1.4)	-0.021
Hemorrhagic	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.023
Ischemic	17 (0.7)	≤ 10	≤ 10	17 (0.7)	0.000
Unknown	21 (0.8)	16 (0.8)	≤ 10	24 (0.9)	-0.013
TIA	≤ 10	≤ 10	≤ 10	≤ 10	-0.025
Diabetes Mellitus[d]	256 (10.0)	191 (9.2)	65 (13.8)	241 (9.4)	0.020
Treated insulin dependent	N/A	N/A	N/A	N/A	
Treated non insulin dependent	N/A	N/A	N/A	N/A	
Dyslipidaemia (not available in SNDS)	N/A	N/A	N/A	N/A	
Hypertension (not available in SNDS)					
History of hypertension	N/A	N/A	N/A	N/A	
Current hypertension	N/A	N/A	N/A	N/A	
Immune disorders	133 (5.2)	94 (4.5)	39 (8.3)	120 (4.7)	0.024
AIDS/HIV	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.046
Antiphospholipid syndrome	N/A	N/A	N/A	N/A	

Characteristics[b]	Baricitinib Any[e] n = 2556	Baricitinib 4 mg n = 2083	Baricitinib 2 mg n = 470	TNFi[a] n = 2556	Std. Diff. (Any vs TNFi)
SLE	32 (1.3)	28 (1.3)	≤ 10	12 (0.5)	0.085
Primary Sjogren Syndrome	106 (4.1)	71 (3.4)	35 (7.4)	108 (4.2)	-0.004
Liver or pancreatic disorder[d]	84 (3.3)	64 (3.1)	19 (4.0)	88 (3.4)	-0.009
Obesity (not available in SNDS)	N/A	N/A	N/A	N/A	
Recent pregnancy (ongoing or having ended in the 90 days prior to cohort entry date)	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.008
RA Severity (CIRAS Index)					0.039
Mean (± SD)	6.5 (1.4)	6.6 (1.3)	5.8 (1.4)	6.4 (1.4)	
Smoking (not available in SNDS)	N/A	N/A	N/A	N/A	
DMARDs, n (%)					
cDMARDs, during baseline period					
n, total (%)	2075 (81.2)	1718 (82.5)	354 (75.3)	2065 (80.8)	0.010
Mean (SD)	1.0 (0.7)	1.0 (0.7)	1.0 (0.8)	1.0 (0.7)	-0.019
Median	1.0	1.0	1.0	1.0	
Min; Max	[0.0;4.0]	[0.0;4.0]	[0.0;4.0]	[0.0;4.0]	
>1 cDMARD concomitantly	305 (11.9)	245 (11.8)	59 (12.6)	279 (10.9)	0.032
Hydroxychloroquine	251 (9.8)	199 (9.6)	51 (10.9)	212 (8.3)	0.053
Chloroquine	≤ 10	≤ 10	≤ 10	≤ 10	-0.023
Azathioprin	21 (0.8)	15 (0.7)	≤ 10	15 (0.6)	0.028
Leflunomid	444 (17.4)	367 (17.6)	76 (16.2)	474 (18.5)	-0.031
Methotrexate	1710 (66.9)	1421 (68.2)	287 (61.1)	1751 (68.5)	-0.034
Mycophenolate mofetil	≤ 10	≤ 10	≤ 10	≤ 10	0.016
Sulfasalazin	175 (6.8)	137 (6.6)	37 (7.9)	183 (7.2)	-0.012
Cyclosporin	≤ 10	≤ 10	≤ 10	≤ 10	0.028
Penicillamin	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.040
bDMARDs, during baseline period					
n, total (%)	1729 (67.6)	1444 (69.3)	282 (60.0)	1678 (65.6)	0.042
Mean (SD)	0.9 (0.8)	1.0 (0.8)	0.8 (0.8)	0.9 (0.8)	0.009
Median	1.0	1.0	1.0	1.0	
Min; Max	[0.0;6.0]	[0.0;4.0]	[0.0;6.0]	[0.0;5.0]	
cDMARDs, concomitant	1161 (45.4)	994 (47.7)	165 (35.1)	1067 (41.7)	0.074

Characteristics[b]	Baricitinib Any[e] n = 2556	Baricitinib 4 mg n = 2083	Baricitinib 2 mg n = 470	TNFi[a] n = 2556	Std. Diff. (Any vs TNFi)
Adalimumab[c]	312 (12.2)	272 (13.1)	40 (8.5)	327 (12.8)	-0.018
Certolizumab pegol[c]	175 (6.8)	151 (7.2)	24 (5.1)	178 (7.0)	-0.005
Etanercept[c]	459 (18.0)	391 (18.8)	67 (14.3)	485 (19.0)	-0.026
Golimumab[c]	142 (5.6)	131 (6.3)	11 (2.3)	147 (5.8)	-0.009
Infliximab[c]	114 (4.5)	105 (5.0)	≤ 10	102 (4.0)	0.023
Rituximab	134 (5.2)	102 (4.9)	31 (6.6)	114 (4.5)	0.036
Sarilumab	27 (1.1)	21 (1.0)	≤ 10	24 (0.9)	0.012
Abatacept	513 (20.1)	401 (19.3)	109 (23.2)	502 (19.6)	0.011
Tocilizumab	471 (18.4)	406 (19.5)	65 (13.8)	451 (17.6)	0.020
Anakinra	20 (0.8)	15 (0.7)	≤ 10	17 (0.7)	0.014
TNFi naïve at baseline	1547 (60.5)	1200 (57.6)	346 (73.6)	1506 (58.9)	0.033
Other prescription medications during baseline period, n (%)					
Antibiotics	2024 (79.2)	1638 (78.6)	383 (81.5)	2014 (78.8)	0.01
Antidiabetic agents	256 (10.0)	192 (9.2)	64 (13.6)	237 (9.3)	0.025
Insulins	111 (4.3)	86 (4.1)	25 (5.3)	89 (3.5)	0.044
Non-insulins	215 (8.4)	160 (7.7)	55 (11.7)	207 (8.1)	0.011
Cardiovascular					
Antithrombotic agents	703 (27.5)	518 (24.9)	183 (38.9)	658 (25.7)	0.04
Anticoagulant	434 (17.0)	314 (15.1)	118 (25.1)	414 (16.2)	0.021
Antiplatelet	340 (13.3)	248 (11.9)	92 (19.6)	325 (12.7)	0.017
Antihypertensives	986 (38.6)	699 (33.6)	286 (60.9)	980 (38.3)	0.005
Angiotensin converting enzyme inhibitors (ACE)	291 (11.4)	205 (9.8)	86 (18.3)	305 (11.9)	-0.017
Angiotensin receptor blockers (ARB)	378 (14.8)	256 (12.3)	122 (26.0)	384 (15.0)	-0.007
Beta blocker	468 (18.3)	323 (15.5)	145 (30.9)	465 (18.2)	0.003
Calcium channel blocker	352 (13.8)	234 (11.2)	117 (24.9)	355 (13.9)	-0.003
Nitrates	58 (2.3)	34 (1.6)	24 (5.1)	67 (2.6)	-0.023
Acyclovir	39 (1.5)	27 (1.3)	12 (2.6)	52 (2.0)	-0.039
Valacyclovir	227 (8.9)	178 (8.5)	49 (10.4)	227 (8.9)	0

Characteristics[b]	Baricitinib Any[e] n = 2556	Baricitinib 4 mg n = 2083	Baricitinib 2 mg n = 470	TNFi[a] n = 2556	Std. Diff. (Any vs TNFi)
Hormonal	585 (22.9)	504 (24.2)	80 (17.0)	563 (22.0)	0.021
HRT	374 (14.6)	310 (14.9)	63 (13.4)	356 (13.9)	0.02
Oral Contraceptives	214 (8.4)	196 (9.4)	18 (3.8)	204 (8.0)	0.014
SERMs	12 (0.5)	11 (0.5)	≤ 10	13 (0.5)	-0.006
Topic with progestogens and/or estrogens	37 (1.4)	35 (1.7)	≤ 10	44 (1.7)	-0.022
Lipid-lowering agents	523 (20.5)	384 (18.4)	139 (29.6)	518 (20.3)	0.005
HMG CoA reductase inhibitors	417 (16.3)	299 (14.4)	118 (25.1)	431 (16.9)	-0.015
Fibrates	55 (2.2)	42 (2.0)	13 (2.8)	47 (1.8)	0.022
Bile acid sequestrants	28 (1.1)	24 (1.2)	≤ 10	25 (1.0)	0.012
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Other lipid modifying agents	46 (1.8)	33 (1.6)	13 (2.8)	38 (1.5)	0.025
Lipid modifying agents, combinations	48 (1.9)	38 (1.8)	≤ 10	32 (1.3)	0.051
Rheumatoid arthritis-related					
Aspirin	84 (3.3)	64 (3.1)	20 (4.3)	87 (3.4)	-0.007
Cox-2 Inhibitor	298 (11.7)	260 (12.5)	37 (7.9)	340 (13.3)	-0.05
NSAIDs	1723 (67.4)	1468 (70.5)	253 (53.8)	1737 (68.0)	-0.012
Glucocorticosteroid	2296 (89.8)	1866 (89.6)	427 (90.9)	2282 (89.3)	0.018
Vaccines	1547 (60.5)	1200 (57.6)	347 (73.8)	1560 (61.0)	-0.010
Antineoplastic agents	18 (0.7)	≤ 10	≤ 10	27 (1.1)	-0.038

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; CNAM = Caisse Nationale de l'Assurance Maladie; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; HMG-CoA = β-Hydroxy β-methylglutaryl-CoA; 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; NSAID = non-steroidal anti-inflammatory drug; 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 Matching ratio 1:1 is applied

b All conditions and characteristics are measured during the 2 years 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 TNF inhibitors.

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

e n=3 subjects were dispensed both baricitinib 4mg and 2mg at index date, are included in the overall « Baricitinib Any » group but not in the strata according to the dosage

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III. 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_SNDS_VRM. Crude rates of incident VTE - VTE cohort (including CIRAS score in propensity score models) [SNDS]

	Unmatched				Matched				
VTE	**Bari. Any[b] n = 3242**	**Bari. 4mg n = 2616**	**Bari. 2mg n = 622**	**TNFi n = 10202**	**Bari. Any[b] n = 2859**	**Bari. 4mg n = 2306**	**Bari. 2mg n = 551**	**TNFi[a] n = 2859**	**Total n = 5718**
Overall									
Person-Years	2114	1734	377	6706	1855	1518	336	1919	3774
VTE	23	16	7	29	20	14	6	12	32
VTE/100 PY	1.1	0.9	1.9	0.4	1.1	0.9	1.8	0.6	0.8
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]	[0.3 ; 1.1]	[0.6 ; 1.2]
IRD[d]	0.7			.	0.5			.	
IRD[d] 95% CI	[0.3 ; 1.0]				[-0.1 ; 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)	1350 (47.2)	2576 (45.1)
Person-Years	1009	860	148	4105	906	773	133	1053	1959
VTE	9	8	1	12	8	7	1	3	11
VTE/100 PY	0.9	0.9	0.7	0.3	0.9	0.9	0.8	0.3	0.6
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]	[0.0 ; 4.2]	[0.1 ; 0.8]	[0.3 ; 1.0]
IRD[d]	0.6			.	0.6			.	
IRD[d] 95% CI	[0.2 ; 1.0]				[-0.1 ; 1.3]				
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)	1509 (52.8)	3142 (54.9)
Person-Years	1105	875	228	2602	949	745	203	866	1814

	Unmatched				Matched				
VTE	**Bari. Any[b] n = 3242**	**Bari. 4mg n = 2616**	**Bari. 2mg n = 622**	**TNFi n = 10202**	**Bari. Any[b] n = 2859**	**Bari. 4mg n = 2306**	**Bari. 2mg n = 551**	**TNFi[a] n = 2859**	**Total n = 5718**
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]	0.6			.	0.3				
IRD[d] 95% CI	[-0.03 ; 1.3]				[-0.6 ; 1.3]				

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

a Variable matching ratio 1:3 is applied, TNFi subjects are weighted by the reciprocal of the number of TNFi subjects within the matched set to which that subjects belong

b n=4 subjects were dispensed both baricitinib 4mg and 2mg 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 48_SNDS_VRM. Comparative risk of incident VTE - VTE matched cohort (including CIRAS score in propensity score models) [SNDS]

VTE	TNFi	Baricitinib, HR [95% CI]	p-value
Base model	Ref	1.68 [0.93 ; 3.04]	0.0845
Adjusted – Model [1]	Ref	1.68 [0.93 ; 3.04]	0.0845
Adjusted – Model [2]	Ref	1.65 [0.92 ; 2.99]	0.0952
Concomitant Glucocorticoid use	Ref	1.57 [0.87 ; 2.86]	0.1373
Concomitant cDMARD use	Ref	0.84 [0.47 ; 1.51]	0.5572
Adjusted – Model [3]	Ref	1.67 [0.93 ; 3.02]	0.0883
Concomitant Glucocorticoid use	Ref	1.56 [0.86 ; 2.83]	0.1475

Abbreviations: cDMARD = conventional disease-modifying antirheumatic drug; CI = confidence interval; CIRAS = claims-based index for rheumatoid arthritis severity; HR = hazard ratio; Ref = referent group; VTE = venous thromboembolism.

Model [1] = propensity score-matched model with outcome and baricitinib exposure, adjusted for any variables that remain unbalanced after PS 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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Table 54_SNDS_VRM. Crude rates of first MACE (including CIRAS score in propensity score models) [SNDS]

	Unmatched				Matched				
MACE	**Bari. Any[b] n = 3236**	**Bari. 4mg n = 2613**	**Bari. 2mg n = 619**	**TNFi n = 10175**	**Bari. Any[b] n = 2864**	**Bari. 4mg n = 2314**	**Bari. 2mg n = 548**	**TNFi[a] n = 2864**	**Total n = 5728**
Overall (MI or stroke)									
Person-Years	2102	1727	372	6681	1848	1521	326	1928	3777
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]	0.8			.	0.8			.	
IRD[d] 95% CI	[0.4 ; 1.2]				[0.2 ; 1.4]				
Overall (MI)									
Person-Years	2102	1727	372	6681	1848	1521	326	1928	3777
MI	16	12	4	23	13	9	4	8	21
MI /100 PY	0.8	0.7	1.1	0.3	0.7	0.6	1.2	0.4	0.6
95% CI	[0.4 ; 1.2]	[0.4 ; 1.2]	[0.3 ; 2.8]	[0.2 ; 0.5]	[0.4 ; 1.2]	[0.3 ; 1.1]	[0.3 ; 3.1]	[0.2 ; 0.8]	[0.3 ; 0.8]
IRD[d]	0.4			.	0.3			.	
IRD[d] 95% CI	[0.1 ; 0.7]				[-0.2 ; 0.8]				
Overall (stroke)									
Person-Years	2102	1727	372	6681	1848	1521	326	1928	3777
Stroke	12	7	5	11	12	7	5	3	15
Stroke /100 PY	0.6	0.4	1.3	0.2	0.6	0.5	1.5	0.2	0.4
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]	[0.0 ; 0.5]	[0.2 ; 0.7]
IRD[d]	0.4			.	0.5			.	
IRD[d] 95% CI	[0.2 ; 0.7]				[0.1 ; 0.9]				
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)	1355 (47.3)	2573 (44.9)
Person-Years	1004	857	145	4093	895	764	130	1047	1942
MACE	9	6	3	23	7	4	3	5	12
MACE/100 PY	0.9	0.7	2.1	0.6	0.8	0.5	2.3	0.5	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]	[0.2 ; 1.1]	[0.3 ; 1.1]
IRD[d]	0.3			.	0.3			.	

	Unmatched				Matched				
MACE	**Bari. Any[b] n = 3236**	**Bari. 4mg n = 2613**	**Bari. 2mg n = 619**	**TNFi n = 10175**	**Bari. Any[b] n = 2864**	**Bari. 4mg n = 2314**	**Bari. 2mg n = 548**	**TNFi[a] n = 2864**	**Total n = 5728**
IRD[d] 95% CI	[-0.2 ; 0.9]				[-0.4 ; 1.0]				
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)	1509 (52.7)	3155 (55.1)
Person-Years	1098	869	227	2589	953	757	196	882	1835
MACE	19	13	6	11	18	12	6	5	23
MACE/100 PY	1.7	1.5	2.6	0.4	1.9	1.6	3.1	0.6	1.3
95% CI	[1.0 ; 2.7]	[0.8 ; 2.6]	[1.0 ; 5.8]	[0.2 ; 0.8]	[1.1 ; 3]	[0.8 ; 2.8]	[1.1 ; 6.7]	[0.2 ; 1.3]	[0.8 ; 1.9]
IRD[d]	1.3			.	1.3	1.3			
IRD[d] 95% CI	[0.7 ; 1.9]				[0.3 ; 2.3]	[0.3 ; 2.3]			

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

a Variable matching ratio 1:3 is applied, TNFi subjects are weighted by the reciprocal of the number of TNFi subjects within the matched set to which that subjects belong

b n=4 subjects were dispensed both baricitinib 4mg and 2mg 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_VRM. Comparative risk of incident MACE (including CIRAS score in propensity score models), matched cohort [SNDS]

MACE	TNFi	Baricitinib, HR [95% CI]	p-value
Base model	Ref	2.30 [1.31 ; 4.02]	0.0036
Adjusted – Model [1]	Ref	2.30 [1.31 ; 4.02]	0.0036
Adjusted – Model [2]	Ref	2.27 [1.29 ; 3.97]	0.0043
Concomitant Glucocorticoid use	Ref	0.91 [0.48 ; 1.72]	0.7764
Concomitant cDMARD use	Ref	0.83 [0.47 ; 1.48]	0.5245
Adjusted – Model [3]	Ref	2.30 [1.31 ; 4.02]	0.0036
Concomitant Glucocorticoid use	Ref	0.90 [0.48 ; 1.70]	0.7499
Adjusted – Model [n]	Ref	N/A	N/A

Abbreviations: cDMARD = conventional disease-modifying antirheumatic drug; CIRAS = claims-based index of rheumatoid arthritis severity; 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 = Referent group; TNFi = tumour necrosis factor inhibitor.

Model [1] = propensity score-matched model with outcome and baricitinib exposure, adjusted for any variables that remain unbalanced after PS 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.

Models 1-n may include additional variables that remain unbalanced after propensity-score matching as well as concomitant cDMARD or glucocorticoid use separately.

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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Table 59_SNDS_VRM. Crude rates of first serious infection event – Serious infection cohort (including CIRAS score in propensity score models) [SNDS]

	Unmatched				Matched				
SI	**Bari. Any [b] n = 3366**	**Bari. 4mg n = 2696**	**Bari. 2mg n = 666**	**TNFi n = 10451**	**Bari. Any[b] n = 2979**	**Bari. 4mg n = 2385**	**Bari. 2mg n = 591**	**TNFi [a] n = 2979**	**Total n = 5958**
Overall									
Person-Years	2188	1785	400	6867	1920	1561	357	2000	3920
VTE	44	29	15	68	36	25	11	30	66
VTE/100 PY	2.0	1.6	3.7	1.0	1.9	1.6	3.1	1.5	1.7
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]	[1.0 ; 2.1]	[1.3 ; 2.1]
IRD [d]	1.0			.	0.4			.	
IRD [d] 95% CI	[0.5 ; 1.6]				[-0.4 ; 1.2]				
Concomitant [c] MTX Use, n (%)	1403 (41.7)	1181 (43.8)	220 (33.0)	5508 (52.7)	1266 (42.5)	1064 (44.6)	200 (33.8)	1403 (47.1)	2669 (44.8)
Person-Years	1035	879	155	4194	941	797	143	1089	2030
VTE	16	11	5	32	14	11	3	14	28
VTE/100 PY	1.5	1.3	3.2	0.8	1.5	1.4	2.1	1.3	1.4
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]	[0.7 ; 2.2]	[0.9 ; 2.0]
IRD [d]	0.8			.	0.2			.	
IRD [d] 95% CI	[0.1 ; 1.4]				[-0.8 ; 1.2]				
No concomitant [c] MTX Use, n (%)	1963 (58.3)	1515 (56.2)	446 (67.0)	4943 (47.3)	1713 (57.5)	1321 (55.4)	391 (66.2)	1576 (52.9)	3289 (55.2)
Person-Years	1153	906	245	2673	979	764	214	911	1890
VTE	28	18	10	36	22	14	8	17	39
VTE/100 PY	2.4	2.0	4.1	1.3	2.2	1.8	3.7	1.9	2.1
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]	[1.1 ; 3.0]	[1.5 ; 2.8]
IRD [d]	1.1			.	0.4				
IRD [d] 95% CI	[0.2 ; 2.0]				[-0.9 ; 1.7]				

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

a Variable matching ratio 1:3 is applied, TNFi subjects are weighted by the reciprocal of the number of TNFi subjects within the matched set to which that subjects belong

b n=4 subjects were dispensed both baricitinib 4mg and 2mg 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 61_SNDS_VRM. Comparative risk of first serious infection event – Serious infection matched cohort (including CIRAS score in propensity score models) [SNDS]

Serious Infections	TNFi	Baricitinib, HR [95% CI]	p-value
Base Model	Ref	1.46 [0.95 ; 2.23]	0.0835
Adjusted – Model [1]	Ref	1.46 [0.95 ; 2.23]	0.0835
Adjusted – Model [2]	Ref	1.46 [0.95 ; 2.25]	0.0819
Concomitant Glucocorticoid use	Ref	0.98 [0.62 ; 1.56]	0.9373
Concomitant cDMARD use	Ref	1.05 [0.70 ; 1.60]	0.8025
Adjusted – Model [3]	Ref	1.46 [0.95 ; 2.24]	0.0836
Concomitant Glucocorticoid use	Ref	0.99 [0.62 ; 1.57]	0.9526
Adjusted – Model [n]	Ref	N/A	N/A

Abbreviations: cDMARD = conventional disease-modifying antirheumatic drug; CI = confidence interval; CIRAS= claims-based index of rheumatoid arthritis severity; HR = hazard ratio; Ref = referent group; TNFi = tumour necrosis factor inhibitor.

Model [1] = propensity score-matched model with outcome and baricitinib exposure, adjusted for any variables that remain unbalanced after PS 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.

Models 1-n may include additional variables that remain unbalanced after propensity-score matching as well as concomitant cDMARD or glucocorticoid use separately.

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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Annex 17. B029 VTE Validation Study in US-based Claims

Presented to:

Eli Lilly

Report	**Claims-linked Medical Chart Abstraction Study of Venous Thrombotic Event Validation among Patients with Rheumatoid Arthritis**	
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Approval Date: 20-Jun-2022 GMT

Study Summary

This study was designed to support study I4V-MC-B023 “Comparative Assessment of VTE and Other Risks among Patients with Rheumatoid Arthritis treated with Baricitinib versus Tumor Necrosis Factor Inhibitors: A Multi-database Observational Cohort Study” by increasing the scientific validity of the real-world data used for that study in two ways:

a) validation of the venous thrombotic event (VTE) outcome definition based on confirmation of presumptive VTEs identified in (i) administrative claims data through traditional chart review and (ii) an innovative approach exploring the use of claims data linked to electronic health record (EHR) to identify and confirm presumptive VTE; and

b) evaluation of the prevalence of risk factors for VTE and MACE, BMI and smoking, for a quantitative bias analysis that will quantify the potential for unmeasured confounding by these factors.

The primary objective of this study was to evaluate the performance of the selected VTE case definition using positive predictive value (PPV) as a measure of performance in a US population of insured adults diagnosed with and treated for rheumatoid arthritis (RA). The secondary objective was to describe the prevalence of smoking and obesity based on information from medical records or charts in a similar population of patients.

The main study population consisted of adults aged ≥18 years in the Optum Research Database (ORD), with commercial or Medicare insurance with medical and Part D coverage who had an International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis code for RA and received treatment for RA between 01 May 2016 – 30 November 2020. Clinical data abstracted from medical charts was used to confirm or refute the presumptive VTE diagnosis in claims using pre-determined case confirmation rules developed under clinical guidance. Patient charts were procured from treating providers for 155 of 254 patients (61%) with presumptive VTE based on the algorithm. The majority of patients were female (74%), with mean age 66 years (standard deviation [SD] 11), and had Medicare insurance coverage (81%). Chronic obstructive pulmonary disease (27%), ever smoking (56%), hypertension (72%), obesity (47%), and prior evidence of VTE (28%) were common. Follow-up ranged from 51 to 1,704 days (mean 912; SD 525 days). A total of 117 patients with presumptive VTE had their event confirmed based on clinical data, with lower DVT and pulmonary embolism being the most common types confirmed. Among confirmed cases, diagnosis was most commonly based on an emergency room (ER) setting, followed by treatment in an inpatient setting. Venous duplex ultrasound and angiogram were the most common diagnostic imaging methods used to confirm VTE; lung ventilation-perfusion scans and all forms of magnetic resonance imaging were used in less than 10 patients. The PPV for the primary VTE case definition was 75.5% (117/155; 95% CI 68.7-82.3%). The secondary case definition, which relied on less stringent criteria, yielded a lower performance with a PPV of 52.6% (40/76; 95% CI 41.4-63.9%).

An additional analysis explored the potential for using claims data linked to Optum’s EHR for case validation. For this analysis, the performance of the primary algorithm was also evaluated by confirming presumptive VTEs identified in administrative health care claims from patients in Optum’s Market Clarity database based on unstructured provider notes from Optum’s EHR database. Using this novel secondary data source yielded a lower PPV of 56.3% (36/64; 95% CI 44.1-68.4%), probably due to insufficient information captured in the providers’ notes to validate VTE; and the open source nature of the data where relevant providers’ records may be captured

in another EHR system. Not all providers or provider networks contribute records to these unstructured notes. Furthermore, the composition of notes is specific to each patient and their interaction with the health care provider(s) who have contributed free-text data.

The secondary objective of this study was to estimate the prevalence of smoking and obesity in a sample of patients with RA and a claim for a tumor necrosis factor inhibitor or Janus kinase inhibitor therapy (N=182). Smoking status was available for 147 patients (95%) in the medical charts. Of 147 patients with smoking status available in the medical charts, 23 were current smokers (16%), and an additional 59 patients (40%) were identified as former smokers, for a total of 56% “ever smokers.” Patient charts indicated that 65 patients (44%) were never smokers. Cigarettes were the most commonly used tobacco product, used by 87% of current smokers. Of the 141 patients with BMI reported in medical charts, the mean was 31 kg/m^2, with 47% obese and nearly one-quarter of patients having a BMI≥35.

This chart validation study estimated an acceptable PPV for the primary VTE case definition based on traditional chart review of presumptive events identified with ICD-10-CM diagnosis codes, clinical setting, and prescription dispensings, from a US population of insured adults diagnosed with and treated for RA. Our findings demonstrate reliability of the selected VTE case definition for identifying true VTE in the target study I4V-MC-B023. This case definition and the estimated prevalence of smoking and BMI (obesity) may also be generalizable to similar US data sources and populations.

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Abbreviations

Abbreviation	Definition
AHRQ	Agency for Healthcare Research and Quality
bDMARD	Biologic Disease Modifying Antirheumatic Drug
BMI	Body Mass Index
CAW	Covariate Assessment Window
cDMARD	Conventional Disease Modifying Antirheumatic Drug
CE	Continuous Enrollment
CMS	Centers for Medicare and Medicaid Services
COPD	Chronic Obstructive Pulmonary Disease
CPT	Current Procedural Terminology
CT	Computed Tomography
DVT	Deep Venous Thromboembolism
EHR	Electronic Health Record
ER	Emergency Room
HIPAA	Health Insurance Portability and Accountability Act
HCPCS	Healthcare Common Procedure Coding System
ICD-10-CM	International Classification of Diseases, Tenth Revision, Clinical Modification
JAKi	Janus Kinase Inhibitor
LDVT	Lower Deep Venous Thromboembolism
MRA	Magnetic Resonance Angiography
MRI	Magnetic Resonance Imaging
MRV	Magnetic Resonance Venography
MTX	Methotrexate
NSAID	Nonsteroidal Anti-Inflammatory Drug
OP	Outpatient
ORD	Optum Research Database
PE	Pulmonary Embolism
RA	Rheumatoid Arthritis
TNFi	Tumor Necrosis Factor Inhibitor
UB	Uniform Billing
UDVT	Upper Deep Venous Thromboembolism
VT	Venous Thrombosis
VTE	Venous Thrombotic Event

1 Background and Rationale

Rheumatoid arthritis (RA) is an immunologic condition characterized by chronic inflammation of the lining of joints. Long-term chronic inflammation may lead to bone loss, joint deformity, and damage to other tissues and organs, including eyes, lungs, kidney, heart and blood vessels, and liver. Symptoms of RA include pain, stiffness, and swelling in one or more joints (typically bilaterally), fatigue, weight loss, and fever. Patients tend to experience bouts of increased activity (flares) and periods of relative remission of symptoms. The goal of RA treatment is to reduce or eliminate inflammation, thereby minimizing damage to joints and organs.[1,2,3] RA poses substantial burden to individual patients with over half of those diagnosed eventually experiencing work disability; burden to the healthcare system occurs through ongoing pharmacologic management in addition to surgical intervention for some patients. RA is associated with a higher comorbidity burden and with increased mortality compared to the general population, which appears to be due largely to increased cardiovascular risk.[4]

RA may be treated with a variety of classes of medication,[5] including nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, conventional disease modifying antirheumatic drugs (cDMARDs [e.g., methotrexate (MTX), hydroxychloroquine]) that target the full immune system, and biologic disease modifying antirheumatic drugs (bDMARDs) (including tumor necrosis factor inhibitor [TNFi] and excluding rituximab) that target specific aspects of inflammatory processes. When cDMARDs are not effective, bDMARDs or Janus kinase inhibitor (JAKi) may be used. Baricitinib is a JAKi that has been shown to be effective in patients for whom cDMARDs have not worked.[6] A network meta-analysis of clinical trials has also suggested that baricitinib shows a higher degree of efficacy compared to other JAKi treatments, tofacitinib and upadacitinib,[7] while maintaining a similar safety profile.[8,9]

RA appears to be a risk factor for the development of major adverse cardiovascular events (MACE) and peripheral artery disease (PAD). A few population studies found increased risk of MACE among RA patients compared with the general population.[9,10] In a study that compared patients with RA to those without, patients with RA had a greater proportion of PAD and the difference could not be explained fully by traditional risk factors.[11] Patients with RA are also at risk to experience a venous thrombotic event (VTE).[12,13] A study utilizing US administrative insurance claims data found a significantly higher incidence of VTE among patients with an RA diagnosis compared with patients without, even after adjusting for other risk factors.[14]

Health insurance claims databases provide an opportunity to study uncommon complications, such as VTE, in a large RA population. To date, however, no prior studies have validated an algorithm based on International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes. Building on a prior validation study of VTE based on ICD-9-CM diagnosis codes,[15] Lilly developed claims-based algorithms for VTE identification including ICD-10-CM diagnosis codes and recent treatments. This study assessed the performance of claims-based algorithms for VTE identification among a US managed care population of insured adults.

2 Study Purpose and Objectives

2.1. Study Objectives

This study was proposed to support study I4V-MC-B023 “Comparative Assessment of VTE and Other Risks among Patients with Rheumatoid Arthritis treated with Baricitinib versus Tumor

Necrosis Factor Inhibitors: A Multi-database Observational Cohort Study" by increasing the scientific validity of the real-world data used for that study in two ways:

a) validation of the VTE outcome definition based on confirmation of presumptive VTE identified in (i) administrative claims data through traditional chart review and (ii) an innovative approach exploring the use of claims data linked to electronic health record (EHR) to identify and confirm presumptive VTE; and

b) evaluation of the prevalence of risk factors for VTE and MACE, body mass index (BMI) and smoking, for a quantitative bias analysis that will evaluate the potential for unmeasured confounding by these factors.

The primary objective of the study was to evaluate the performance of the selected VTE case definition using positive predictive value (PPV) as a measure of performance in a US population of insured adults diagnosed with and treated for RA. An additional exploratory analysis evaluated the potential for using claims data and linked clinical notes from EMR for case validation by estimating the PPV of the selected algorithm.

The secondary objective was to estimate the prevalence of smoking and obesity from medical records or charts in a sample of patients with RA and a claim for a TNFi or JAKi therapy. This information, which is not typically available in administrative claims data, was collected to support a quantitative bias analysis conducted as part of the main B023 study analyses. The objectives of this study were:

- **Primary objective:** To validate VTEs identified in administrative claims data using a primary case definition based on traditional medical chart review and

- **Secondary objective:** To estimate the prevalence of BMI and smoking status in a cohort of patients diagnosed with RA.

3 Study Design

3.1. Study Design Overview

The study utilized retrospective administrative health care claims data, including medical and pharmacy claims and enrollment information linked at the patient level with medical chart data. Data from 01 January 2016 through 30 November 2019 was used. Study subjects were adults with evidence of RA diagnosis and treatment with a TNFi or JAKi who had commercial or Medicare Advantage medical and pharmacy coverage. Medical chart abstraction evaluated the performance of two claims-based algorithms for identifying VTEs based on combinations of codes for diagnosis and treatment by site of care. Abstraction included review of three months of chart data to validate presumptive VTE cases. Abstraction was also used to collect clinical and behavioral variables not available in claims data from patients with a presumptive VTE as well as a population of patients meeting the study inclusion criteria but without claims evidence of a VTE. This study was reviewed and approved by an institutional review board and privacy board (WCG IRB #1284955).

Protocol Revision

The original protocol I4V-MC-B029, Claims-linked Medical Chart Abstraction Study of Venous

Thrombotic Event Validation among Patients with Rheumatoid Arthritis, was approved on 04-Aug-2020. The protocol was revised twice: Revision 1A [I4V-MC-B029(a)] on 23-Jul-2021, and Revision 2B [I4V-MC-B029(b)] on 13-Aug-2021. The revisions were prompted by the limited number of cases identified to validate the primary VTE algorithm using the initial approach. Accordingly, while the study purpose and objectives remained unchanged, an expanded date range and an additional data source were pursued to expand the number of qualifying VTE events available for validation. Additionally, the revisions removed specific eligibility requirements that were not required to assess the performance of the VTE algorithm. Important changes made in the protocol amendments are summarized below.

Revision 1A

Using the same administrative claims data described for the original protocol, Revision 1A increased the size of the primary VTE algorithm cohort via three mechanisms: (1) expanding the date range of permissible claims to 01 November 2015 through 31 December 2020; (2) expanding the medications of interest beyond TNFi and JAKi to include non-TNFi bDMARDs (abatacept, tocilizumab, sarilumab or anakinra); and (3) removing exclusion criteria that forced cohort participants to be new users of the index therapy. All patients identified for inclusion in Revision 1A were those with a presumptive VTE identified via the primary study algorithm.

Revision 2B

To further increase the size of the primary VTE algorithm cohort, Revision 2B explored a new data source, namely Optum's Market Clarity integrated clinical records + claims database. The claims data in the Market Clarity database was not as current as the data available in the Optum Research Database (ORD) (utilized by the original protocol and Revision 1A); therefore, a date range modification to the end of the identification and observation period was required. The observation period for claims data using the Market Clarity database was 01 November 2015 to 30 September 2020. The expanded medications of interest and revised inclusion criteria implemented for Revision 1A was carried forward for Revision 2B. Again, only the primary VTE algorithm was being assessed as part of this revision.

A summary of the modifications to the study sample are described in the Table 1. Modified criteria are italicized and include the date ranges, data source, and therapies of interest. Modifications to the exclusion criteria include deletion of the new user criteria and updates to the implementation of age and diagnostic services for Revision 2B.

Table 1. Summary of Inclusion/Exclusion Criteria by Protocol Version

	Original (Version 1)	Revision 1A	Revision 2B
Inclusion Criteria			
Date range for sample identification periods	01 July 2016 through 30 October 2019	*01 May 2016 through 30 November 2020*	*01 May 2016 through 31 August 2020*
Date range for observation periods	01 January 2016 through 30 November 2019	*01 November 2015 through 31 December 2020*	*01 November 2015 through 30 September 2020*
Data source	ORD	ORD	Market Clarity
≥1 pharmacy claim for a therapy of interest	TNFi therapy (adalimumab, certolizumab pegol, etanercept, golimumab, or infliximab), or a JAKi	TNFi therapy (adalimumab, certolizumab pegol, etanercept, golimumab, or infliximab), *a non-*	TNFi therapy (adalimumab, certolizumab pegol, etanercept, golimumab, or infliximab), *a non-TNFi*

	Original (Version 1)	Revision 1A	Revision 2B
	therapy (baricitinib, tofacitinib, or upadacitinib) during the sample identification period	*TNFi bDMARD (abatacept, tocilizumab, sarilumab and anakinra),* or a JAKi therapy (baricitinib, tofacitinib, or upadacitinib) during the sample identification period	*bDMARD (abatacept, tocilizumab, sarilumab and anakinra),* or a JAKi therapy (baricitinib, tofacitinib, or upadacitinib) during the sample identification period
≥1 medical claim with diagnosis of interest	Diagnosis of RA, excluding claims for diagnostic services, during the covariate assessment window (CAW)	Diagnosis of RA, excluding claims for diagnostic services, during the covariate assessment window (CAW)	Diagnosis of RA,[a] during the covariate assessment window (CAW)
Age eligibility requirement	≥18 years age as of index date	≥18 years age as of index date	≥18 years age as of index date[b]
Covariate assessment window (CAW) enrollment eligibility requirement	6 months of continuous enrollment with medical and pharmacy coverage during the CAW	6 months of continuous enrollment with medical and pharmacy coverage during the CAW	6 months of continuous enrollment with medical and pharmacy coverage during the CAW
Post-index enrollment eligibility requirement	≥31 days of continuous enrollment from the date of the qualifying event (post-index)	≥31 days of continuous enrollment from the date of the qualifying event (post-index)	≥31 days of continuous enrollment from the date of the qualifying event (post-index)
Patient chart abstraction identification criteria	Patient and provider identifiable information available to support medical chart identification and abstraction; only one provider will be identified and contacted for chart procurement	Patient and provider identifiable information available to support medical chart identification and abstraction; *expanded to include identification of a secondary treating provider whenever possible*[c]	*Criteria deleted since chart abstraction will not be completed*[c]
Exclusion Criteria			
New user (index therapy)	Patients with ≥1 pharmacy claim for the index therapy (TNFi or JAKi) in the 6-months prior to index date will be excluded	*Deleted this criterion*	*Deleted this criterion*
≥1 claim for anticoagulant therapy	Patients with ≥1 claim for anticoagulant therapy prior to the	Patients with ≥1 claim for anticoagulant therapy prior to the	Patients with ≥1 claim for anticoagulant therapy prior to the date of the

[a] Diagnostic service claims were excluded if this level of service granularity was available in the Market Clarity data.

[b] Age as of index year was approximated if the Market Clarity data source did not support calculation of age as of index date.

[c] Revision 1A and 2B sample identification was limited to patients with a presumptive VTE based on the primary algorithm only.

	Original (Version 1)	Revision 1A	Revision 2B
	date of the qualifying VTE whose runout date[d] overlaps with the date of the qualifying VTE will be excluded. Anticoagulants that will be assessed include apixaban, dabigatran, dalteparin, edoxaban, enoxaparin, fondaparinux, rivaroxaban, tinzaparin, and warfarin	date of the qualifying VTE whose runout date overlaps with the date of the qualifying VTE will be excluded. Anticoagulants that will be assessed include apixaban, dabigatran, dalteparin, edoxaban, enoxaparin, fondaparinux, rivaroxaban, tinzaparin, and warfarin	qualifying VTE whose runout date overlaps with the date of the qualifying VTE will be excluded. Anticoagulants that will be assessed include apixaban, dabigatran, dalteparin, edoxaban, enoxaparin, fondaparinux, rivaroxaban, tinzaparin, and warfarin
≥1 claim for cancer treatment	Patients with ≥1 pharmacy or medical claim for cancer treatment on the index date will be excluded	Patients with ≥1 pharmacy or medical claim for cancer treatment on the index date will be excluded	Patients with ≥1 pharmacy or medical claim for cancer treatment on the index date will be excluded

3.2. Study Sample

3.2.1. Patient Population

This study included patients with commercial and Medicare Advantage with Part D medical and pharmacy claims with evidence of RA and a treatment of interest. To be included in the final study sample, subjects must have met all inclusion/exclusion criteria below. A single-step sample identification approach was applied: all patients were identified at one time and assigned to one of three cohorts at the time of sample identification.

Note: Final diagnosis and treatment code lists for sample identification are included in Appendix C.

The **index date** was the date of the first pharmacy or medical claim for an RA therapy of interest during the identification period (01 July 2016 through 30 October 2019). The 6-month pre-index period was used for sample identification and as the covariate assessment window (CAW).[16] The pre-index period included the index date.

The **qualifying event** refers to the presumptive claims-based VTE that established the cohort each patient was assigned to at the time of sample identification for algorithm validation (cohorts and hierarchy of VTE assignment are addressed below). The **qualifying event date** was the date of the qualifying event and defines the chart abstraction period. The first possible date of the qualifying event was defined as index date + 1 day.

[d] The approximate last date that the medication was available to the patient based on the number of days since the most recent refill and days supply.

Inclusion Criteria

- ≥1 pharmacy claim for a TNFi therapy (adalimumab, certolizumab pegol, etanercept, golimumab, or infliximab), or a JAKi therapy (baricitinib, tofacitinib, or upadacitinib) during the sample identification period. The first observed therapy of interest was defined as the index therapy unless the identification period also included a claim for a JAKi therapy. The index therapy was defined as baricitinib for all patients with a claim for baricitinib during the identification period even if baricitinib was not the first observed therapy of interest, followed by tofacitinib and upadacitinib;

- ≥1 medical claim with diagnosis of RA, excluding medical claims for diagnostic services, during the CAW through the index date plus 1-month post-index;

- ≥18 years of age as of index date;

- 6 months of continuous enrollment (CE) with medical and pharmacy coverage during the CAW (including index date);

- ≥31 days of CE post-index (starting on the day after index date); and

- Patient and provider identifiable information available to support medical chart identification and abstraction.

Exclusion Criteria

- ≥1 pharmacy claim for the index therapy (TNFi or JAKi) in the 6-months prior to and excluding index date;

- ≥1 claim for anticoagulant therapy prior to the date of the qualifying VTE whose runout date (approximate last date that the medication was available to the patient) overlapped with the date of the qualifying VTE. Anticoagulants that were assessed included apixaban, dabigatran, dalteparin, edoxaban, enoxaparin, fondaparinux, rivaroxaban, tinzaparin, and warfarin; or

- ≥1 pharmacy or medical claim for cancer treatment on the index date.

These criteria established the target universe from which the sample was drawn as shown in Figure 1. Criteria for identification of VTEs (primary algorithm and secondary algorithm) by type of VTE and treatment setting for diagnosis were then applied. As shown in Figure 2, the algorithms for identification of VTEs included four categories: pulmonary embolism (PE), lower extremity deep venous thromboembolism (DVT), upper extremity DVT, and other venous thrombosis (VT) (other). A combination of variables (site of care, position of code on the claims, and type of VTE) determined the need for a claim for an anticoagulant to be included in the primary algorithm.

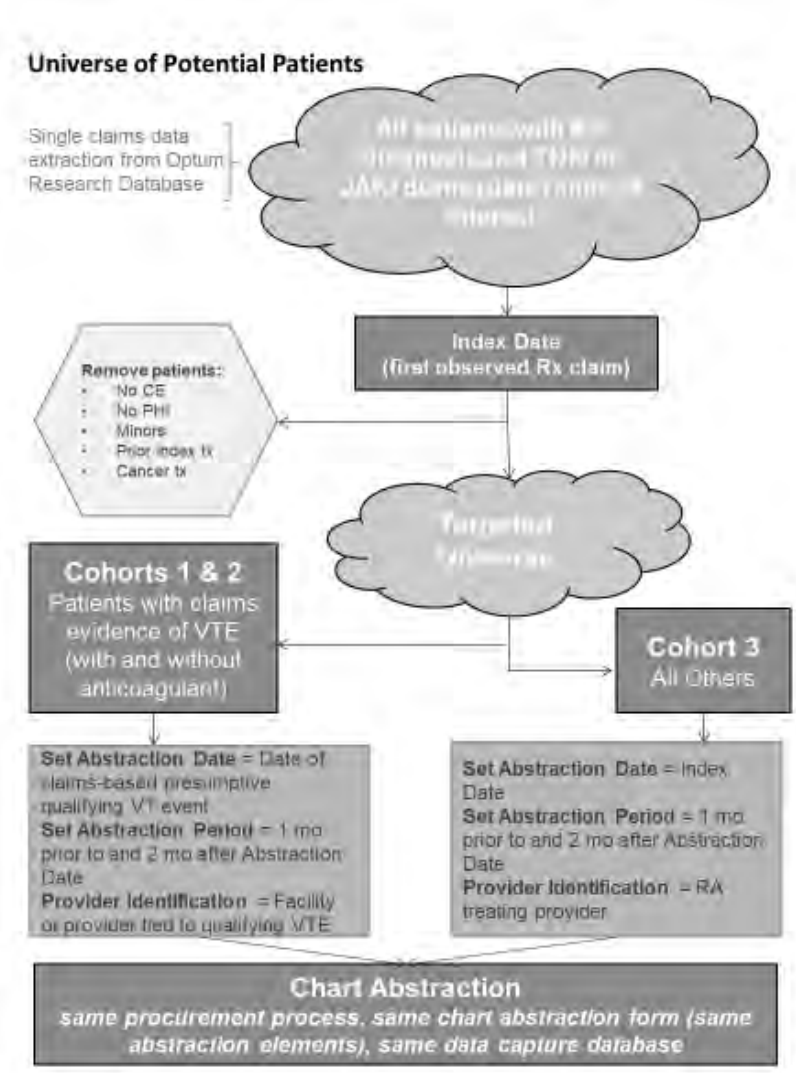

Figure 1. Study Process Diagram: Patient Flow and Stratification Prior to Chart Abstraction

Presumptive Claims-based VTE, Primary Definition		
Pulmonary Embolism	**Deep Vein Thromboembolism**	**Other Venous Thrombosis**
Hospital or ER diagnosis: 1. PE in primary position, OR 2. PE in secondary position + anticoagulant dispensing within 31 days	**Hospital or ER diagnosis:** 1. Lower extremity DVT in primary position, OR 2. Upper extremity DVT + anticoagulant dispensing within 31 days, OR 3. Lower extremity DVT in secondary position + anticoagulant dispensing within 31 days, OR **Outpatient diagnosis:** 4. Lower extremity DVT + anticoagulant dispensing within 31 days, OR 5. Upper extremity DVT in primary position + anticoagulant dispensing within 31 days	1. Diagnoses in any care setting + anticoagulant dispensing within 31 days

Presumptive Claims-based VTE, Secondary Definition (Applied to remaining sample following identification of patients using primary definition)		
Pulmonary Embolism	**Deep Vein Thromboembolism**	**Other Venous Thrombosis**
Hospital or ER diagnosis: 1. PE in secondary position **Outpatient diagnosis:** 2. PE in any position + anticoagulant dispensing within 31 days	**Hospital or ER diagnosis:** 1. Lower extremity DVT in secondary position, OR 2. Upper extremity DVT in primary position, OR 3. Upper extremity DVT in secondary position + anticoagulant dispensing within 31 days **Outpatient diagnosis:** 4. Lower extremity DVT	**Hospital or ER diagnosis:** 1. Diagnosis of other VTE in any care setting

Figure 2. Claims-based Presumptive VTE Cohorts for Chart Abstraction

3.2.2. Revision 1A

The identification period for the index date was expanded from 01 July 2016 through 30 October 2019 to 01 May 2016 through 30 November 2020. The definition of the index date and the pre-index period remained unchanged.

The definition of the Qualifying Event for Revision 1A remained the same. Cohort assignment and hierarchy of the algorithm definition were not implemented in Revision 1A because only patients meeting the primary algorithm definition were identified and included in the study analysis.

Revision 1A included an update to the first inclusion criteria (addition of the non-TNFi bDMARDs abatacept, tocilizumab, sarilumab, and anakinra) and removal of the first exclusion criterion which required patients to be new users of the index therapy.

Only the primary VTE algorithm cohort (Cohort 1 in Figure 1) was populated. The primary algorithm definition described in Figure 2 was unchanged in Revision 1A.

3.2.3. Revision 2B

The criteria for Revision 2B were built on the Revision 1A modifications to the medications of interest and other inclusion/exclusion criteria. Patients with commercial insurance, Medicare or Medicaid health care coverage were identified from the Market Clarity database. The identification period for the index date reflected the date ranges available in the Market Clarity database (01 May 2016 through 31 August 2020). Use of the Market Clarity database also eliminated the need to limit the study population to those with identifying information available since direct outreach to providers was not utilized for validation. This inclusion criterion, found in both the original protocol and Revision 1A, has been removed from 2B. The definition of the index date and the pre-index period remained the same.

The definition of the Qualifying Event for Revision 2B remained the same. Cohort assignment and hierarchy of the algorithm definition was not implemented in Revision 2B because only patients meeting the primary algorithm definition were identified and included in the study analysis. Only the primary VTE algorithm cohort (Cohort 1 in Figure 1) was populated. The primary algorithm definition described in Figure 2 was unchanged in Revision 2B.

Additionally, after the inclusion/exclusion criteria had been implemented, the study population size was reviewed, and it was determined sufficient to support the next steps in the process. Thus, the population identified from the Market Clarity data source was mapped to Optum's EHR database to search for patients with free-text provider clinical notes with dates of service within 90 days of the presumptive VTE date. Patients without applicable (either by date range or relevancy) provider clinical notes available for abstraction were excluded.

3.3. Cohort Assignment

After the broad population of patients who met the initial inclusion/exclusion criteria was identified, administrative claims data from the variable post-index period was used to create 3 cohorts.

- Patients whose claims observation period included claims consistent with a primary VTE algorithm (Cohort 1)
- Patients whose claims observation period included claims consistent with a secondary VTE algorithm (Cohort 2)
- Patients whose claims observation period did not include claims consistent with a VTE (Cohort 3)

The cohort assignment was performed in a hierarchical fashion using the criteria from the primary and secondary algorithms. Criteria falling into the primary algorithm were considered before applying the secondary algorithm. Criteria for identification of VTEs (primary algorithm only) were based on the work of Fang et al.[15] and included diagnosis codes (ICD-10-CM),

position of the diagnostic code when they were discharge codes, drug dispensing records, and the service location (site of care) captured in administrative claims. Diagnosis codes and the type of care setting are required elements for reimbursement and routinely populated in administrative claims data submitted to insurers for payment. The claims-based VTE algorithm included four VTE categories: PE, lower extremity DVT, upper extremity DVT, and other VT (other). Within each algorithm, a hierarchy was applied by type of VTE, position of the diagnosis code on the claim for inpatient claims, and site of care. The earliest date for a VTE claim defined the qualifying event. If multiple inpatient claims meeting the algorithm criteria for a VTE fell on the same day, and one of the VTE types was a PE, the PE was defined as the qualifying event. If multiple claims for a VTE fell on the same day in different settings, the VTE that occurred in an inpatient setting was set as the qualifying event followed by claims for emergency room (ER) care. The position of a diagnosis code on a claim was defined as primary if it was the first diagnosis code listed on the claim (and presumably represented the constellation of symptoms of greatest importance to the clinical service). A secondary diagnosis code is any diagnosis code not in the first position on the claim. The **primary algorithm hierarchy**, which applied when different events or different sites of care all met the VTE primary algorithm criteria and occurred on the same day, included:

- Hospital setting with PE diagnosis in primary position on the claim
- ER setting with PE diagnosis in the primary position on the claim
- Hospital setting with PE diagnosis in a secondary position on the claim and a claim for an anticoagulant within 31 days
- ER setting with PE diagnosis in secondary position and a claim for an anticoagulant within 31 days
- Hospital setting with a lower DVT (LDVT) diagnosis in primary position on the claim
- ER setting LDVT diagnosis in primary position on the claim
- Hospital setting with upper extremity DVT diagnosis in primary position and a claim for an anticoagulant within 31 days
- ER setting with an upper DVT (UVDT) diagnosis in primary position on the claim and a claim for an anticoagulant within 31 days
- Hospital setting with a diagnosis of LDVT in a secondary position and a claim for an anticoagulant within 31 days
- ER setting with a diagnosis of LDVT in a secondary position and a claim for an anticoagulant within 31 days
- Outpatient (OP) setting with a diagnosis of LDVT in any position (primary or secondary) and a claim for an anticoagulant within 30 days
- OP setting with a diagnosis of UDVT in any position and a claim for an anticoagulant within 31 days
- Hospital setting with a diagnosis of other VT in primary position and a claim for an

anticoagulant within 31 days

- ER setting with a diagnosis of other VT in primary position and a claim for an anticoagulant within 31 days
- Hospital setting with a diagnosis of other VT in secondary position and a claim for an anticoagulant within 31 days
- ER setting with a diagnosis of other VT in secondary position and a claim for an anticoagulant within 31 days
- OP setting with a diagnosis of other VT in any position with and a claim for an anticoagulant within 31 days

The deep veins considered in the study definition of UDVT and LDVT as well as other VT included but were not limited to the renal, splenic, subclavian, vena cava, brachiocephalic, cerebral, hepatic, jugular, mesenteric, ophthalmic, penile and other peripheral deep veins. The purpose of the primary algorithm hierarchy during sample identification was to facilitate identification of the treating provider. Higher levels of care (inpatient and ER) are more likely to include multidisciplinary treatment teams and imaging/radiology. Since imaging was required to confirm VTE, the hierarchy prioritized the provider associated with those patient charts that were most likely to include documentation of imaging results for procurement and abstraction.

For patients without a qualifying event after applying the primary algorithm, the secondary algorithm was applied to identify qualifying events. The criteria that fall under **secondary algorithm hierarchy** but are *not* included in the primary algorithm are as follows (and applies as above, for different events or sites of care occurring on the same day):

- Hospital PE in secondary position
- ER PE in secondary position
- Hospital UDVT in primary position
- ER UDVT in primary position
- Hospital LDVT in secondary position
- ER LDVT in secondary position
- Hospital UDVT in secondary position with anticoagulant
- ER UDVT in secondary position with anticoagulant
- OP PE in any position with anticoagulant
- OP LDVT in any position
- Hospital other VT in primary position
- ER Other VT in primary position

There are identical qualifying event identification criteria that are in both primary and secondary algorithms. If a patient had a qualifying event identified by any of the overlapping criteria, patients were included in the primary algorithm cohort (Cohort 1). The following criteria fall within the definition for **both algorithms**:

- Hospital PE in primary position
- ER PE in primary position
- Hospital LDVT in primary position
- ER LDVT in primary position
- OP UDVT in any position with anticoagulant
- Hospital Other VT in secondary position with anticoagulant
- ER Other VT in secondary position with anticoagulant
- OP Other VT in any position with anticoagulant

Table 2. Summary of Claims-identified Patient Cohorts

	RA	TNFi or JAKi	VTE	Anticoagulation therapy
Cohort 1	✓	✓	✓	✓*
Cohort 2	✓	✓	✓	✓*
Cohort 3	✓	✓**		

*Not all primary algorithm VTE categories included anticoagulants.
**Patients whose index therapy was tofacitinib or upadacitinib were not included in Cohort 3.

Revisions 1A and 2B

Cohort assignment described in Section 3.3 was not implemented in Revisions 1A or 2B since only patients meeting the primary algorithm (Cohort 1) were included in the revision studies. The hierarchy for VTE assignment described for Cohort 1 was retained for Revisions 1A and 2B.

3.4. Sample Identification Period

Patients were identified for the study if they met the inclusion/exclusion criteria during the identification period. Figure 3 presents the sample identification period for the original study population and Revisions 1A and 2B.

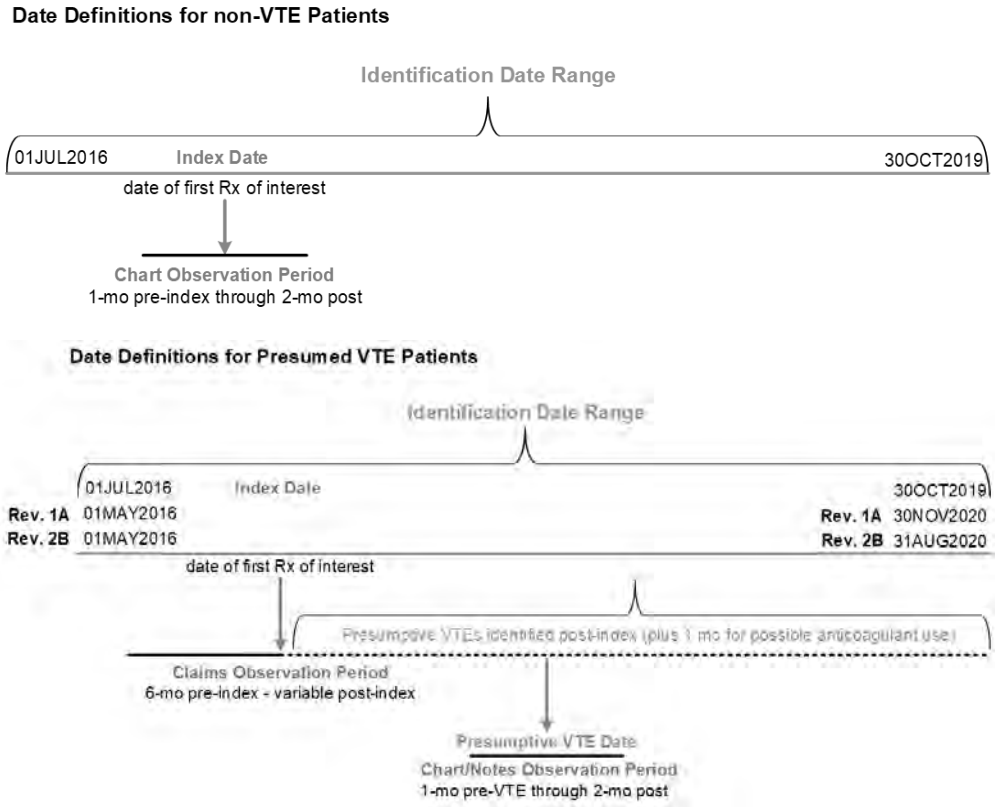

Figure 3. Sample Identification and Chart Abstraction Periods by non-VTE (Cohort 3) and presumptive VTE patients (Cohort 1 and Cohort 2)

3.5. Observation Periods, Claims and Charts

Each patient had two periods of observation, one that was claims-based and one in the medical chart.

- Each patient was observed for a minimum of 7 months in the claims data. This was comprised of 6 months pre-index and a minimum of 1 month from the date of the qualifying event. The post-index period was variable and continued for as long as the patient was continuously enrolled or until a VTE was observed. Patients may have been observed for evidence of a VTE for the total length of post-index CE minus 1 month. The final 1 month after the date of the qualifying event was for observation of anticoagulant use. For example, a patient with 14 months of post-index CE was observed for evidence of a VTE for months 1-13 and evidence of anticoagulant use, if required as part of the algorithm, during month 14.

- Patients' chart observation period comprised 90 days (where available). The period of observation for medical chart data describes the timeframe during which patient/provider

encounters were abstracted. It was not a guarantee that the patient had received services during this time period or that the chart was available for abstraction. Among patients without a presumptive VTE, the chart observation period corresponded to the 3-month period at index date. Among patients with a presumptive VTE identified from the claims data, the chart observation period corresponded with the qualifying event date.[e] As shown in Figure 3, the chart observation period was 3 months, which included 1 month prior to the date of interest (index pharmacy fill [non-VTE cohort] or date of qualifying event [VTE cohort]) and 2 months post.

Revision 1A

The observation periods for each patient were implemented consistent with the original protocol; however, only patients meeting the criteria for VTE based on the primary algorithm were included in the Revision 1A sample. The observation periods described in Figure 3 for the VTE cohort reflect the expanded start and end dates for Revision 1A. The observation periods described in Figure 3 for the non-VTE cohort are not applicable to Revision 1A.

Revision 2B

The observation periods for each patient were implemented consistent with the original protocol. Only patients meeting the criteria for VTE based on the primary algorithm were included in the Revision 2B sample. The notes observation period (for validation) consisted of the 3-month period (1-month prior to and 2-months post presumptive VTE date). During the notes observation period, provider notes available in the EHR database were extracted from the database for each identified patient. Figure 3 has been updated to reflect the modification to the end date of the observation period and the data source (provider notes) specific to Revision 2B.

3.6. Patient Chart Abstraction Identification Criteria

Patient samples eligible for chart abstraction (all cohorts) were identified using the claims-based inclusion and exclusion criteria described in Section 3.2. The criteria described below were then applied to the patient samples with and without presumptive VTE(s) in preparation for chart data collection.

Patients with Presumptive Qualifying Event (VTE)

All patients with evidence of a VTE (primary or secondary algorithms) were considered for medical chart abstraction.

Patients without Presumptive Qualifying Event (VTE)

A random sample of patients meeting the study inclusion/exclusion criteria but whose claims observation period did not include claims consistent with the primary or secondary VTE algorithms were identified for medical chart abstraction for the secondary study objective (smoking status and BMI). The 3-month period of medical chart abstraction included the index

[e] This standard approach, illustrated in **Error! Reference source not found.**, improves the programming and data collection efficiency by standardizing the chart abstraction period for all patients.

date. The purpose of abstraction was to collect personal (height, weight, BMI) and behavioral (smoking status) variables not well populated in claims data.

Medical Chart Eligibility

- Medical charts that did not include reference to RA or a TNFi/JAKi therapy were considered invalid and were not abstracted. This criterion applied to all cohorts.

- Medical charts for patients whose claims did not indicate a VTE (Cohort 3) were required to have BMI (or its components) or smoking data available. This eligibility criterion introduces selection bias by only including those patients whose providers have recorded (and by proxy, inquired about) smoking status and/or height/weight. However, abstraction of medical charts that do not include this information do not support the study objective.

Provider Selection

For each patient, one provider was identified to be contacted for chart procurement. Among patients whose claims indicate evidence of a VTE, a combination of VTE diagnosis codes, dates of service, and provider site codes was used to identify the providers of interest for medical chart abstraction. Claims for diagnostic testing were excluded from provider identification. Among patients whose claims did not indicate evidence of a VTE, a combination of RA diagnosis and site codes was used to identify providers most likely to be treating the patient's RA symptoms with one of the medications of interest.

Among patients with a presumptive VTE, personal identifying information (such as name and date of birth) as well as provider identifying information (name and practice address) were merged with the study dataset to support procurement of each patient's clinical chart from a provider for abstraction of VTE-related confirmatory data. The provider of interest (including inpatient hospitals, emergency department providers, and OP providers) was identified based on the claims data for each patient and contacted directly to request the medical chart for the identified patient over a 90-day period that included the VTE date (date of the presumptive VTE identified from the claims data). The provider most likely to have rendered services for the presumptive VTE was the primary target for chart procurement and abstraction. Provider participation was voluntary and was limited to providing the patient's chart over the date range of interest to a professional medical abstraction firm who conducted the abstraction of the procured charts using an IRB approved chart abstraction form.

Revision 1A

Patient chart abstraction identification criteria were modified for Revision 1A to include only patients meeting the primary VTE algorithm (referred to as Cohort 1 in the original protocol), remove the medical chart eligibility requirement of RA diagnosis and TNFi/JAKi therapy for abstraction, and identify an alternative provider for each patient (when possible).

Revision 1A patient sample eligible for chart abstraction was identified using the claims-based inclusion and exclusion criteria for Revision 1A described in Section 3.2.2.

Patients with Presumptive Qualifying Event (VTE) Revision 1A

In the original protocol, medical charts that did not include reference to RA or a TNFi/JAKi therapy were considered invalid and were not abstracted. However, the initial execution of the original protocol informed that these charts contained sufficient information to validate VTE. Thus, this requirement was removed in Revision 1A, and all patients with evidence of a VTE (primary algorithm only) were considered for medical chart abstraction regardless of RA diagnosis or therapy reference.

Provider Selection Revision 1A

For each patient in the Revision 1A sample, one provider was identified to be contacted for chart procurement. A combination of VTE diagnosis codes, dates of service, and provider types were used to identify the provider of interest for medical chart abstraction. In addition, an alternative provider was also identified whenever possible for each patient in the Revision 1A sample. The purpose of identifying an alternative provider was to mitigate the number of patients whose clinical information could not be included in the study simply because a chart could not be procured. Alternative providers for some patients from the initial sample who were identified as part of the original protocol, but whose charts were not procured, were also identified as part of Revision 1A. Specific provider identification steps were described in the statistical analysis plan.

Revision 2B

Provider selection was not required for Revision 2B because of use of electronic provider notes for validation. Patients meeting the Revision 2B study inclusion/exclusion criteria (primary VTE algorithm only) were included in the validation dataset if:

- The patient's provider(s) had contributed free-text clinical notes from an EHR database that could be extracted and redacted for abstraction
- The patient's free-text clinical notes fell within the 3-month observation period described in Section 3.5 (Revision 2B notes and Figure 3)

4 Data Sources

4.1. Optum Research Database Data Source

The ORD is fully de-identified and Health Insurance Portability and Accountability Act (HIPAA) compliant and comprises medical and pharmacy claims data (including linked enrollment) from 1993-present on more than 73 million lives. The ORD is the data source for patient identification in the original protocol and Revision 1A.

4.1.1. Commercially Insured Patient Data

In 2019, approximately 19% of the US commercially enrolled population and 21% of the Medicare Advantage population (with medical and pharmacy claims) were represented in the ORD.

4.1.2. Medical and Pharmacy Claims

Medical claims or encounter data are collected from all available health care sites (inpatient hospital, OP hospital, ER, physician's office, surgery center, etc.) for virtually all types of provided services. Medical claims and coding conform to insurance industry standards. Claims for ambulatory services submitted by individual providers, e.g., physicians, use the Centers for Medicare and Medicaid Services (CMS)-1500 form, or submit electronically using the 837P format. Claims for facility services submitted by institutions, e.g., hospitals, use the Uniform Billing (UB)-82, UB-92, UB-04, or CMS-1450 formats. Medical claims include multiple diagnosis codes recorded with the International Classification of Diseases, Ninth Revision and ICD-10-CM diagnosis codes; procedures recorded with ICD-9 and ICD-10-CM procedure codes, Current Procedural Terminology (CPT), or Healthcare Common Procedure Coding System (HCPCS) codes; site of service codes; provider specialty codes; revenue codes (for facilities); paid amounts; and other information. Typically, facility claims do not include medications dispensed in hospital. Approximately six months following the delivery of services is required for complete medical data.

Claims for pharmacy services are typically submitted electronically by the pharmacy at the time prescriptions are filled. The claims history is a profile of all OP prescription pharmacy services provided and covered by the health plan. Pharmacy claims data include drug name, dosage form, drug strength, fill date, days of supply, financial information, and de-identified patient and prescriber codes, allowing for longitudinal tracking of medication refill patterns and changes in medications.

Pharmacy claims are typically added to the research database within six weeks of dispensing. Approximately six months following the delivery of services are required for complete medical data.

4.2. Market Clarity Integrated Clinical + Claims Database

Optum’s Market Clarity integrated clinical + claims database was used for Revision 2B sample identification. Market Clarity is a de-identified and deterministically-linked claims data integrated with Optum’s Clinical EHR Data. The clinical data combined with adjudicated medical and pharmacy claims from both Optum affiliated and non-affiliated payers can provide deep insight into patterns of care and patient clinical profiles, and offers increased geographic and payment heterogeneity.

Market Clarity Data includes:

- More than 150 complete payer data sets, spans all therapeutic areas and has greater breadth and diversity of coverage including cash payments and Medicaid.
- More than 60 million patients, with visibility into more than 20 thousand different clinical variables

The integrated database was de-identified in compliance with HIPAA using the ‘statistical’ method and includes: historical, linked administrative claims data, including pharmacy claims, physician claims, facility claims, and health plan enrollment data. Optum’s proprietary deterministic matching capabilities ensure an eligibility-controlled resource. The Market Clarity database includes approximately 30 million matched patients with complete health plan eligibility, which allows for in-depth understanding of the patient journey from start to finish.

4.2.1. Provider Notes Data

Providers and provider networks (or health systems) can opt to include free-text fields in the EHR data provided to Optum. Provider notes include free-text remarks logged in a patient's electronic chart. Notes for a single patient may include multiple providers interacting with the patient within a clinical system. Various clinical providers and specialties may contribute notes for a single patient (for example, specialty clinics such a rheumatology as well as provider types such as physicians, nurses, or physical therapists). Notes often capture consultations, treatment planning, suspected conditions, or other clinically relevant remarks not otherwise captured in a structured field. Thus, when notes are available, review and abstraction can provide valuable insights. However, not all providers or provider networks contribute these unstructured notes (or not uniformly for all patients), meaning that the sample of patients with notes for review is smaller than the population of patients identified initially from the Market Clarity database. The composition of notes is specific to each patient and their interaction with the health care provider(s) who have contributed free-text data. Since Market Clarity is a deidentified data source, the specific provider(s) contributing notes was unknown.

For the purposes of Revision 2B, the unstructured notes were redacted and utilized in much the same way that medical charts were used for the original study and Revision 1A.

4.2.2. Notes Extraction

Extraction of the provider notes included 2 strategic quality checkpoints. To assess the quality of the notes, a random sample of 7 patients' notes were redacted and reviewed by the chart abstraction vendor. The quality of the data observed was sufficient to support the study objectives; however, the vendor suggested focusing the notes for review using search terms relevant to the study objectives similar to the targeted provider selection criteria utilized by Protocol 1A. A list of VTE and RA-related search terms was created (see below) and implemented, reducing the number of notes from 4,293 to 1,494. Of the 73 patients with notes during the 3-month observation period, 5 did not have notes that contained VTE or RA-related search terms and were excluded. A quality review of one of the five patients found that all 7 notes identified for this patient represented telephonic exchanges between the patient and the service provider requesting refills of non-RA, non-VTE medications.

Given the widely variable number of notes per patient, many of which are not relevant to this study, targeted search terms were used to focus abstraction on clinical data related to the study population and objectives. Search terms used to identify relevant clinical notes included:

- Embol…
- Defect
- Thromb…
- Phlebitis
- Pulmon…
- Vein
- Subsegmental
- Budd-Chiari
- Clot
- Blockage
- Restriction
- Thrombophlebitis
- D-dimer
- DVT
- PE
- CT
- Ultrasound
- MRI
- X-ray
- Anticoagulant
- Anticoagulation
- Angiogram
- Perfusion
- Computed Tomography

- Venogram
- MRA
- MRV
- Venous Duplex
- Iliac
- Occlusion
- Femoral
- Popliteal
- Posterior tibial
- Brachial
- Radial
- Ulnar
- Subclavian
- Doppler
- Deep
- Profunda
- Lung
- Duplex
- Homan's
- Venography
- VQ Scan
- Ventilation
- Plethysmography
- Magnetic Resonance
- Computed Axial
- Segmental
- Extremity
- Portal
- Mesentery
- Geneva Score
- Calf
- Leg
- Arm
- Rheumatoid
- RA
- Baricitinib
- Tofacitinib
- Upadacitinib
- Abatacept
- Tocilizumab
- Sarilumab
- Anakinra
- Adalimumab
- Certolizumab
- Etanercept
- Golimumab
- Infliximab
- DMARD
- Apixaban
- Dabigatran
- Edoxaban
- Enoxaparin
- Fondaparinux
- Rivaroxaban
- Tinzaparin
- Warfarin
- Arthritis

After the notes to be included were identified, they were redacted using a two-stage process prior to abstraction.

5 Variable Definitions

5.1. Claims Data Variables

Descriptions of claims data variables are provided below. Diagnosis codes, procedure codes, and medication lists are provided in Appendix C.

Presumptive VTE Identification

Variables were created to identify presumptive VTEs that satisfied one of two algorithms, primary and secondary. Both algorithms identified VTEs by site of care (hospital, ER, OP), diagnosis type (PE, upper extremity DVT, lower extremity DVT, and other VT), and diagnosis position (primary, secondary, or any). Primary diagnosis was defined as a diagnosis in Position 1. Secondary diagnosis was defined as any diagnosis other than Position 1.

For hospital and ER site of care, variables with all possible diagnosis positions (primary and secondary) were created. Outpatient site of care included variables for diagnosis in any position, not separated by primary and secondary. All flag and date variables allowed for stratification by diagnosis and site of care.

- **Primary algorithm presumptive VTE date** – date variable identifying the earliest date of presumptive VTE that met qualifying criteria from the primary algorithm by site of care, diagnosis type, and diagnosis position.

- **Primary algorithm presumptive VTE flag** – dichotomous variable identifying the presumptive VTE identifying qualification for the primary algorithm by site of care, diagnosis type, and diagnosis position.

- **Secondary algorithm presumptive VTE date** – date variable identifying the earliest date of presumptive VTE that met qualifying criteria from the secondary algorithm by site of care, diagnosis type, and diagnosis position.

- **Secondary algorithm presumptive VTE flag** – dichotomous variable identifying the presumptive VTE identifying qualification for the secondary algorithm by site of care, diagnosis type, and diagnosis position.

- **Anticoagulant therapy flag** – dichotomous variables identifying anticoagulant treatment(s) within 31 days of presumptive VTE date.

- **VTE date** – date variable indicating the earliest date of presumptive VTE that met qualifying criteria from either the primary algorithm (VTE_DATE1), the secondary algorithm (VTE_DATE2), or did not qualify as presumptive VTE on either algorithm (VTE_DATE3). These are mutually exclusive date variables. These three date variables were harmonized into a single variable called VTE_DATE, which was operationalized as the abstraction date.

- **VTE type** – categorical variable identifying the specific site of care, diagnosis type, diagnosis position combination on the patient's presumptive VTE date. There was only a VTE_TYPE1 and VTE_TYPE2 since Cohort 3, by definition, did not include patients with a presumptive VTE.

- **Total follow-up time** – days from index date +1 to death, disenrollment, or end of the study period [30November2019] (minimum = 31 and maximum = varied by patient up to approximately 1,200 days).

- **VTE Algorithm 1** – number of primary algorithm criteria the patient met (e.g. met criteria for a hospital PE and for an ER PE in the primary position).

- **VTE Algorithm 2** – number of secondary algorithm criteria the patient met.

- **Total time at VTE risk** – days from the index date +1 to death, disenrollment, presumptive VTE, or end of the study period [30November2019] (minimum = 0 and maximum = end of per patient follow-up period).

- **Time to VTE** – days from index date to VTE for those patients meeting primary or secondary algorithms (minimum = 0 and maximum = end of per patient follow-up).

- **Time from VTE to end** – days from the VTE event date to death, disenrollment, or end of the study period (minimum = 0 and maximum = total follow- up time - time to VTE).

- **Time from last index claim to VTE date** – days from the end of medication coverage for an index therapy to the VTE date. This value could be negative.

- **Number of index treatments** – the number of claims observed for the index therapy during the follow-up period.

Revisions 1A and 2B

All time-to-event variables (Total follow-up time, Total time at VTE risk, and Time to VTE) were calculated as days from the index date. The modified definitions of Total time at VTE risk and Total follow-up time as from the index date were applied to the original study cohorts in addition to Revisions 1A and 2B. Time to VTE was equivalent to Total time at VTE risk among patients meeting the primary VTE algorithm. Therefore, only one of these two measures (Total time at VTE risk) was reported in Revisions 1A and 2B.

Protocol

- **Protocol number** – a categorical variable identifying each patient as identified under the original protocol, Revision 1A or Revision 2B.

Patient Characteristics

The following characteristics were assessed during the 6-month CAW prior to and inclusive of the index date.

- **Age** – age was defined as of the index year. Mean, median, and SD were provided.

- **Age groups** – subjects were assigned to one of the following age groups: 18-34, 35-54, 55- 64, 65-74, and 75+.

- **Gender** – gender was captured from enrollment data; subjects with undefined gender were removed from the study sample prior to chart procurement.

- **Pre-index TNFi treatment** – a dichotomous variable identifying patients who had evidence of treatment with a TNFi that differed from their index TNFi treatment.

- **Baseline Charlson comorbidity score** – a comorbidity score was calculated based on the presence of diagnosis codes on medical claims in the baseline period. The Quan-Charlson comorbidity score was also categorized into the following groups: 0, 1-2, 3-4, and 5+.

- **Baseline general comorbid conditions** – general comorbid conditions were identified during the baseline period using the Clinical Classifications Software managed by the Agency for Healthcare Research and Quality (AHRQ).[17] This measure generated indicator variables for specific disease conditions based on ICD-10-CM diagnoses. The top 15 comorbid conditions were presented.

- **Condition-related comorbid conditions or treatments** – comorbidities related to RA and/or VTE were assessed from the claims. A dichotomous variable for evidence of ICD-10-CM based diagnosis of up to 10 comorbidities or treatments of interest during the 6-month CAW was created. The following comorbidities are planned for this analysis: major

adverse cardiac events (MACE), atrial fibrillation, chronic obstructive pulmonary disease (COPD), obesity, and genetic polymorphism associated with VTE. Dichotomous variables for treatments of interest were assessed for hormone use (oral contraceptives and hormone replacement therapy), MTX, selective estrogen receptor modulator, cancer treatment, and Cox-2 inhibitors.

- **Smoking status** – a dichotomous variable for evidence of ICD-10-based diagnosis, CPT, or HCPCS code identifying patients as a smoker (current or former).

- **Geographic location** – the US region in which the study subject was enrolled in medical and pharmacy benefits were determined and reported. States are categorized into a geographic region in accordance with the US Census Bureau's region designations. The regions are presented below.

Table 3. Geographic Regions

Region	State
Northeast	CT, MA, ME, NH, RI, VT, NJ, NY, PA
Midwest	IL, IN, MI, OH, WI, IA, KS, MN, MO, ND, NE, SD
South	AL, AR, DC, DE, FL, GA, KY, LA, MD, MS, NC, OK, SC, TN, TX, VA, WV
West	AZ, CO, ID, MT, NM, NV, UT, WY, AK, CA, HI, OR, WA

5.2. Chart/Notes-based Data Variables

General descriptions of chart data variables are provided below. Medical charts represent a clinical accounting of each unique patient/provider presenting symptom/treatment pattern combination. Not all variables described below were available in the medical chart for every patient. Missing data was not imputed.

RA Experience Characteristics

The following variables were collected at the beginning of abstraction:

- **RA diagnosis.** A diagnosis of RA on a medical chart.

- **RA treatment of interest**. This included evidence of a TNFi (adalimumab, certolizumab pegol, etanercept, golimumab, or infliximab), a JAKi(baricitinib, tofacitinib, or upadacitinib), a cDMARD (MTX, hydroxychloroquine, leflunomide, sulfasalazine) or sarilumab.

Revisions 1A and 2B

The RA treatment of interest was expanded beyond TNFi and JAKi to include non-TNFi bDMARDs (abatacept, tocilizumab, sarilumab or anakinra). All other variables have the same operational definitions as the original study. For 2B, notes rather than medical charts were used. See Appendix A for summary of operational definitions in the original study and the revisions 1A and 2B.

VTE Characteristics

The following variables were collected from the medical chart, when available.

- **Evidence of prior VTE** – a dichotomous variable indicating if the patient had a history of having a VTE prior to the start of the abstraction period. This variable was reported separately for the non-VTE cohort.
    - Location/type of prior VTE – PE, UDVT, LDVT, or other VT (with an associated open-ended please specify); this variable was recorded missing if the information was not recorded in the chart
    - Date of prior VTE – this variable was recorded as missing if the information was not recorded in the chart
- **Evidence of current VTE** – a categorical variable indicating Yes, No, or Unclear. This variable was reported separately for the non-VTE cohort.
    - Location where VTE was first *observed* (place of diagnosis) - OP clinic, inpatient, ER, other, or unknown
    - Location where VTE was *treated* (place of service) - OP clinic, inpatient, ER, other, or unknown
- **Evidence of VTE-related diagnostic evaluation** – a dichotomous variable indicating if the patient had any imaging or diagnostic procedures performed to confirm a VTE during the abstraction period.
    - Diagnostic testing modalities included the following: angiogram; computed tomography (CT) scan; lung ventilation-perfusion scan; magnetic resonance imaging (MRI)/magnetic resonance angiography (MRA)/magnetic resonance venography (MRV); venogram; or venous duplex ultrasound. A dichotomous variable and date variable, if available, was collected for each type of diagnostic test
    - Results of the diagnostic test(s) was collected, when available, and if possible, was categorized as confirming the VTE, ruling out the VTE, or neither confirm nor rule out the VTE
- **Evidence of VTE-related laboratory tests** – a dichotomous variable indicating if the patient had a D-dimer laboratory test.
    - Date and results[f] of laboratory testing were collected when available. Result units were measured in mg/L or µg/ml, µg/L or ng/mL, nmol/L, or an open-ended please specify other
- **VTE adjudication variables** – a dichotomous variable indicating that the patient was classified as having a possible VTE requiring clinical adjudication. Among patients whose

[f] One patient had a D-dimer lab result of >4.0 mg/L. This result was assigned a value of 4.0 mg/L.

VTE required clinical adjudication, a three-level variable was created to indicate the medical director's judgement, categorized as 'Positive' or 'Negative'.

- **Proportion of patients having more than one confirmed VTE** – a dichotomous variable indicating that the patient was classified as having more than one VTE confirmed by a VTE-related diagnostic evaluation.
    - Count of VTEs per patient
- **Proportion of patients having an unconfirmed VTE** – a dichotomous variable indicating that the patient was classified as having at least one unconfirmed VTE
    - Count of unconfirmed VTEs per patient

VTE characteristics were recorded separately for each VTE observed in the chart. One patient may have multiple VTE events or multiple values for a single VTE event (i.e., multiple diagnostic evaluations).

Patient Clinical Characteristics

- **Smoking status** – among subjects for whom this data was available in the chart, the following variables were collected
    - Smoking status (current smoker, former smoker, never smoked, or not documented)
    - Type of product smoked (cigarettes, cigars, pipe, or unknown)
- **BMI** – patient height and weight[g] (or BMI) closest to the index date was collected. For patients with height and weight recorded but no BMI, BMI was calculated from the height and weight values using the following equation:

$$\frac{weig.\ t\ (lb)}{height\ (in)^2} * 703$$

- **Obesity** – among subjects for whom BMI could be recorded or calculated, a dichotomous variable for whether the patient was obese (or severely obese) or not. Patients were considered obese if BMI ≥30 kg/m^2, the minimum level definition for class I obesity.
- **RA treatments of interest** – evidence of treatment with a conventional or bDMARD (MTX, hydroxychloroquine, leflunomide, sulfasalazine), sarilumab, non-TNFi (abatacept, anakinra, tocilizumab, or sarilumab), TNFi (adalimumab, certolizumab pegol, etanercept, golimumab, or infliximab), and/or JAKi (baricitinib, tofacitinib, or upadacitinib) was recorded as separate dichotomous variables. All treatments received had their most recent date of receipt recorded.

[g] One patient had a recorded weight of >400 pounds. This result was assigned a value of 400 pounds.

- **Pregnancy status** – a categorical variable indicating that patient was pregnant or recently gave birth (Yes, No, or Not Applicable) during the abstraction period.

- **Mortality** – a dichotomous variable indicating if the patient expired, if known, during the abstraction period.

    - A categorical variable indicating that the patient died as the result of a VTE; that a VTE (or multiple VTEs) contributed to the patient's death; or the medical chart does not list VTE as the cause of death.

Comorbidities

- Comorbidities or other conditions/treatments of interest observed in the chart during the 3-month abstraction period included the following: atrial fibrillation, autoimmune disease, cancer (with cancer diagnosis date), COPD, COX-2 inhibitor use, hormone replacement therapy, hypertension, intra-abdominal surgery, hip surgery, or oral contraceptive use.

5.3. Missing Data

Missing data were not imputed. Outliers identified in the chart data were confirmed with the chart abstraction vendor to ensure the quality of the abstracted data.

6 Analytic Strategy

6.1. Analytic Preparation

Prior to the analysis, all medical chart data received from the abstraction vendor underwent data cleaning and edit checking in order to ensure that there were no inconsistent or out of range values, and that the final evaluable sample is complete. This final analytic dataset was then linked with administrative claims data, as well as with the medical director's determination from clinical adjudication, using a unique patient identifier. Invalid chart/notes were excluded from the final analytic sample.

6.2. General Statistical Considerations

This study conducted a descriptive analysis of linked medical chart and administrative claims data at the patient level. The final analytic results were provided in summary table form. All study variables, including baseline and outcome measures, were analyzed descriptively. Numbers and percentages were provided for dichotomous and polychotomous variables. Means, medians, standard deviations, and percentiles were provided for continuous variables. The planned stratification by index therapy (JAKi and TNFi) in the original protocol was not implemented due to the small sample size. The planned stratification by type of VTE in the original protocol was also not implemented after the descriptive results revealed that many patients experienced more than one type of VTE. Appropriate tests (e.g., t-test, Mann Whitney-U test, chi-square test) were used based on the distribution of the measure.

Revision 1A

The analytic approach remains unchanged for patients meeting the primary VTE algorithm. The analyses will utilize the Revision 1A data only. After review of the results by the study team, the

results of the Revision 1A analyses may be combined with the previously completed study results (Cohort 1 only).

Revision 2B

The analytic approach remains unchanged for patients meeting the primary VTE algorithm. The analyses will utilize the Revision 2B data only. After review of the results by the study team, the results of Revision 2B may be combined with the Revision 1A results and/or with the primary study results primary study and Revision 1A results (Cohort 1 only).

6.2.1 Amendments to the Statistical Analysis Plan

The primary objective of this study was to evaluate the performance of the main VTE case definition used in the B023 study (referred to as the primary VTE algorithm in the B029 study) among a US population of insured adults diagnosed with and treated for RA. In addition, the B029 study also evaluated the performance of an alternative, less stringent, VTE case definition proposed for sensitivity analyses in the B023 study (referred to as the secondary VTE algorithm in B029 study).

Cohort 2 in the original sample of B029 study was specifically defined for the purpose of identifying patients with claims evidence of a presumptive VTE based on the secondary algorithm. The secondary VTE algorithm comprises 20 unique qualifying criteria (unique diagnosis, diagnosis position and treatment setting combinations, as well as drug dispensing records), of which 8 criteria also fall under qualifying criteria of the primary VTE algorithm. For operational purposes, however, Cohort 2 was identified after selecting patients into Cohort 1 (See Section 3.3). This allowed for mutually exclusive cohorts to be created, thereby allowing statistical comparisons to be made between the cohorts. However, this resulted in unintentional exclusion of patients with claims evidence of presumptive VTE based on qualifying for both the primary and secondary algorithms from Cohort 2.

In order to correctly estimate the PPV of the secondary algorithm, Cohort 2 was recreated to include all patients with claims evidence of a presumptive VTE based on the secondary algorithm (N=76). It now includes 40 patients who were originally selected into Cohort 2 and 36 patients who were additionally identified from Cohort 1. The PPV of the secondary algorithm calculated from the updated Cohort 2 was reported.

6.3. Primary Objectives

6.3.1. Use Abstracted Medical Chart Data to Validate VTEs Identified from Administrative Claims Data

The primary objective was to validate the VTEs identified from administrative claims data using the abstracted medical chart data. Results of presumptive VTE identification from the primary and secondary algorithms in the claims database were compared to the results generated by chart abstraction.

The validity of the algorithm to identify VTE was assessed by calculating the positive predictive value (PPV). PPV was calculated as true positives / (true positives + false positives).

- Positive predictive value (PPV) = TP / (TP + FP)

Table 4. Table for Assessing the VTE Algorithm

	Reference Gold Standard		
	Chart positive	Chart negative	Total
Claims positive	True positive (TP)	False positive (FP)	TP + FP

True positives were cases identified from the claims algorithm and confirmed by chart analysis; false positives were cases identified using the claims algorithm where the chart analysis did not identify a VTE. Cases where not enough information was present in the chart to confirm whether a VTE occurred (either using the case rules, or clinical adjudication by Optum's medical director) were not included in PPV computation. The VTE case confirmation rules were developed based on clinical consultation and were specific to each type of VTE (PE, UDVT, LDVT, and other thrombosis). To be categorized as a confirmed VTE, the abstracted patient chart data had to fulfill the confirmation rule specific to the VTE observed in the chart. Specifically, a positive VTE was assigned if the available abstracted medical chart data for the patient met at least one of the following criteria:

- The patient's abstracted chart data indicated that the patient died as a result of a VTE or that a VTE contributed to the patient's death; and death occurred on or within 30 days of the VTE date (fromclaims)
- Chart indicated that the patient had a diagnosis of PE within +/- 7 days of the claims-based VTE date AND had at least one of the following diagnostic tests within +/- 30 days of the VTE date (from claims) where the result confirmed a finding of VTE:
    - Angiogram
    - CT
    - MRI/MRA/MRV
- Chart indicated that the patient had a diagnosis of an upper and/or a LDVT within +/- 7 days of the claims-based VTE date AND had at least one of the following diagnostic tests within +/- 30 days of the VTE date (from claims) where the result confirmed a finding of VTE:
    - MRI/MRA/MRV
    - CT
    - Venogram
    - Venous Duplex Ultrasound
- Chart indicated that the patient had a diagnosis of other VTE within +/- 7 days of the claims-based VTE date AND had at least one of the following diagnostic tests within +/- 30 days of the VTE date (from claims) where the result confirmed a finding of VTE:
    - MRI/MRA/MRV

- CT
- Venogram
- Venous Duplex Ultrasound

- Chart required a clinical review and was subsequently classified by Optum's medical director as a positive VTE. These included cases that had a documented VTE, where diagnostic tests were not performed, or they were performed but the results did not confirm nor rule out a VTE. It also included cases that had an unknown VTE type, place of diagnosis, or place of service from the chart.

Algorithm validation results were stratified by primary versus secondary algorithms.

Revision 1A and Revision 2B

To maximize efficiency, simple case rules were developed and implemented within the abstraction database. The case rules, developed with clinical consultation for the original protocol, are applied following initial edit checks for data completeness and quality. The same process and case rules utilized by the original protocol and Revision 1A were utilized for Revision 2B. Final VTE adjudication was completed analytically by Optum after all patient notes were abstracted. The medical director's determination was linked with the abstracted data at the patient level and included in the analytic dataset.

The PPV of the primary VTE algorithm was calculated separately for Revision 1A and Revision 2B. The PPV results from Revision 1A were combined with the results of the original study.

6.4. Secondary Objectives

6.4.1. Describe Body Mass Index and Smoking Status

A secondary objective was to assess the distribution of BMI and smoking status as collected from the chart data. Data were presented for all patients, as well as stratified by study cohort (i.e., patients with a presumptive VTE versus patients with no evidence of a VTE). Patient height and weight (or BMI), and obesity indicator (BMI ≥30 kg/m^2) were presented.

A sensitivity analysis was performed to consider other BMI values for analysis (i.e., BMI ≥35 kg/m^2).

6.5. Multiple Comparisons

No adjustments for multiple comparisons were made.

6.6. Statistical Significance

When appropriate, two-sided tests with a p-value less than or equal to 0.05 were considered significant.

6.7. Software

All analysis was conducted using SAS version 9.4 (SAS Inc., Cary, NC, USA).

7 Results

7.1. Cohort Attrition/Sample Size

7.1.1. Original Study

A total of 28,757 RA patients with at least one pharmacy claim for a TNFi therapy or a JAKi therapy during the sample identification period 1 July 2016 to 30 October 2019 and at least one medical claim with diagnosis of RA during the CAW through 1 month post-index were identified. 18,466 patients were at least 18 years of age as of their index date, had no missing or invalid demographic or insurance information, and met the CE with medical and pharmacy coverage requirements of 6 months pre-index and at least 31 days index. 15,452 patients were eligible for re-identification with provider identifiable information available to support medical chart identification and abstraction. Patients with at least 1 pharmacy claim for the index therapy in the 6 months pre-index, at least 1 claim for anticoagulant therapy prior to the date of VTE, or at least 1 pharmacy or medical claim for cancer treatment on the index date were excluded (N. Excluded = 6,457). Patients with no presumptive VTE whose index RA JAKi medication was either tofacitinib or upadacitinib were also excluded from chart abstraction; for patients with no presumptive VTE, only patients with TNFi therapy (n=5,073) or baricitinib (n=119) were included.

After initial patient selection criteria were applied, 453 patients were identified as eligible for chart abstraction. Of those, 134 patients with a presumptive VTE and 319 without a presumptive VTE (includes all 119 patients with baricitinib on index, plus a random sample of 200 patients with TNFi on index) were identified. Direct outreach to treating providers resulted in the procurement of 289 charts. After removing invalid charts, 260 patients with eligible abstracted medical charts were included in the study. Charts were not procured for a variety of reasons (n=164), including provider non-response or refusal or not at given address (38%), lack of requested information (57%), or request for patient consent (4%). A comparison of age, gender, geographic region, and insurance coverage type did not reveal statistically significant differences between patients whose charts were procured versus those that were not procured.

Cohort 1: Primary VTE Algorithm

A sample of 70 patients were identified, and, of those, a total of 38 patients (out of 46 charts procured) were included in the study with eligible abstracted medical charts.

Cohort 2: Secondary VTE Algorithm

A sample of 126 patients were identified, and, of those, a total of 76 patients (out of 85 charts procured) were included in the study with eligible abstracted medical charts.

Cohort 3: Non-VTE Patients

A sample of 319 patients were identified. Of those, 199 charts were procured and a total of 182 patients were included in the study with eligible abstracted medical charts.

7.1.2. Revision 1A

A total of 41,605 RA patients with at least one pharmacy claim for a TNFi therapy, a JAKi therapy, or a non-TNFi therapy during the sample identification period 1 May 2016 to 30 November 2020 and at least one medical claim with diagnosis of RA during the CAW through 1 month post-index were identified. Initially, 22,174 patients were at least 18 years of age as of their index date, had no missing or invalid demographic or insurance information, and met the CE with medical and pharmacy coverage requirements of 6 months pre-index and at least 31 days index. Of these, 18,477 patients were eligible for re-identification with provider identifiable information available to support medical chart identification and abstraction. Patients with at least 1 claim for anticoagulant therapy prior to the date of VTE or at least pharmacy or medical claim for cancer treatment on the index date were excluded.

For Revision 1A, 222 patients were identified eligible for chart abstraction. 184 charts were procured. After removing invalid charts, 117 patients were included in the study with eligible abstracted medical charts.

7.1.3. Revision 2B

A total of 95,587 RA patients with at least one pharmacy claim for a TNFi therapy, a JAKi therapy, or a non-TNFi therapy during the sample identification period 1 May 2016 to 31 August 2020 and at least one medical claim with diagnosis of RA during the CAW through 1 month post-index were identified. 42,858 patients were at least 18 years of age as of their index date, had no missing or invalid demographic or insurance information, and met the CE with medical and pharmacy coverage requirements of 6 months pre-index and at least 31 days index. 28,554 patients had available data as partner claims or ASO-only plans. Patients with at least 1 claim for anticoagulant therapy prior to the date of VTE or at least pharmacy or medical claim for cancer treatment on the index date were excluded.

A total of 253 patients were identified from the Market Clarity claims data meeting the study criteria for the primary algorithm. Optum's Natural Language Processing (NLP) team was able to identify 73 of the 253 patients whose providers had contributed unstructured provider notes during the 3-month observation period. 68 had unstructured provider notes that contained VTE or RA-related search terms. The list of search terms was broad to capture as many provider notes as possible that may be related to this study. 4 patients were ineligible because their notes were unrelated to RA, even though their notes were identified by the NLP team. 64 patients were included in the study with eligible abstracted provider notes.

Table 5. Chart/Notes Abstraction Disposition

Patients	Original Study			Rev. 1A (Primary VTE algorithm validation)	Rev. 2B (Primary VTE algorithm validation)
	Cohort 1 (Primary VTE algorithm validation)	Cohort 2 (Secondary VTE algorithm validation)	Cohort 3 (Estimation of smoking and BMI prevalence)		
Eligible for chart/notes abstraction	70	126	319	222	253
Chart procured/notes available	46	85	199	184	73
Abstract completed	38	76	182	117	64

7.1.4. Missing Data

Charts and provider notes that did not contain relevant/sufficient information for VTE validation were considered invalid and were not counted in the PPV calculation. For the original study, 29 charts of 289 procured were incomplete/invalid. For Revision 1A, 67 charts of 184 procured were incomplete/invalid. For Revision 2B, 4 of 68 provider notes were incomplete/invalid.

7.2. Primary Objective

7.2.1. Primary Algorithm Validation Sample

Two hundred ninety two presumptive VTE events were identified in the ORD, of which valid patient charts were procured from treating providers for 155 patients (38 from cohort 1 from the original sample and 117 from Revision 1A). They formed the primary algorithm validation sample. Although the Market Clarity database was explored as an additional source to identify and validate claims-based VTE per the primary algorithm definition, the Revision 2B sample (N=64) was not combined with the ORD sample due to limitations unique to the Market Clarity database in the outcome validation, discussed in Sections 7.4 and 9.

7.2.2. Claims-Based Patient and Clinical Characteristics

The mean age of those 155 patients was 66 years (standard deviation [SD] 11) with 35% of the population between ages 65 and 74 and 28% aged 75 years or older. The population was predominantly female (74%) and covered by a Medicare insurance with medical and Part D coverage insurance plan (81%). Over half of patients (55%) resided in the southern United States, 25% in the Midwest and 10% in each of the northeast and the western United States regions. Follow-up time available to observe a primary algorithm VTE ranged from 51 days to 1,704 days after index date with a mean of 912 days (SD=525).

The mean Charlson comorbidity score during the CAW was 2.5 (SD 1.7) with nearly 40% having a Charlson comorbidity score of 3 or higher. The most common comorbidities identified from claims data during the CAW (using AHRQ[18] classification software) were consistent with a population of older RA patients. Common comorbid conditions included: hypertension (67%), diseases of the heart (58%), nervous system disorders (54%), disorders of lipid metabolism (53%) and spondylosis and back problems (51%). The claims data identified only 3 patients with evidence of a MACE (myocardial infarction or stroke), 9 patients (6%) with atrial fibrillation, 36 patients (23%) with evidence of COPD, and 7 patients (5%) with a genetic polymorphism

associated with VTE. Evidence of smoking was present in the claims data for 36 patients (23%).[h] About 42% of patients in the sample had ≥1 claim for MTX therapy during the CAW. During the follow-up period starting on index date the most common bDMARDs were adalimumab (30%), tocilizumab (24%), and etanercept (19%).

7.2.3. Claims-Based VTE Characteristics

The time to presumptive (claims-identified) VTE ranged from 2 days to 1,676 days with a mean of 482 days (SD 418). There were 17 unique primary algorithm criteria (unique diagnosis, diagnosis position and treatment setting combinations), and many patients were identified by more than one. Among the 155 patients identified, the mean number of primary algorithm VTE criteria met was 2.6 (number of criteria met ranged from 1 to 9).

7.2.4. Chart-Based Patient and Clinical Characteristics

During the 3-month chart abstraction period, a diagnosis of hypertension was mentioned in the charts of 72% of patients. Chronic obstructive pulmonary disease was identified among 27% of the chart-based population. Atrial fibrillation was noted in 16% of patient charts, and autoimmune diseases were listed in 19% of charts. There was evidence in the abstracted chart data that 8 of the 155 patients expired and, of those, 2 charts indicated that a VTE may have contributed to the patient's death.

The most common RA-related treatments documented in patient charts included cDMARDs (52% of patients), adalimumab (18% of patients), and tofacitinib (10% of patients).

7.2.5. Chart-Based VTE Characteristics

Patient charts indicated a history of VTE among 44 of the 155 patients (28%). An LDVT was the most common prior VTE (27 patients) followed by a prior PE (19 patients). (Note that patients can experience more than one type of prior VTE.)

Among patient charts, there were 117 patients with confirmed VTE. The types of confirmed VTE were nearly evenly split between LDVT (N=75) and PE (N=67). The total number of confirmed VTEs (n=147) exceeds the number of patients with a confirmed VTE (n=117) because 30 patients had 2 confirmed VTEs captured in the abstracted medical charts. When patients had more than 2 VTEs confirmed, the most frequent combination was PE and LDVT.

[h] Claims-based evidence of smoking based on ICD-10-CM diagnosis codes, CPT codes, and Healthcare Common Procedure Coding System (HCPCS) codes. Please see **Error! Reference source not found.** Appendix C. Claims Codes for Study for codes.

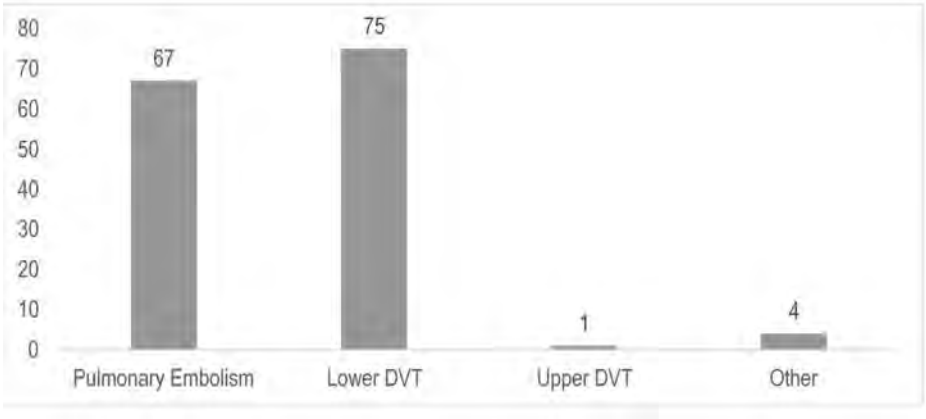

Figure 4. VTE by Type from ORD Charts

The diagnosis of VTE was most commonly made in an ER setting followed by treatment in an inpatient setting. Venous duplex ultrasound was the most common diagnostic imaging used to confirm VTE followed by angiogram. Lung ventilation-perfusion scan and all forms of MRI were used in less than 10 patients.

Abstracted medical chart information for a total of 38 presumptive cases (25%) did not confirm VTE. The most common reasons that claims-based VTE was not confirmed included:

- Patient's symptoms were consistent with VTE, but final disposition included alternative diagnosis (rule-out VTE);
- Patient history of VTE considered when making treatment decisions for alternative diagnosis (history of VTE);
- Patient's abstracted medical chart data did not include evidence of imaging or imaging results (lack of imaging);
- Patient's abstracted medical chart data included ineligible imaging for the type of VTE (inappropriate imaging);
- Patient's abstracted medical chart data indicates the patient was diagnosed with an alternative, but related, condition such as an arterial thrombosis or fat embolus (miscoded VTE).

Clinical review was required for 27 of the 155 patients with a presumptive VTE (17% of the 155 patients). Just under half (48%, or 13 out of the 27) of the charts reviewed were categorized as VTE confirmed.

7.2.6. Algorithm Performance

In the ORD sample (original study+Revision 1A population), the PPV for the primary VTE algorithm was 75.5% (95% CI: 68.7-82.3). The PPV was 76.3% and 75.2% in the original study and Revision 1A sample alone, respectively.

Table 6. Performance of the Primary Algorithm for Chart-Sourced Patients from ORD

Algorithm and Study Sample		Total	Chart positive	Chart negative
Presumptive Primary Algorithm VTE (original study population)	n	38	29	9
	%	100.00	**76.32**	23.68
Presumptive Primary Algorithm VTE (Revision 1A population)	n	117	88	29
	%	100.00	**75.21**	24.79
Presumptive Primary Algorithm VTE (original study+Revision 1A population)	n	155	117	38
	%	100.00	**75.48**	24.52

The original study also evaluated the secondary algorithm. The PPV for the secondary algorithm was 52.6% (40/76; 95% CI 41.4-63.9%). The magnitude of the PPV and its use in determining the performance of an algorithm are dependent on the prevalence of the condition in the selected population so there are no commonly accepted benchmarks for PPV. However, other published studies show that a PPV=75% indicates “adequate” algorithm performance in detecting “true positives.”[19]

7.3. Secondary Objective

7.3.1. Chart-Based BMI and Smoking Status among Non-VTE Patients (Cohort 3)

The original study sample included charts abstracted from 182 patients in Cohort 3. Among those with valid charts (n=164), the mean BMI was 31 (valid N=164) with about one-quarter (26%) having a BMI ≥35. BMI data were missing for 18 patients.

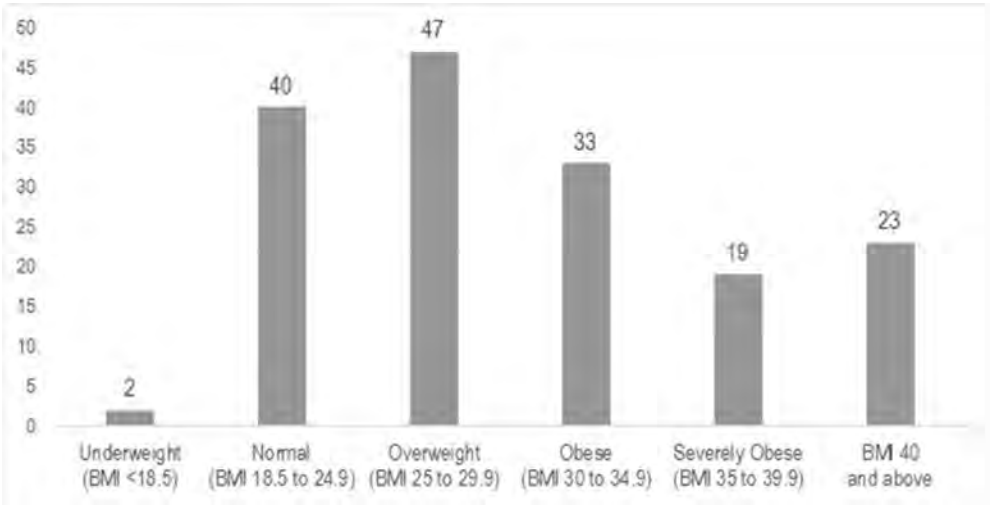

Figure 5. Chart Sourced Number of Non-VTE Patients by BMI Category

Of the 182 non-VTE patients with abstracted chart data from ORD, smoking status was unknown for 37 patients (20%). Among the 145 patients with known smoking status, 30 (21%) were current smokers, with half using cigarettes. An additional 37 patients (26%) were identified as former smokers. The charts indicated that 78 patients (54%) were never smokers.

7.3.2. Chart-Based BMI and Smoking Status among Patients with Presumptive VTE

In the ORD sample (original study+Revision 1A population), patient height, weight and/or BMI was collected from patient charts for nearly all patients. Among the 141 valid charts, the mean BMI was 31 with nearly one-quarter (24%) of patients having a BMI ≥35, similar to non-VTE patients.

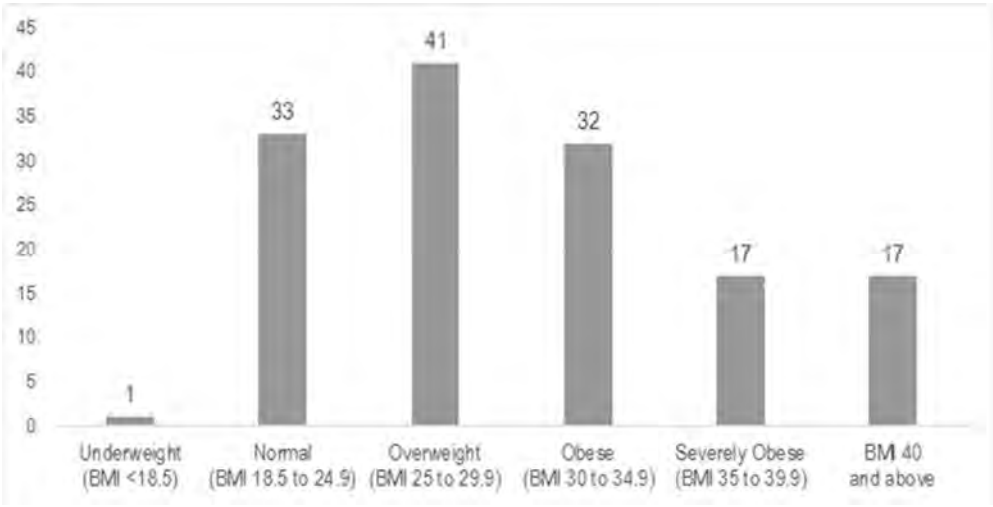

Figure 6. Chart Sourced Number of Patients with presumptive VTE from ORD by BMI Category

Smoking status was unknown for 8 (5%) patients. 23 of 147 patients with known smoking status (16%) were current smokers. Cigarettes were the most commonly used tobacco product (87% of current smokers). An additional 59 patients (40%) were identified as former smokers. The charts indicated that 65 patients (44%) never smoked. Compared to non-VTE patients, the percentages of current/former smokers were higher (56% of VTE patients versus 46% of non-VTE patients) and the percent of never smokers was lower among non-VTE patients (54% of non-VTE patients versus 44% of VTE patients).

7.4. Results from Exploratory Approach: Market Clarity

Revision 2B was an effort to evaluate the primary VTE algorithm using a non-conventional data source. This secondary data source, Market Clarity, includes provider notes from a variety of providers rather than medical charts.

7.4.1. Claims-Based Patient and Clinical Characteristics

Sixty four patients identified from the Market Clarity database had unstructured notes available for abstraction. The majority of patients were female (75%). The mean age was younger than the ORD population (60 years [SD=13] vs. 66 years [SD=11]). 31% of the patients identified from the Market Clarity database had Medicare insurance coverage, and 19% were covered by a Medicaid plan. Nearly half of the patients (44%) resided in the Midwest United States. Follow-up time available to observe the primary algorithm VTE ranged from 131 days to 1,612 days after index date, with a mean of 1,134 days (SD=466 days).

The mean Charlson comorbidity score among the 64 Market Clarity patients was 1.9, with the majority of patients (78%) having a score between 1-2. The mean comorbidity score was lower for Market Clarity patients compared to ORD patients (mean 2.5), likely reflecting the lower mean age for this population. Common comorbid conditions included: hypertension (50%); nutritional, endocrine, and metabolic disorders (48%); spondylosis and other back problems

(45%); disorders of lipid metabolism (44%); and diseases of the heart (44%). The most common bDMARDs on or after index date (variable follow-up time period) were etanercept (28%), adalimumab (27%), and infliximab (22%); 50% of this population had ≥1 claim for MTX therapy during the CAW. In this population 8 patients (13%) had claims-based evidence of smoking.

7.4.2. Claims-Based VTE Characteristics

The time to presumptive VTE ranged from 8 to 1,584 days with a mean of 546 days (SD 455). Among the 64 patients identified, the mean number of primary algorithm VTE criteria met was 1.6 (ranged from 1 to 4).

7.4.3. Provider Note-Based Patient and Clinical Characteristics

Patients from Market Clarity had a mean BMI of 33.4 (valid N=53) with almost half (47%) of patients having a BMI ≥35. BMI was unknown for 11 patients in clinical notes.

Of the 64 patients with abstracted provider notes from Market Clarity, smoking status was unknown for 11 patients (17%). Only 2 patients of 53 patients with known smoking status (4%) were identified as current smokers. 27 patients (51%) were identified as former smokers, and 24 patients (45%) never smoked.

Related comorbid conditions identified in the provider notes include diagnoses of hypertension for 58% of patients, COPD for 14% of patients, atrial fibrillation for 9%, autoimmune diseases for 13%, and cancer for 9%. From the abstracted provider notes data, there was no evidence of VTE-related patient death.

The most common RA-related treatments documented in patient notes included cDMARDs (52% of patients), etanercept (19%), and adalimumab (9%).

7.4.4. Provider Note-Based VTE Characteristics

Eighteen of the 64 patients (28%) had evidence of a prior VTE, of which 10 patients had prior LDVT and 10 had prior PE. (Note that patients can experience more than one type of prior VTE.)

Lower DVT and PE were the most observed types of VTE; 7 patients had 2 confirmed VTEs in their notes. The diagnosis of VTE was most commonly made in an ER setting and treatment was most commonly in an inpatient location or an ER setting.

A total of 28 patients' abstracted notes data (44%) did not confirm VTE. The most common reasons that claims-based VTE was not confirmed were similar to the reasons in the chart-based analysis. Clinical review was required for 14 of the 64 patients with a presumptive VTE (22%), with 6 of the notes reviewed categorized as VTE confirmed.

7.4.5. Algorithm Performance

Of the 64 abstracted notes, a VTE corresponding with the VTE date identified by the presumptive primary VTE claims-based algorithm was confirmed for 36 patients (56.3%; 95% CI 44.1-68.4%).

8 Discussion

Administrative claims data, available for large populations of patients, are an effective tool to evaluate safety and effectiveness of treatment in the real-world. Claims-based algorithms are commonly used to identify the outcome in studies of treatment effect in a healthcare database. Thus, validity and relevance of the selected algorithms to a target study are critical to increase the validity and reliability of the target study.

Although there is not a recommended range for what would be considered an adequate PPV in RWE algorithms,[19] the FDA has recommended a threshold of 70% or greater as indicating an acceptable algorithm performance.[20] In this study, 75.5% of VTEs identified from a claims-based algorithm were confirmed with abstracted medical chart data using rigorous clinical criteria, highlighting the accuracy of the primary VTE algorithm in its ability to correctly identify VTE in RA patients. It is not unexpected that the PPV of the less stringent secondary algorithm was lower at 52.6%. The superior performance of the primary algorithm is likely attributable to the inclusion of a higher number of diagnostic and other criteria in its definition.[21] In addition to the 8 qualifying criteria shared with the primary VTE algorithm, the secondary VTE algorithm included 12 unique qualifying criteria. These criteria are distinct from those qualified for the primary VTE algorithm by relaxing anticoagulant requirement or allowing OP diagnosis for PE.

There is no definitive recommendation for an appropriate sample size for outcome validation studies. Given that PPV is a primary measure of accuracy in this study, precision of PPV could be considered reflecting adequacy of sample size. The precision of PPV observed in this study was 6.8%, estimated from the width of 95% confidence intervals. This post hoc estimation shows that the sample size of the outcome validation study was sufficient to generate a PPV with an adequate precision.

The PPV estimates in our study fall within a range of what has been reported in previous chart validation studies of claims-based algorithms for VTE. In Fang et al.'s[15] study of adult patients with VTE diagnoses between 2004-2010 from the Cardiovascular Research Network Venous Thromboembolism, the overall PPV of any VTE code, based on ICD-9-CM coding, was 51.9%, but varied widely by clinical setting and VTE type. Primary discharge diagnosis codes obtained from a hospital/ED encounter had high positive predictive values (78.9%) compared to codes in secondary positions (44.4%) and OP codes (30.9%). Fang et al.'s study further demonstrated the importance of the diagnosis setting, the position of codes used in inpatient settings, and evidence of anticoagulation to the PPV of the case definition. These factors formed the basis of the primary and secondary algorithms based on ICD-10-CM coding in our study.

Recently, a population-based study of patients with RA from the Swedish National Patient Register (2009-2018) reported a higher PPV of 87% for incident VTE using their main algorithm, based on ICD-10 coding. It is difficult to pinpoint a reason for difference in the PPVs. However, there are differences in the Swedish and U.S. healthcare systems that may contribute to differences in PPV. Perhaps there is better consistency among physicians for the codes that are used in Sweden, making it easier for an algorithm to be refined and accounting for the higher PPV. It is also notable that the U.S healthcare systems use ICD-10-CM codes, which are more granular than ICD-10 codes used in Sweden, although the impact on the observed PPVs is unknown. Lastly, PPV is impacted by prevalence of the VTE in the study population, with improved performance at higher prevalence. However, both studies were based on patients with RA, who were at an increased risk of VTE compared to the general population. Although the average age of the study population was older in the Swedish Study than our study (mean age

at VTE was 71 years versus 66 years)[22], it is unlikely that differences in age and other risk factors between the study populations account for the observed difference in PPVs

Validation of claims-based outcome definitions involves verification of the outcome in a gold standard (e.g., medical records), and typically requires a time and labor-intensive process of procurement of medical charts, manual data extraction and adjudication. While conducting a traditional outcome validation study based on medical charts, this study also experimented with a novel alternative to this process using Optum's Market Clarity database that contains EHR data with provider notes where available. Because the validation exercises were conducted on samples drawn from two different claims systems (ORD vs. multi-payer Market Clarity), it has provided an interesting case for comparison of validation methods, based on either abstracted charts and abstracted physician notes.

It is informative that the same algorithm validated using charts produced a higher PPV compared to the PPV calculated using clinical notes, even though the PPV from notes were still considered to indicate "moderate" algorithm performance[20]. There could be several reasons for the lower PPV for the algorithm validated with the abstracted clinical notes:

- The EHR data come from an "open" data source that captures patient encounters from the providers/provider networks that submit their electronic medical records to this data source. Specific providers were not identified for procurement and notes abstraction, as with the traditional ORD-chart review approach. Patients included in 2B analyses may have VTE diagnoses documented in other clinical systems that are not part of Optum's Market Clarity database or provider's records that were not captured in the current notes.

- The algorithm validation using the abstracted clinical notes relied on the abstracted free text notes submitted as part of the electronic medical records. It is possible that the notes did not provide sufficient information to validate VTE.

- The patients from the Market Clarity data were younger on average and could have lower prevalence of VTE. In general, as prevalence decreases, the PPV will also decrease.

This finding suggests that abstracted charts may still be the "gold standard" for algorithm validation in retrospective research since they contain the most comprehensive information about a condition of interest. While not an objective of this particular study, this result also provides additional insight into future utility of abstracted physician notes. First, abstracted physician notes could be considered an alternative for claims-based algorithm validation when charts are not available. Second, abstracted physician notes may be useful for creating a claims-based algorithm (and subsequent algorithm validation) for conditions without specific diagnosis codes because natural language processing can be leveraged to identify free-text references to diagnoses.

Applicability of this outcome validation study to the target B023 study (I4V-MC-B023: "Comparative Assessment of VTE and Other Risks among Patients with Rheumatoid Arthritis treated with Baricitinib versus Tumor Necrosis Factor Inhibitors: A Multi-database Observational Cohort Study") can be evaluated in consideration of their similarities in the data sources, time frame, and prevalence and definition of the outcome under validation. Using administrative database of insured patients in the US, this outcome validation study identified patients treated for RA using the same conceptual and operational definitions of VTE in the target study.

Moreover, the administrative claims data source used in the validation study is reflective of other US administrative data sources in terms of health care delivery and coding practice. Thus, the PPV of the VTE algorithm in this study is expected to be applicable to the target B023 study.

9 Limitations

While claims data are valuable for the efficient and effective examination of health care outcomes, such as VTE, they are collected for the purpose of payment and not research. In general, the presence of a claim for a filled prescription does not indicate that the medication was consumed or that it was taken as prescribed, although this limitation is less of a concern for patients with RA in this study. Also, presence of a diagnosis code on a medical claim may not indicate positive presence of disease, as the diagnosis code may be incorrectly coded or included as rule-out criteria rather than actual disease. Procurement of medical charts or provider notes for patients meeting the VTE algorithms can address these limitations. The study design further mitigates the limitations of claims data presented by potentially missing claims by requiring patients to have CE around the index date.

For the data used in Revision 2B, it is important to consider that EHR data in the Market Clarity database also has limitations for purposes of research. First, like most other EHR databases, Optum's EHR data represents "data of opportunity" and does not necessarily reflect all treatment an RA/VTE patient is receiving. Unlike a closed system data source such as enrollment controlled administrative claims, an open EHR database will only include information provided by contributing providers. Second, not all EHR platforms capture data uniformly (by variable, variable type or allowed values). Most research databases that utilize EHR data from multiple platforms have taken steps to normalize incoming data streams; however, some differences may persist.

This study used abstracted medical chart and clinical notes data to confirm clinical finding of a VTE identified from administrative claims data. Case confirmation criteria required the chart to indicate a diagnosis of VTE and corresponding imaging confirmation. These rigorous case confirmation criteria may have omitted some true VTEs, which were diagnosed using alternative or less rigorous approaches.

Additionally, when inappropriate imaging was undertaken by the clinical provider to diagnose VTE, it is unclear if this represented a lack of diagnostic resources available to the clinician or a lack of awareness of best practice standards. Had these patients received appropriate diagnostic imaging, the final case finding results of the claims-based algorithm may have been improved.

Some of the charts selected for abstraction lacked critical evidence necessary to meet the case confirmation criteria established for the study. Among these patients, procurement of an alternative chart with additional clinical insight might have resulted in confirmation. Direct consultation with the provider might have also resulted in confirmation but could not be implemented for this study without patient consent.

10 Conclusions

Overall, this chart validation study reports an adequate PPV for the VTE algorithm based on ICD-10-CM diagnosis codes using data from a US population of insured adults diagnosed with and treated for RA. Our findings demonstrate reliability of the selected VTE algorithm in the

target study I4V-MC-B023 and will be generalizable to other comparative observational studies of similar target population and data source.

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Appendix A. Operational Definitions

Table 7. Summary of Operational Definitions

Variable	Original Definition (Version 1)	Revision 1A Definition	Revision 2B Definition
Index Date	The date of the first observed RA therapy of interest during the sample identification period (01July2016 – 30October2019).	The date of the first observed RA therapy of interest during the sample identification period *(01May2016 – 30November2020).*	The date of the first observed RA therapy of interest during the sample identification period *(01May2016 – 31August2020).*
RA Identification Period	The 180-day period extending backward in time from (and including) the Index Date through 30 days after the Index Date. This time period represents the window during which a claim with a diagnosis of RA was observed as part of the inclusion criteria.	The 180-day period extending backward in time from (and including) the Index Date through 30 days after the Index Date. This time period represents the window during which a claim with a diagnosis of RA was observed as part of the inclusion criteria.	The 180-day period extending backward in time from (and including) the Index Date through 30 days after the Index Date. This time period represents the window during which a claim with a diagnosis of RA was observed as part of the inclusion criteria.
Covariate Assessment Window (CAW)	The 180-day period extending backward in time from (and including) the Index Date. All patients were required to have health insurance coverage for the entire CAW.	The 180-day period extending backward in time from (and including) the Index Date. All patients were required to have health insurance coverage for the entire CAW.	The 180-day period extending backward in time from (and including) the Index Date. All patients were required to have health insurance coverage for the entire CAW.
Study Cohort	Describes patients with and without a claims-observed VTE.	Describes patients with ~~*and without*~~ a claims-observed VTE *consistent with the primary algorithm.*	Describes patients with ~~*and without*~~ a claims-observed VTE *consistent with the primary algorithm.*
Presumptive Qualifying Event Date	The date of service on a claim (or combination of claims) that met the study criteria/algorithm for a VTE of interest.	The date of service on a claim (or combination of claims) that met the *primary* study criteria/algorithm for a VTE of interest.	The date of service on a claim (or combination of claims) that met the *primary* study criteria/algorithm for a VTE of interest.
Follow-up Continuous Enrollment Period	The 31 days after the Index Date. Continuous health insurance coverage was required of all patients for at least 31 days after the Index Date.	The 31 days after the Index Date. Continuous health insurance coverage was required of all patients for at least 31 days after the Index Date.	The 31 days after the Index Date. Continuous health insurance coverage was required of all patients for at least 31 days after the Index Date.

Variable	Original Definition (Version 1)	Revision 1A Definition	Revision 2B Definition
Observation Period (claims)	Represents the amount of time when a patient is continuously enrolled in health insurance coverage and claims can be observed. Each patient was observed for a minimum of 7 months (6-mo CAW and 1-mo follow-up). If additional follow-up time was available, it was included.	Represents the amount of time when a patient is continuously enrolled in health insurance coverage and claims can be observed. Each patient was observed for a minimum of 7 months (6-mo CAW and 1-mo follow-up). If additional follow-up time was available, it was included.	Represents the amount of time when a patient is continuously enrolled in health insurance coverage and claims can be observed. Each patient was observed for a minimum of 7 months (6-mo CAW and 1-mo follow-up). If additional follow-up time was available, it was included.
Observation Period (chart *or EHR notes*)	The date range requested from the provider for review of all services rendered. Providers were asked to supply all encounters/services over a 3-month period.[i]	The date range requested from the provider for review of all services rendered *for patients meeting the criteria for VTE based on the primary algorithm.* Providers identified from claims data *(one or two providers for each patient)* were asked to supply all encounters/services over a 3-month period.[i]	*The date range during which unstructured provider notes with VTE or RA-related terms were identified and extracted from the electronic health record (EHR) database. EHR notes observation period consists of the 3-month period.*[i]
VTE Risk Period	The period from index date through the earlier of death, health plan disenrollment, presumptive VTE, or end of the study period (30November2019).	The period from index date through ~~*the earlier of death, health plan disenrollment,*~~ presumptive VTE, ~~*or end of the study period (31December2020).*~~[j]	The period from index date through ~~*the earlier of death, health plan disenrollment,*~~ presumptive VTE, ~~*or end of the study period (30September2020).*~~

Note: Modified variables are italicized.

Appendix B. Descriptive Result Tables

Tables are available upon request.

Appendix C. Claims Codes for Study

Tables of claims codes are available upon request.

[i] Among non-VTE patients, the 3-month chart observation period includes 1 month pre-index to 2 months post-index. Among presumptive VTE patients, the 3-month chart or notes observation period includes 1 month pre-VTE date to 2 months post-VTE date.

[j] The purpose of this table is to serve as a quick reference. Additional detail describing the modification to the VTE risk period for Revisions 1A and 2B can be found in Section 5.1.

Annex 18. VTE Case Definition: Validation in French Patients with RA and Prevalence of Smoking and Obesity

This annex includes information about results for the following:

I. **Validation of VTE case definition in French patients with RA**

Safety Outcomes in Patients Treated for RA

Comparative Assessment of VTE Risk among Patients with Rheumatoid Arthritis treated with Baricitinib versus Tumor Necrosis Factor Inhibitors

French part of the study program

Minutes of the Adjudication Committee

Version 1.0, May 17th, 2021

Bordeaux PharmacoEpi
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DATES & PLACE

March 17, 2021 14h00-17h00, on BPE site (Bordeaux)

March 26, 2021 14h00-17h00, on BPE site (Bordeaux)

April 7, 2021 14h00-17h00, on BPE site (Bordeaux)

April 9, 2021 14h00-17h00, on BPE site (Bordeaux)

April 28, 2021 15h30-16h30, held by videoconference (zoom)

PARTICIPANTS

Adjudication Committee

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- Dr. Eléonore Brunetti-Cassasus, Vascular physician, Bordeaux
- Pr. Joël Constans, Vascular physician, CHU de Bordeaux, Bordeaux
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- Régis LASSALLE, Chief of biostatistics & data-management
- Nicolas THURIN, Scientific officer

CONDUCT OF THE STUDY

1. Context

The study "Safety Outcomes in Patients Treated for RA" aims to evaluate the safety of patients with rheumatoid arthritis (RA) treated with baricitinib or Tumor Necrosis Factor Inhibitors (TNFi) in France, using postmarketing data from the French national healthcare database (SNDS). The study objectives are to compare among RA patients treated with baricitinib *vs*. TNFi the risk of:

- Venous thromboembolism (VTE)
- Major Adverse Cardiovascular Events
- Incident serious infections
- Tuberculosis requiring hospitalization

To address study objectives, an algorithm was design to identify VTEs from inpatient and outpatient settings in the SNDS. This algorithm relied on hospital discharge ICD-10 codes, drug dispensing and imaging procedures. To ensure results robustness a validation study was set-up to check for the positive predictive value (PPV) of the algorithm main definition, and if necessary, to review and adjust its parameters.

2. General Method

Among patients to whom baricitinib or TNFi were dispensed between September 1st 2017 and December 31st 2018, patients with VTE over the same period were identified by the algorithm according to the two following definitions:

- VTE primary definition:
    - Hospitalization with VTE primary or linked discharge diagnosis, **or**
    - Hospitalization with VTE associated diagnosis and a dispensing of anticoagulant[1] dispensing with curative dosage within 31 days from the date of discharge, **or**
    - Imaging procedure[2] and a dispensing of anticoagulant with curative dosage within 2 days before or after the date of imaging procedure.
- VTE secondary definition without anticoagulant dispensing requirement:
    - Hospitalization with VTE primary, linked or associated diagnosis, **or**
    - Imaging procedure[2]

[1] See Appendix 5 of the statistical analysis plan 'List of codes of anti-coagulant used in the VTE definition (curative dosage)': *apixaban (B01AF02), dalteparin (B01AB04), enoxaparin (B01AB05), parnaparin (B01AB06), tinzaparin (B01AB10), dabigatran (B01AE07), rivaroxaban (B01AF01), warfarin (B01AA03), acenocoumarol (B01AA07), heparin (B01AB01), fondaparinux (B01AX05).*

[2] See Appendix 6 of the statistical analysis plan 'List of codes used for the identification of medical imaging for deep vein thrombosis or pulmonary embolism': *Lung scintigraphy: GFQL002, GFQL005, GFQL006, GFQL007, DFQL001; Lower limb compression ultrasound (=compression ultra-sonography): EJQM001, EJQM003, EJQM004; Phlebography (=venography): DHQH001, DHQH002, DHQH003, DHQH004, DHQH005, DHQH006, DHQH007, EJQH002, EJQH003, EJQH004, EJQH005, EJQH006; Thorax scanner (=thoracic CT angiogram): ECQH010.*

Among the 1 103 patients identified according to the VTE primary definition and the 8 749 identified according to the VTE secondary definition a total of 200 cases were selected in order to have:

- 150 patients meeting the VTE primary definition, including the 26 cases of the main comparison cohorts of the study completed by a random selection of others VTE cases identified in the dataset,
- 50 patients meeting the VTE secondary definition.

The overall validation process followed the methodology introduced by Thurin, N.H., Bosco-Levy, P., Blin, P. et al. *Intra-database validation of case-identifying algorithms using reconstituted electronic health records from healthcare claims data* published in BMC Medical Research Methodology in 2021 (https://doi.org/10.1186/s12874-021-01285-y).

Medical history available in the SNDS (e.g. drug dispensing, procedure codes including surgery and imaging, hospital discharge diagnoses, laboratory tests) were used to generate rEHRs (Figure 1) with a 6-month look back period prior to the supposed VTE onset and a 12-month follow-up period after. To ensure that individual data contained in these rEHRs did not lead to patient re-identification, new patient identifiers were assigned, calendar dates were replaced by the delay elapsed since the outcome outset, location details were deleted and only age classes were displayed.

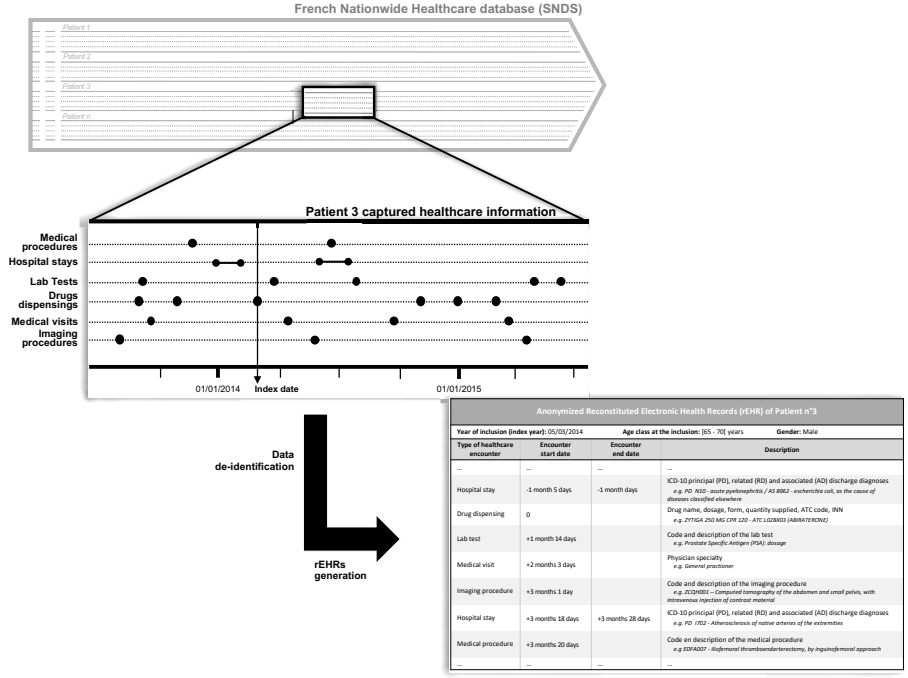

Figure 1: Generation of an anonymized reconstituted Electronic Health Record (rEHR) from data of the French Nationwide Healthcare database (SNDS)

The adjudication committee was constituted by 4 medical experts divided into two pairs. Each pair of experts blindly adjudicated the status of 100 patients (75 defined with VTE primary definition; 25 with the VTE secondary definition). In case of disagreement within a pair, the cases were assessed by all four experts to reach consensus. Experts adjudicated patients according to their own medical knowledge and the rEHR content. In addition to confirm or not the event, experts had to categorize patients according to 4 different clinical definitions: pulmonary embolism, lower extremity deep vein thrombosis, upper extremity deep venous thrombosis, deep venous thrombosis with unspecified localization, or unspecified thromboembolic event.

Experts' conclusions and algorithm results were compared. The PPV was calculated as the number of experts-confirmed VTE events divided by the number of cases identified by the algorithm as meeting the VTE main definition. The corresponding 95% confidence interval [95%CI] was calculated as follow:

$$\hat{A}\,\mathrm{BDE}\;\tilde{A}_{\mathrm{MMN}}\mathrm{Y}\;\;\mathrm{FFG}\;\;\mathrm{X}\;\bar{A}_{\mathrm{JL}}\;\frac{\mathrm{V}}{\mathrm{K}}\;\mathrm{C}\,\mathrm{Z}\,\overline{\frac{\mathrm{FFG}\,\grave{\mathrm{A}}\;\;\mathrm{WFFG}\,\acute{\mathrm{A}}}{\mathrm{H}_{\mathrm{RQSPTPUO}}}}$$

where $n_{positive}$ is the number of algorithm-based positive assessed cases, and $z_{(1-\alpha/2)}$ the z-value for standard normal distribution with left-tail probability (1-α/2). Here $z_{(1-\alpha/2)} = 1.96$ for a type-1 error $\alpha = 0.05$.

The review of the 50 cases meeting the VTE secondary definition aimed to provide potential clue for VTE sensitivity improvement and was not use to generate PPV.

3. Results

Case review took place between March 17th, and April 9th, 2021.
On the 150 patients meeting the VTE primary definition, the adjudication committee confirmed 92 cases, resulting in a PPV of 61% (95%CI = [54-69]) (Table 1).

Table 1: Contingency table for the primary original definition of VTE

		Experts		
		VTE +	**VTE -**	**Total**
Algorithm	**VTE +**	92	58	150
	VTE -	0	0	0
	Total	92	58	150

Out of the 92 cases confirmed, experts are able to identify:

- 38 pulmonary embolisms
- 65 lower extremity deep vein thrombosis
- 6 upper extremity deep venous thrombosis
- 4 deep venous thrombosis (unspecified localization)
- 1 unspecified thromboembolic event

Among these cases, experts identified 22 cases with both pulmonary embolism and lower extremity deep vein thrombosis at the same time.

On April 30th, results of the algorithm validation were presented to the expert committee. Adjustments were proposed to improve algorithm performance. The following updated definitions were approved:

- Updated definition v1:
  - Hospitalization with VTE primary or linked discharge diagnosis, **or**
  - Imaging procedure[3]
    - **And** an anticoagulant[4] dispensing with curative dosage within 3 days before or after the date of imaging procedure and no more than one dispensing of the same drug in the previous 6 months,
    - **And** an anticoagulant coverage period of at least 56 days in the following 120 days (at least of 70% of coverage in case of death), or a hospitalization with VTE primary/linked/associated discharge diagnosis in the following 120 days.

- Updated definition v2:
  - Hospitalization with VTE primary or linked discharge diagnosis, **or**
  - Imaging procedure[3] or hospitalization with VTE associated discharge diagnosis
    - **And** an anticoagulant[4] dispensing with curative dosage within 3 days before or after the date of imaging procedure, and no more than one dispensing of the same drug in the previous 6 months.
    - **And** an anticoagulant coverage period of at least 30 days in the following 120 days (at least of 50% of coverage in case of death); or a hospitalization with VTE primary/linked/associated diagnosis in the following 120 days,

The updated definition v1 showed a PPV of 91% (95%CI = [83-98]) with 58 cases confirmed by experts out of 64 identified by the algorithm. However, this definition only allowed to identify 58 VTE cases from the 92 confirmed by experts (Table 2).

[3] Two codes were added to the Appendix 6 of the statistical analysis plan upon the recommendation of the experts: 'EFQM001' and 'ECQH011'.

[4] One anticoagulant drug available in France was added to the Appendix 5 of the statistical analysis plan upon the recommendation of the experts: Previscan® (fluindione, B01AA12).

Table 2: Contingency table for the updated definition v1 of VTE

		Experts		
		VTE +	**VTE -**	**Total**
Algorithm	**VTE +**	58	6	64
	VTE -	34	52	86
	Total	92	58	150

The updated definition v2 showed a PPV of 92% (95%CI = [86-98]) with 80 cases confirmed by experts out of 87 identified by the algorithm. This definition also allowed to retrieve 80 VTE cases from the 92 confirmed by experts (Table 3), suggesting a better sensitivity in the top of the slightly improved PPV.

Table 3: Contingency table for the updated definition v2 of VTE

		Experts		
		VTE +	**VTE -**	**Total**
Algorithm	**VTE +**	80	7	87
	VTE -	12	51	63
	Total	92	58	150

Performances of algorithm according to VTE definition are summarized in Table 4.

Table 4: Algorithm performances before and after adjustment, according to VTE definitions

		After adjustment	
	Primary definition	Updated definition v1	Updated definition v2
PPV	0.61	0.91	0.92

4. Conclusion

Initial VTE-identifying algorithms had a low VPP (61%). The adjustment of the algorithm based on expert feedbacks (updated definition v2) led to a PPV of 92% for VTE identification in the SNDS, with a restricted number of false positives (12/80) and false negatives (7/58). Experts highlighted the good performances of this new algorithm in view of the complexity of the outcome to be identified. Thus, the updated definition v2 appears as a valuable alternative to the initial primary definition for the identification of VTE in the SNDS, in the frame of the 'Safety Outcomes in Patients Treated for RA' study.

II. Prevalence of Smoking and Obesity in French Patients with RA

ESPOIR

Etude et Suivi des Polyarthrites Indifférenciées Récentes

Statistical Analysis Report

Version 1.0 – 04 June 2021

Sponsor: Aetion, Inc

Bordeaux PharmacoEpi
Plateforme de recherche en Pharmaco-épidémiologie
CIC Bordeaux CIC1401
INSERM – Université de BORDEAUX – CHU de Bordeaux – Adera
Bâtiment Le Tondu case 41 – 146 rue Léo Saignat – 33076 Bordeaux cedex

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1 The espoir study

ESPOIR (Etude et Suivi Des POlyarthrites Indifférenciées Récentes) is a national multicenter, longitudinal cohort that was initiated by the French Society of Rheumatology in order to allow various investigations on diagnosis, prognostic markers, epidemiology, pathogenesis and medico-economic factors in the field of early arthritis and rheumatoid arthritis. Patients were recruited if they had undifferentiated arthritis or rheumatoid arthritis, of less than 6 months disease duration and if they were disease modifying anti-rheumatic drugs and steroids naïve. Patients have then to be followed every 6 months during the first 2 years then every year during at least 10 years. A total of 813 patients were included between November 2002 and April 2005, and the follow-up is still active. Note that one paper has been published on the association of tobacco exposure and RA.

2 Flowchart

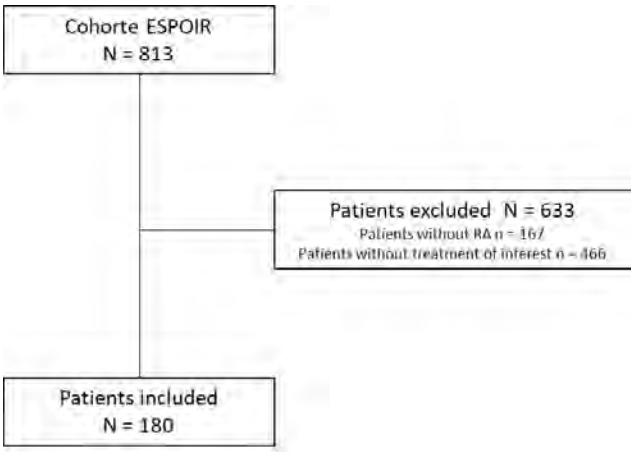

Figure 1. Analysis flow chart

3 Descriptive tables

3.1 BY 1ST LINE OF TREATMENT

The considered unit is the patient but only the first prescription in the considered treatment group (column of the following tables) is taken into account. It should be noted that a patient recorded in the column " TNFi " is also in the column “All drugs of interest".

Age is calculated on the date of the first prescription. Weight, height and smoking status were collected from the CRF closest to that date. The same strategy was carried out for the HAQ self-questionnaire completed by the patient.

3.1.1 BMI

Table 1. Description of Body Mass Index (BMI) among patients with Rheumatoid Arthritis aged ≥18 years for overall population and by group of patients treated by therapeutic class (TNFi and JAK inhibitors)[1] according to age at the date of initiation of the first treatment line

	All drugs of interest[1]			TNFi[2]		
	ALL n = 180	**Women n = 134**	**Men n = 46**	**ALL n = 172**	**Women n = 127**	**Men n = 45**
Total						
BMI (kg/m2)						
Size (missing)	180 (0)	134 (0)	46 (0)	172 (0)	127 (0)	45 (0)
Mean (± SD)	25.3 (4.8)	25.0 (4.9)	26.1 (4.6)	25.2 (4.9)	24.9 (5.0)	26.1 (4.6)
Median	24.4	24.0	25.9	24.3	23.9	25.9
[p25% - p75%]	[21.7;27.8]	[21.6;27.7]	[22.2;28.0]	[21.6;27.8]	[21.3;27.7]	[22.2;28.0]
[Min - Max]	[16.4;43.5]	[16.4;43.5]	[19.0;38.2]	[16.4;43.5]	[16.4;43.5]	[19.0;38.2]
[18-30[	**14 (7.8)**	**10 (7.5)**	**4 (8.7)**	**14 (8.1)**	**10 (7.9)**	**4 (8.9)**
BMI (kg/m2)						
Size (missing)	14 (0)	10 (0)	4 (0)	14 (0)	10 (0)	4 (0)
Mean (± SD)	21.8 (2.8)	21.0 (2.6)	23.8 (2.3)	21.8 (2.8)	21.0 (2.6)	23.8 (2.3)
Median	21.9	20.8	23.9	21.9	20.8	23.9
[p25% - p75%]	[19.8;24.0]	[19.1;22.8]	[21.8;25.8]	[19.8;24.0]	[19.1;22.8]	[21.8;25.8]
[Min - Max]	[16.4;25.8]	[16.4;24.8]	[21.5;25.8]	[16.4;25.8]	[16.4;24.8]	[21.5;25.8]
[30-40[	**22 (12.2)**	**18 (13.4)**	**4 (8.7)**	**22 (12.8)**	**18 (14.2)**	**4 (8.9)**
BMI (kg/m2)						
Size (missing)	22 (0)	18 (0)	4 (0)	22 (0)	18 (0)	4 (0)
Mean (± SD)	23.3 (3.2)	23.3 (3.1)	23.6 (3.9)	23.3 (3.2)	23.3 (3.1)	23.6 (3.9)
Median	22.6	22.6	22.6	22.6	22.6	22.6
[p25% - p75%]	[20.8;25.7]	[20.8;25.7]	[20.9;26.3]	[20.8;25.7]	[20.8;25.7]	[20.9;26.3]
[Min - Max]	[19.6;29.6]	[19.6;29.6]	[20.2;29.0]	[19.6;29.6]	[19.6;29.6]	[20.2;29.0]
[40-50[	**45 (25.0)**	**36 (26.9)**	**9 (19.6)**	**44 (25.6)**	**35 (27.6)**	**9 (20.0)**
BMI (kg/m2)						
Size (missing)	45 (0)	36 (0)	9 (0)	44 (0)	35 (0)	9 (0)
Mean (± SD)	24.8 (4.9)	24.2 (4.4)	27.2 (6.3)	24.8 (5.0)	24.1 (4.5)	27.2 (6.3)
Median	23.8	23.8	26.8	23.8	23.7	26.8
[p25% - p75%]	[21.5;26.3]	[21.3;25.4]	[21.5;31.4]	[21.3;26.4]	[21.0;25.2]	[21.5;31.4]
[Min - Max]	[18.6;39.8]	[18.6;39.8]	[19.1;38.2]	[18.6;39.8]	[18.6;39.8]	[19.1;38.2]

	All drugs of interest[1]			TNFi[2]		
	ALL n = 180	**Women n = 134**	**Men n = 46**	**ALL n = 172**	**Women n = 127**	**Men n = 45**
[50-60[	**56 (31.1)**	**38 (28.4)**	**18 (39.1)**	**55 (32.0)**	**37 (29.1)**	**18 (40.0)**
BMI (kg/m2)						
Size (missing)	56 (0)	38 (0)	18 (0)	55 (0)	37 (0)	18 (0)
Mean (± SD)	26.4 (5.2)	26.4 (5.9)	26.4 (3.7)	26.4 (5.3)	26.5 (5.9)	26.4 (3.7)
Median	25.3	25.1	26.3	25.5	25.2	26.3
[p25% - p75%]	[22.8;29.0]	[22.7;29.7]	[22.9;28.0]	[22.7;29.1]	[22.7;29.7]	[22.9;28.0]
[Min - Max]	[17.2;43.5]	[17.2;43.5]	[21.3;34.2]	[17.2;43.5]	[17.2;43.5]	[21.3;34.2]
[60-65[	**22 (12.2)**	**16 (11.9)**	**6 (13.0)**	**19 (11.0)**	**14 (11.0)**	**5 (11.1)**
BMI (kg/m2)						
Size (missing)	22 (0)	16 (0)	6 (0)	19 (0)	14 (0)	5 (0)
Mean (± SD)	26.9 (4.9)	26.9 (4.2)	27.0 (6.8)	27.0 (5.2)	27.0 (4.4)	27.0 (7.6)
Median	27.4	28.2	25.0	27.7	28.2	22.9
[p25% - p75%]	[23.3;30.0]	[24.0;29.7]	[22.9;33.2]	[22.9;30.5]	[24.4;30.0]	[22.9;33.2]
[Min - Max]	[17.9;36.8]	[17.9;34.3]	[19.0;36.8]	[17.9;36.8]	[17.9;34.3]	[19.0;36.8]
≥65	**21 (11.7)**	**16 (11.9)**	**5 (10.9)**	**18 (10.5)**	**13 (10.2)**	**5 (11.1)**
BMI (kg/m2)						
Size (missing)	21 (0)	16 (0)	5 (0)	18 (0)	13 (0)	5 (0)
Mean (± SD)	26.0 (4.4)	26.0 (4.8)	25.9 (3.2)	25.9 (4.3)	25.9 (4.8)	25.9 (3.2)
Median	26.7	25.8	26.8	26.8	26.7	26.8
[p25% - p75%]	[21.9;29.2]	[21.9;29.7]	[25.1;27.8]	[21.9;29.2]	[21.9;29.4]	[25.1;27.8]
[Min - Max]	[19.7;35.8]	[19.7;35.8]	[20.8;29.2]	[19.7;35.8]	[19.7;35.8]	[20.8;29.2]

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB
2. TNFi: ADALIMUMAB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB
   JAK inhibitors: BARICITINIB, TOFACITINIB (not available in the database)

Table 2. Description of Body Mass Index (BMI) in categories among patients with Rheumatoid Arthritis aged ≥18 years for overall population and by group of patients treated by therapeutic class (TNFi and JAK inhibitors) [1] according to age at the date of initiation of the first treatment line

	All drugs of interest[1]						TNFi[2]					
	ALL n = 180		Women n = 134		Men n = 46		ALL n = 172		Women n = 127		Men n = 45	
Total												
BMI (kg/m2) (in categories), n (%)												
<18.5	4	(2.2)	4	(3.0)	0	(0.0)	4	(2.3)	4	(3.1)	0	(0.0)
[18.5-25[	93	(51.7)	74	(55.2)	19	(41.3)	89	(51.7)	70	(55.1)	19	(42.2)
[25-30[	54	(30.0)	35	(26.1)	19	(41.3)	51	(29.7)	33	(26.0)	18	(40.0)
≥30	29	(16.1)	21	(15.7)	8	(17.4)	28	(16.3)	20	(15.7)	8	(17.8)
[18-30[	**14**	**(7.8)**	**10**	**(7.5)**	**4**	**(8.7)**	**14**	**(8.1)**	**10**	**(7.9)**	**4**	**(8.9)**
BMI (kg/m2) (in categories), n (%)												
<18.5	1	(7.1)	1	(10.0)	0	(0.0)	1	(7.1)	1	(10.0)	0	(0.0)
[18.5-25[	11	(78.6)	9	(90.0)	2	(50.0)	11	(78.6)	9	(90.0)	2	(50.0)
[25-30[	2	(14.3)	0	(0.0)	2	(50.0)	2	(14.3)	0	(0.0)	2	(50.0)
≥30	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
[30-40[	**22**	**(12.2)**	**18**	**(13.4)**	**4**	**(8.7)**	**22**	**(12.8)**	**18**	**(14.2)**	**4**	**(8.9)**
BMI (kg/m2) (in categories), n (%)												
<18.5	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
[18.5-25[	14	(63.6)	11	(61.1)	3	(75.0)	14	(63.6)	11	(61.1)	3	(75.0)
[25-30[	8	(36.4)	7	(38.9)	1	(25.0)	8	(36.4)	7	(38.9)	1	(25.0)
≥30	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
[40-50[	**45**	**(25.0)**	**36**	**(26.9)**	**9**	**(19.6)**	**44**	**(25.6)**	**35**	**(27.6)**	**9**	**(20.0)**
BMI (kg/m2) (in categories), n (%)												
<18.5	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
[18.5-25[	29	(64.4)	26	(72.2)	3	(33.3)	29	(65.9)	26	(74.3)	3	(33.3)
[25-30[	9	(20.0)	6	(16.7)	3	(33.3)	8	(18.2)	5	(14.3)	3	(33.3)
≥30	7	(15.6)	4	(11.1)	3	(33.3)	7	(15.9)	4	(11.4)	3	(33.3)

	All drugs of interest[1]				TNFi[2]			
	ALL n = 180		Women n = 134		Men n = 46		ALL n = 172		Women n = 127		Men n = 45	
[50-60[	**56**	**(31.1)**	**38**	**(28.4)**	**18**	**(39.1)**	**55**	**(32.0)**	**37**	**(29.1)**	**18**	**(40.0)**
BMI (kg/m2) (in categories), n (%)												
<18.5	2	(3.6)	2	(5.3)	0	(0.0)	2	(3.6)	2	(5.4)	0	(0.0)
[18.5-25[	23	(41.1)	16	(42.1)	7	(38.9)	22	(40.0)	15	(40.5)	7	(38.9)
[25-30[	19	(33.9)	11	(28.9)	8	(44.4)	19	(34.5)	11	(29.7)	8	(44.4)
≥30	12	(21.4)	9	(23.7)	3	(16.7)	12	(21.8)	9	(24.3)	3	(16.7)
[60-65[	**22**	**(12.2)**	**16**	**(11.9)**	**6**	**(13.0)**	**19**	**(11.0)**	**14**	**(11.0)**	**5**	**(11.1)**
BMI (kg/m2) (in categories), n (%)												
<18.5	1	(4.5)	1	(6.3)	0	(0.0)	1	(5.3)	1	(7.1)	0	(0.0)
[18.5-25[	7	(31.8)	4	(25.0)	3	(50.0)	6	(31.6)	3	(21.4)	3	(60.0)
[25-30[	8	(36.4)	7	(43.8)	1	(16.7)	6	(31.6)	6	(42.9)	0	(0.0)
≥30	6	(27.3)	4	(25.0)	2	(33.3)	6	(31.6)	4	(28.6)	2	(40.0)
≥65	**21**	**(11.7)**	**16**	**(11.9)**	**5**	**(10.9)**	**18**	**(10.5)**	**13**	**(10.2)**	**5**	**(11.1)**
BMI (kg/m2) (in categories), n (%)												
<18.5	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
[18.5-25[	9	(42.9)	8	(50.0)	1	(20.0)	7	(38.9)	6	(46.2)	1	(20.0)
[25-30[	8	(38.1)	4	(25.0)	4	(80.0)	8	(44.4)	4	(30.8)	4	(80.0)
≥30	4	(19.0)	4	(25.0)	0	(0.0)	3	(16.7)	3	(23.1)	0	(0.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB
2. TNFi: ADALIMUMAB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB
   JAK inhibitors: BARICITINIB, TOFACITINIB (not available in the database)

3.1.2 SMOKING STATUS

Table 3. Description of smoking status among patients with Rheumatoid Arthritis aged ≥18 years for overall population and by group of patients treated by therapeutic class (TNFi and JAK inhibitors)[1] according to age at the date of initiation of the first treatment line

	All drugs of interest[1]						TNFi[2]					
	ALL n = 180		Women n = 134		Men n = 46		ALL n = 172		Women n = 127		Men n = 45	
Total												
Smoking status, n (%)												
Never smoker	96	(53.3)	77	(57.5)	19	(41.3)	93	(54.1)	74	(58.3)	19	(42.2)
Former smoker	49	(27.2)	32	(23.9)	17	(37.0)	45	(26.2)	29	(22.8)	16	(35.6)
Current smoker	35	(19.4)	25	(18.7)	10	(21.7)	34	(19.8)	24	(18.9)	10	(22.2)
[18-30[	**14**	**(7.8)**	**10**	**(7.5)**	**4**	**(8.7)**	**14**	**(8.1)**	**10**	**(7.9)**	**4**	**(8.9)**
Smoking status, n (%)												
Never smoker	11	(78.6)	7	(70.0)	4	(100.0)	11	(78.6)	7	(70.0)	4	(100.0)
Former smoker	1	(7.1)	1	(10.0)	0	(0.0)	1	(7.1)	1	(10.0)	0	(0.0)
Current smoker	2	(14.3)	2	(20.0)	0	(0.0)	2	(14.3)	2	(20.0)	0	(0.0)
[30-40[	**22**	**(12.2)**	**18**	**(13.4)**	**4**	**(8.7)**	**22**	**(12.8)**	**18**	**(14.2)**	**4**	**(8.9)**
Smoking status, n (%)												
Never smoker	11	(50.0)	10	(55.6)	1	(25.0)	11	(50.0)	10	(55.6)	1	(25.0)
Former smoker	5	(22.7)	5	(27.8)	0	(0.0)	5	(22.7)	5	(27.8)	0	(0.0)
Current smoker	6	(27.3)	3	(16.7)	3	(75.0)	6	(27.3)	3	(16.7)	3	(75.0)
[40-50[	**45**	**(25.0)**	**36**	**(26.9)**	**9**	**(19.6)**	**44**	**(25.6)**	**35**	**(27.6)**	**9**	**(20.0)**
Smoking status, n (%)												
Never smoker	24	(53.3)	21	(58.3)	3	(33.3)	24	(54.5)	21	(60.0)	3	(33.3)
Former smoker	15	(33.3)	10	(27.8)	5	(55.6)	14	(31.8)	9	(25.7)	5	(55.6)
Current smoker	6	(13.3)	5	(13.9)	1	(11.1)	6	(13.6)	5	(14.3)	1	(11.1)
[50-60[	**56**	**(31.1)**	**38**	**(28.4)**	**18**	**(39.1)**	**55**	**(32.0)**	**37**	**(29.1)**	**18**	**(40.0)**
Smoking status, n (%)												

	All drugs of interest[1]			TNFi[2]		
	ALL n = 180	**Women n = 134**	**Men n = 46**	**ALL n = 172**	**Women n = 127**	**Men n = 45**
Never smoker	27 (48.2)	20 (52.6)	7 (38.9)	27 (49.1)	20 (54.1)	7 (38.9)
Former smoker	18 (32.1)	11 (28.9)	7 (38.9)	17 (30.9)	10 (27.0)	7 (38.9)
Current smoker	11 (19.6)	7 (18.4)	4 (22.2)	11 (20.0)	7 (18.9)	4 (22.2)
[60-65[	**22 (12.2)**	**16 (11.9)**	**6 (13.0)**	**19 (11.0)**	**14 (11.0)**	**5 (11.1)**
Smoking status, n (%)						
Never smoker	10 (45.5)	8 (50.0)	2 (33.3)	8 (42.1)	6 (42.9)	2 (40.0)
Former smoker	7 (31.8)	3 (18.8)	4 (66.7)	6 (31.6)	3 (21.4)	3 (60.0)
Current smoker	5 (22.7)	5 (31.3)	0 (0.0)	5 (26.3)	5 (35.7)	0 (0.0)
≥65	**21 (11.7)**	**16 (11.9)**	**5 (10.9)**	**18 (10.5)**	**13 (10.2)**	**5 (11.1)**
Smoking status, n (%)						
Never smoker	13 (61.9)	11 (68.8)	2 (40.0)	12 (66.7)	10 (76.9)	2 (40.0)
Former smoker	3 (14.3)	2 (12.5)	1 (20.0)	2 (11.1)	1 (7.7)	1 (20.0)
Current smoker	5 (23.8)	3 (18.8)	2 (40.0)	4 (22.2)	2 (15.4)	2 (40.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB
2. TNFi: ADALIMUMAB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB
   JAK inhibitors: BARICITINIB, TOFACITINIB (not available in the database)

3.1.3 HAQ

Table 4. Description of the Health Assessment Questionnaire functional disability index (HAQ) among patients with Rheumatoid Arthritis aged ≥18 years for overall population and by group of patients treated by therapeutic class (TNFi and JAK inhibitors)[1] according to age at the date of initiation of the first treatment line

	All drugs of interest[1]			TNFi[2]		
	ALL n = 180	**Women n = 134**	**Men n = 46**	**ALL n = 172**	**Women n = 127**	**Men n = 45**
Total						
HAQ [0-3]						
Size (missing)	180 (0)	134 (0)	46 (0)	172 (0)	127 (0)	45 (0)
Mean (± SD)	0.9 (0.7)	0.9 (0.7)	0.7 (0.6)	0.9 (0.7)	0.9 (0.7)	0.7 (0.6)
Median	0.9	0.9	0.6	0.9	0.9	0.6
[p25% - p75%]	[0.3;1.4]	[0.4;1.4]	[0.1;1.1]	[0.3;1.4]	[0.4;1.4]	[0.1;1.1]
[Min - Max]	[0.0;2.6]	[0.0;2.6]	[0.0;2.4]	[0.0;2.6]	[0.0;2.6]	[0.0;2.4]
[18-30[	**14 (7.8)**	**10 (7.5)**	**4 (8.7)**	**14 (8.1)**	**10 (7.9)**	**4 (8.9)**
HAQ [0-3]						
Size (missing)	14 (0)	10 (0)	4 (0)	14 (0)	10 (0)	4 (0)
Mean (± SD)	0.5 (0.5)	0.6 (0.5)	0.3 (0.6)	0.5 (0.5)	0.6 (0.5)	0.3 (0.6)
Median	0.3	0.6	0.0	0.3	0.6	0.0
[p25% - p75%]	[0.0;1.0]	[0.1;1.0]	[0.0;0.6]	[0.0;1.0]	[0.1;1.0]	[0.0;0.6]
[Min - Max]	[0.0;1.1]	[0.0;1.1]	[0.0;1.1]	[0.0;1.1]	[0.0;1.1]	[0.0;1.1]
[30-40[	**22 (12.2)**	**18 (13.4)**	**4 (8.7)**	**22 (12.8)**	**18 (14.2)**	**4 (8.9)**
HAQ [0-3]						
Size (missing)	22 (0)	18 (0)	4 (0)	22 (0)	18 (0)	4 (0)
Mean (± SD)	0.8 (0.6)	0.7 (0.5)	1.0 (1.0)	0.8 (0.6)	0.7 (0.5)	1.0 (1.0)
Median	0.7	0.7	0.8	0.7	0.7	0.8
[p25% - p75%]	[0.3;1.1]	[0.3;1.1]	[0.3;1.7]	[0.3;1.1]	[0.3;1.1]	[0.3;1.7]
[Min - Max]	[0.0;2.4]	[0.0;1.5]	[0.1;2.4]	[0.0;2.4]	[0.0;1.5]	[0.1;2.4]
[40-50[	**45 (25.0)**	**36 (26.9)**	**9 (19.6)**	**44 (25.6)**	**35 (27.6)**	**9 (20.0)**
HAQ [0-3]						
Size (missing)	45 (0)	36 (0)	9 (0)	44 (0)	35 (0)	9 (0)
Mean (± SD)	0.8 (0.6)	0.9 (0.6)	0.4 (0.4)	0.8 (0.6)	0.9 (0.6)	0.4 (0.4)
Median	0.8	0.9	0.3	0.8	0.9	0.3
[p25% - p75%]	[0.3;1.1]	[0.5;1.3]	[0.0;0.6]	[0.3;1.2]	[0.6;1.3]	[0.0;0.6]

	All drugs of interest[1]			TNFi[2]		
	ALL n = 180	**Women n = 134**	**Men n = 46**	**ALL n = 172**	**Women n = 127**	**Men n = 45**
[Min - Max]	[0.0;2.4]	[0.0;2.4]	[0.0;1.0]	[0.0;2.4]	[0.0;2.4]	[0.0;1.0]
[50-60[	**56 (31.1)**	**38 (28.4)**	**18 (39.1)**	**55 (32.0)**	**37 (29.1)**	**18 (40.0)**
HAQ [0-3]						
Size (missing)	56 (0)	38 (0)	18 (0)	55 (0)	37 (0)	18 (0)
Mean (± SD)	1.0 (0.7)	1.0 (0.7)	0.8 (0.6)	1.0 (0.7)	1.0 (0.7)	0.8 (0.6)
Median	1.0	1.1	0.9	1.1	1.1	0.9
[p25% - p75%]	[0.3;1.4]	[0.5;1.5]	[0.3;1.4]	[0.3;1.4]	[0.5;1.5]	[0.3;1.4]
[Min - Max]	[0.0;2.5]	[0.0;2.5]	[0.0;1.8]	[0.0;2.5]	[0.0;2.5]	[0.0;1.8]
[60-65[	**22 (12.2)**	**16 (11.9)**	**6 (13.0)**	**19 (11.0)**	**14 (11.0)**	**5 (11.1)**
HAQ [0-3]						
Size (missing)	22 (0)	16 (0)	6 (0)	19 (0)	14 (0)	5 (0)
Mean (± SD)	1.1 (0.7)	1.2 (0.8)	0.9 (0.5)	1.1 (0.8)	1.2 (0.9)	0.9 (0.6)
Median	1.3	1.4	0.9	1.3	1.4	1.0
[p25% - p75%]	[0.6;1.6]	[0.5;1.7]	[0.6;1.0]	[0.4;1.6]	[0.4;1.8]	[0.9;1.0]
[Min - Max]	[0.0;2.6]	[0.0;2.6]	[0.0;1.6]	[0.0;2.6]	[0.0;2.6]	[0.0;1.6]
≥65	**21 (11.7)**	**16 (11.9)**	**5 (10.9)**	**18 (10.5)**	**13 (10.2)**	**5 (11.1)**
HAQ [0-3]						
Size (missing)	21 (0)	16 (0)	5 (0)	18 (0)	13 (0)	5 (0)
Mean (± SD)	1.0 (0.7)	1.1 (0.8)	0.7 (0.5)	1.0 (0.8)	1.1 (0.8)	0.7 (0.5)
Median	0.8	1.1	0.8	0.8	0.8	0.8
[p25% - p75%]	[0.4;1.4]	[0.4;1.5]	[0.1;1.1]	[0.4;1.5]	[0.4;1.5]	[0.1;1.1]
[Min - Max]	[0.0;2.6]	[0.0;2.6]	[0.1;1.1]	[0.1;2.6]	[0.1;2.6]	[0.1;1.1]

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB
2. TNFi: ADALIMUMAB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB
   JAK inhibitors: BARICITINIB, TOFACITINIB (not available in the database)

Table 5. Description of RA severity among patients with Rheumatoid Arthritis aged ≥ 18 years for overall population and by group of patients treated by therapeutic class (TNFi and JAK inhibitors)[1] according to age at the date of initiation of the first treatment line

	All drugs of interest[1]						TNFi[2]					
	ALL n = 180		Women n = 134		Men n = 46		ALL n = 172		Women n = 127		Men n = 45	
Total												
RA severity, n (%)												
Not severe RA	57	(31.7)	39	(29.1)	18	(39.1)	55	(32.0)	37	(29.1)	18	(40.0)
Severe RA	123	(68.3)	95	(70.9)	28	(60.9)	117	(68.0)	90	(70.9)	27	(60.0)
[18-30[	**14**	**(7.8)**	**10**	**(7.5)**	**4**	**(8.7)**	**14**	**(8.1)**	**10**	**(7.9)**	**4**	**(8.9)**
RA severity, n (%)												
Not severe RA	8	(57.1)	5	(50.0)	3	(75.0)	8	(57.1)	5	(50.0)	3	(75.0)
Severe RA	6	(42.9)	5	(50.0)	1	(25.0)	6	(42.9)	5	(50.0)	1	(25.0)
[30-40[	**22**	**(12.2)**	**18**	**(13.4)**	**4**	**(8.7)**	**22**	**(12.8)**	**18**	**(14.2)**	**4**	**(8.9)**
RA severity, n (%)												
Not severe RA	8	(36.4)	7	(38.9)	1	(25.0)	8	(36.4)	7	(38.9)	1	(25.0)
Severe RA	14	(63.6)	11	(61.1)	3	(75.0)	14	(63.6)	11	(61.1)	3	(75.0)
[40-50[	**45**	**(25.0)**	**36**	**(26.9)**	**9**	**(19.6)**	**44**	**(25.6)**	**35**	**(27.6)**	**9**	**(20.0)**
RA severity, n (%)												
Not severe RA	14	(31.1)	9	(25.0)	5	(55.6)	13	(29.5)	8	(22.9)	5	(55.6)
Severe RA	31	(68.9)	27	(75.0)	4	(44.4)	31	(70.5)	27	(77.1)	4	(44.4)
[50-60[	**56**	**(31.1)**	**38**	**(28.4)**	**18**	**(39.1)**	**55**	**(32.0)**	**37**	**(29.1)**	**18**	**(40.0)**
RA severity, n (%)												
Not severe RA	15	(26.8)	9	(23.7)	6	(33.3)	15	(27.3)	9	(24.3)	6	(33.3)
Severe RA	41	(73.2)	29	(76.3)	12	(66.7)	40	(72.7)	28	(75.7)	12	(66.7)
[60-65[	**22**	**(12.2)**	**16**	**(11.9)**	**6**	**(13.0)**	**19**	**(11.0)**	**14**	**(11.0)**	**5**	**(11.1)**
RA severity, n (%)												
Not severe RA	5	(22.7)	4	(25.0)	1	(16.7)	5	(26.3)	4	(28.6)	1	(20.0)
Severe RA	17	(77.3)	12	(75.0)	5	(83.3)	14	(73.7)	10	(71.4)	4	(80.0)
≥65	**21**	**(11.7)**	**16**	**(11.9)**	**5**	**(10.9)**	**18**	**(10.5)**	**13**	**(10.2)**	**5**	**(11.1)**
RA severity, n (%)												
Not severe RA	7	(33.3)	5	(31.3)	2	(40.0)	6	(33.3)	4	(30.8)	2	(40.0)

	All drugs of interest[1]			TNFi[2]		
	ALL n = 180	**Women n = 134**	**Men n = 46**	**ALL n = 172**	**Women n = 127**	**Men n = 45**
Severe RA	14 (66.7)	11 (68.8)	3 (60.0)	12 (66.7)	9 (69.2)	3 (60.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB
2. TNFi: ADALIMUMAB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB
   JAK inhibitors: BARICITINIB, TOFACITINIB (not available in the database)

3.2 BY TREATMENT OF INTEREST

As with the previous tables, **the unit** is always the **patient**. Here, the first prescription of each treatment of interest is taken into account. Thus, a patient could be counted several times if he has had several treatments of interest during the follow-up.

Age is calculated on the **date of the first prescription of each treatment**. **Weight, height and smoking status** were collected from the **CRF** closest to that date. Same strategy was carried out for the HAQ self-questionnaire completed by the patient. The variable "RA severity" is categorized according to the value of HAQ ('Not severe RA' if HAQ < 0.5, 'Severe RA' if HAQ ≥ 0.5).

3.2.1 BMI

Table 6. Description of Body Mass Index (BMI) among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and according to age at the date of initiation of the considered drug, whatever the rank of treatment line

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	Women n = 72	Men n = 24	ALL n = 103	Women n = 80	Men n = 23	ALL n = 21	Women n = 15	Men n = 6	ALL n = 11	Women n = 8	Men n = 3
Total												
BMI (kg/m2)												
Size (missing)	96 (0)	72 (0)	24 (0)	103 (0)	80 (0)	23 (0)	21 (0)	15 (0)	6 (0)	11 (0)	8 (0)	3 (0)
Mean (± SD)	25.2 (5.0)	24.6 (4.8)	27.2 (5.1)	25.2 (4.6)	25.4 (4.9)	24.6 (3.1)	25.6 (6.6)	26.3 (7.1)	23.9 (5.3)	25.4 (6.3)	24.4 (4.6)	28.0 (10.5)
Median	24.7	23.8	26.8	24.2	24.1	24.5	23.8	24.3	21.8	22.6	23.5	22.6
[p25% - p75%]	[21.6;27.4]	[21.1;26.2]	[22.9;30.2]	[21.8;27.9]	[21.7;28.4]	[21.8;27.3]	[21.5;28.3]	[21.7;30.1]	[20.8;26.0]	[20.9;29.0]	[20.5;28.2]	[21.1;40.1]
[Min - Max]	[17.2;43.5]	[17.2;43.5]	[19.0;38.2]	[17.6;39.8]	[17.6;39.8]	[19.4;30.9]	[16.4;46.6]	[16.4;46.6]	[19.1;33.7]	[19.4;40.1]	[19.4;31.6]	[21.1;40.1]
[18-30[	**5 (5.2)**	**3 (4.2)**	**2 (8.3)**	**8 (7.8)**	**7 (8.8)**	**1 (4.3)**	**3 (14.3)**	**2 (13.3)**	**1 (16.7)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
BMI (kg/m2)												
Size (missing)	5 (0)	3 (0)	2 (0)	8 (0)	7 (0)	1 (0)	3 (0)	2 (0)	1 (0)			
Mean (± SD)	23.3 (2.5)	22.9 (2.9)	24.0 (2.6)	22.3 (2.4)	21.8 (2.1)	25.7	19.0 (2.6)	17.7 (1.9)	21.5			
Median	22.8	22.8	24.0	22.1	21.6	25.7	19.1	17.7	21.5			
[p25% - p75%]	[22.2;25.8]	[20.0;25.8]	[22.2;25.8]	[20.4;24.4]	[19.8;24.0]	[25.7;25.7]	[16.4;21.5]	[16.4;19.1]	[21.5;21.5]			
[Min - Max]	[20.0;25.8]	[20.0;25.8]	[22.2;25.8]	[18.9;25.7]	[18.9;24.8]	[25.7;25.7]	[16.4;21.5]	[16.4;19.1]	[21.5;21.5]			
[30-40[	**18 (18.8)**	**14 (19.4)**	**4 (16.7)**	**8 (7.8)**	**6 (7.5)**	**2 (8.7)**	**3 (14.3)**	**3 (20.0)**	**0 (0.0)**	**1 (9.1)**	**1 (12.5)**	**0 (0.0)**
BMI (kg/m2)												
Size (missing)	18 (0)	14 (0)	4 (0)	8 (0)	6 (0)	2 (0)	3 (0)	3 (0)		1 (0)	1 (0)	

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	**Women n = 72**	**Men n = 24**	**ALL n = 103**	**Women n = 80**	**Men n = 23**	**ALL n = 21**	**Women n = 15**	**Men n = 6**	**ALL n = 11**	**Women n = 8**	**Men n = 3**
Mean (± SD)	22.6 (2.8)	22.3 (2.5)	23.6 (3.9)	23.0 (3.0)	22.9 (3.5)	23.5 (0.0)	25.4 (3.4)	25.4 (3.4)		21.8	21.8	
Median	21.8	21.4	22.6	22.7	21.6	23.5	26.0	26.0		21.8	21.8	
[p25% - p75%]	[20.2;25.3]	[20.1;25.3]	[20.9;26.3]	[21.0;23.5]	[20.9;23.4]	[23.5;23.6]	[21.7;28.3]	[21.7;28.3]		[21.8;21.8]	[21.8;21.8]	
[Min - Max]	[19.6;29.0]	[19.6;26.3]	[20.2;29.0]	[20.2;29.6]	[20.2;29.6]	[23.5;23.6]	[21.7;28.3]	[21.7;28.3]		[21.8;21.8]	[21.8;21.8]	
[40-50[	**26 (27.1)**	**23 (31.9)**	**3 (12.5)**	**20 (19.4)**	**17 (21.3)**	**3 (13.0)**	**7 (33.3)**	**4 (26.7)**	**3 (50.0)**	**3 (27.3)**	**2 (25.0)**	**1 (33.3)**
BMI (kg/m2)												
Size (missing)	26 (0)	23 (0)	3 (0)	20 (0)	17 (0)	3 (0)	7 (0)	4 (0)	3 (0)	3 (0)	2 (0)	1 (0)
Mean (± SD)	24.8 (5.0)	23.8 (4.1)	32.1 (5.7)	24.8 (5.0)	25.0 (5.3)	23.3 (3.5)	29.3 (9.1)	31.6 (10.6)	26.3 (7.3)	26.8 (11.5)	20.2 (1.0)	40.1
Median	24.0	23.7	31.4	23.3	23.4	21.5	26.0	27.9	26.0	20.9	20.2	40.1
[p25% - p75%]	[21.6;26.8]	[21.0;24.9]	[26.8;38.2]	[21.3;26.5]	[22.6;25.8]	[21.1;27.3]	[23.8;33.7]	[24.1;39.1]	[19.1;33.7]	[19.4;40.1]	[19.4;20.9]	[40.1;40.1]
[Min - Max]	[18.7;38.2]	[18.7;34.6]	[26.8;38.2]	[18.6;39.8]	[18.6;39.8]	[21.1;27.3]	[19.1;46.6]	[23.8;46.6]	[19.1;33.7]	[19.4;40.1]	[19.4;20.9]	[40.1;40.1]
[50-60[	**31 (32.3)**	**22 (30.6)**	**9 (37.5)**	**39 (37.9)**	**29 (36.3)**	**10 (43.5)**	**4 (19.0)**	**3 (20.0)**	**1 (16.7)**	**2 (18.2)**	**2 (25.0)**	**0 (0.0)**
BMI (kg/m2)												
Size (missing)	31 (0)	22 (0)	9 (0)	39 (0)	29 (0)	10 (0)	4 (0)	3 (0)	1 (0)	2 (0)	2 (0)	
Mean (± SD)	27.3 (5.7)	27.2 (6.3)	27.4 (4.0)	26.1 (4.6)	26.3 (5.0)	25.6 (3.3)	23.5 (2.8)	24.0 (3.2)	22.1	29.6 (2.9)	29.6 (2.9)	
Median	26.2	25.5	27.4	25.0	25.0	25.5	22.6	23.0	22.1	29.6	29.6	
[p25% - p75%]	[23.5;30.1]	[23.5;30.1]	[25.9;29.0]	[22.3;29.0]	[22.7;29.7]	[22.3;28.0]	[21.7;25.3]	[21.3;27.5]	[22.1;22.1]	[27.5;31.6]	[27.5;31.6]	
[Min - Max]	[17.2;43.5]	[17.2;43.5]	[21.3;34.2]	[19.0;38.2]	[19.0;38.2]	[21.0;30.9]	[21.3;27.5]	[21.3;27.5]	[22.1;22.1]	[27.5;31.6]	[27.5;31.6]	
[60-65[	**10 (10.4)**	**6 (8.3)**	**4 (16.7)**	**12 (11.7)**	**10 (12.5)**	**2 (8.7)**	**2 (9.5)**	**2 (13.3)**	**0 (0.0)**	**4 (36.4)**	**2 (25.0)**	**2 (66.7)**
BMI (kg/m2)												
Size (missing)	10 (0)	6 (0)	4 (0)	12 (0)	10 (0)	2 (0)	2 (0)	2 (0)		4 (0)	2 (0)	2 (0)
Mean (± SD)	25.7 (6.1)	24.1 (4.0)	28.0 (8.4)	25.9 (4.9)	26.4 (5.3)	23.6 (0.9)	27.0 (5.2)	27.0 (5.2)		23.2 (4.0)	24.5 (6.3)	21.9 (1.1)
Median	24.7	24.7	28.0	26.0	28.2	23.6	27.0	27.0		21.9	24.5	21.9
[p25% - p75%]	[21.3;28.6]	[21.3;27.5]	[20.9;35.0]	[22.1;29.7]	[21.3;30.0]	[22.9;24.2]	[23.3;30.6]	[23.3;30.6]		[20.6;25.8]	[20.1;29.0]	[21.1;22.6]
[Min - Max]	[17.9;36.8]	[17.9;28.6]	[19.0;36.8]	[17.6;34.3]	[17.6;34.3]	[22.9;24.2]	[23.3;30.6]	[23.3;30.6]		[20.1;29.0]	[20.1;29.0]	[21.1;22.6]
≥65	**6 (6.3)**	**4 (5.6)**	**2 (8.3)**	**16 (15.5)**	**11 (13.8)**	**5 (21.7)**	**2 (9.5)**	**1 (6.7)**	**1 (16.7)**	**1 (9.1)**	**1 (12.5)**	**0 (0.0)**
BMI (kg/m2)												
Size (missing)	6 (0)	4 (0)	2 (0)	16 (0)	11 (0)	5 (0)	2 (0)	1 (0)	1 (0)	1 (0)	1 (0)	
Mean (± SD)	25.4 (3.3)	24.4 (3.7)	27.3 (0.7)	25.5 (4.6)	26.2 (4.9)	24.1 (4.0)	25.5 (6.6)	30.1	20.8	25.2	25.2	
Median	26.8	25.0	27.3	25.5	27.6	25.1	25.5	30.1	20.8	25.2	25.2	
[p25% - p75%]	[23.3;27.8]	[21.5;27.4]	[26.8;27.8]	[21.4;28.8]	[21.9;29.4]	[20.8;25.9]	[20.8;30.1]	[30.1;30.1]	[20.8;20.8]	[25.2;25.2]	[25.2;25.2]	

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	**Women n = 72**	**Men n = 24**	**ALL n = 103**	**Women n = 80**	**Men n = 23**	**ALL n = 21**	**Women n = 15**	**Men n = 6**	**ALL n = 11**	**Women n = 8**	**Men n = 3**
[Min - Max]	[19.7;28.0]	[19.7;28.0]	[26.8;27.8]	[19.4;35.8]	[19.8;35.8]	[19.4;29.2]	[20.8;30.1]	[30.1;30.1]	[20.8;20.8]	[25.2;25.2]	[25.2;25.2]	

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 7. Description of Body Mass Index (BMI) in categories among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and according to age at the date of initiation of the considered drug, whatever the rank of treatment line

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	Women n = 72	Men n = 24	ALL n = 103	Women n = 80	Men n = 23	ALL n = 21	Women n = 15	Men n = 6	ALL n = 11	Women n = 8	Men n = 3
Total												
BMI (kg/m2) (in categories), n (%)												
<18.5	3 (3.1)	3 (4.2)	0 (0.0)	1 (1.0)	1 (1.3)	0 (0.0)	1 (4.8)	1 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
[18.5-25[	48 (50.0)	40 (55.6)	8 (33.3)	57 (55.3)	44 (55.0)	13 (56.5)	11 (52.4)	7 (46.7)	4 (66.7)	6 (54.5)	4 (50.0)	2 (66.7)
[25-30[	30 (31.3)	20 (27.8)	10 (41.7)	30 (29.1)	21 (26.3)	9 (39.1)	4 (19.0)	3 (20.0)	1 (16.7)	3 (27.3)	3 (37.5)	0 (0.0)
≥30	15 (15.6)	9 (12.5)	6 (25.0)	15 (14.6)	14 (17.5)	1 (4.3)	5 (23.8)	4 (26.7)	1 (16.7)	2 (18.2)	1 (12.5)	1 (33.3)
[18-30[	**5 (5.2)**	**3 (4.2)**	**2 (8.3)**	**8 (7.8)**	**7 (8.8)**	**1 (4.3)**	**3 (14.3)**	**2 (13.3)**	**1 (16.7)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
BMI (kg/m2) (in categories), n (%)												
<18.5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
[18.5-25[	3 (60.0)	2 (66.7)	1 (50.0)	7 (87.5)	7 (100.0)	0 (0.0)	2 (66.7)	1 (50.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
[25-30[	2 (40.0)	1 (33.3)	1 (50.0)	1 (12.5)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
≥30	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)	0 (0.0)	0 (0.0)	0 (0.0)
[30-40[	**18 (18.8)**	**14 (19.4)**	**4 (16.7)**	**8 (7.8)**	**6 (7.5)**	**2 (8.7)**	**3 (14.3)**	**3 (20.0)**	**0 (0.0)**	**1 (9.1)**	**1 (12.5)**	**0 (0.0)**
BMI (kg/m2) (in categories), n (%)												
<18.5	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)	0 (0.0)	0 (0.0)	0 (0.0)
[18.5-25[	13 (72.2)	10 (71.4)	3 (75.0)	7 (87.5)	5 (83.3)	2 (100.0)	1 (33.3)	1 (33.3)	0 (0.0)	1 (100.0)	1 (100.0)	0 (0.0)
[25-30[	5 (27.8)	4 (28.6)	1 (25.0)	1 (12.5)	1 (16.7)	0 (0.0)	2 (66.7)	2 (66.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
≥30	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)	0 (0.0)	0 (0.0)	0 (0.0)
[40-50[	**26 (27.1)**	**23 (31.9)**	**3 (12.5)**	**20 (19.4)**	**17 (21.3)**	**3 (13.0)**	**7 (33.3)**	**4 (26.7)**	**3 (50.0)**	**3 (27.3)**	**2 (25.0)**	**1 (33.3)**
BMI (kg/m2) (in categories), n (%)												
<18.5	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)	0 (0.0)	0 (0.0)	0 (0.0)
[18.5-25[	18 (69.2)	18 (78.3)	0 (0.0)	13 (65.0)	11 (64.7)	2 (66.7)	3 (42.9)	2 (50.0)	1 (33.3)	2 (66.7)	2 (100.0)	0 (0.0)
[25-30[	3 (11.5)	2 (8.7)	1 (33.3)	5 (25.0)	4 (23.5)	1 (33.3)	1 (14.3)	0 (0.0)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)
≥30	5 (19.2)	3 (13.0)	2 (66.7)	2 (10.0)	2 (11.8)	0 (0.0)	3 (42.9)	2 (50.0)	1 (33.3)	1 (33.3)	0 (0.0)	1 (100.0)
[50-60[	**31 (32.3)**	**22 (30.6)**	**9 (37.5)**	**39 (37.9)**	**29 (36.3)**	**10 (43.5)**	**4 (19.0)**	**3 (20.0)**	**1 (16.7)**	**2 (18.2)**	**2 (25.0)**	**0 (0.0)**

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	Women n = 72	Men n = 24	ALL n = 103	Women n = 80	Men n = 23	ALL n = 21	Women n = 15	Men n = 6	ALL n = 11	Women n = 8	Men n = 3
BMI (kg/m2) (in categories), n (%)												
<18.5	2 (6.5)	2 (9.1)	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)	0 (0.0)
[18.5-25[	8 (25.8)	6 (27.3)	2 (22.2)	19 (48.7)	14 (48.3)	5 (50.0)	3 (75.0)	2 (66.7)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
[25-30[	13 (41.9)	8 (36.4)	5 (55.6)	12 (30.8)	8 (27.6)	4 (40.0)	1 (25.0)	1 (33.3)	0 (0.0)	1 (50.0)	1 (50.0)	0 (0.0)
≥30	8 (25.8)	6 (27.3)	2 (22.2)	8 (20.5)	7 (24.1)	1 (10.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	1 (50.0)	
[60-65[	**10 (10.4)**	**6 (8.3)**	**4 (16.7)**	**12 (11.7)**	**10 (12.5)**	**2 (8.7)**	**2 (9.5)**	**2 (13.3)**	**0 (0.0)**	**4 (36.4)**	**2 (25.0)**	**2 (66.7)**
BMI (kg/m2) (in categories), n (%)												
<18.5	1 (10.0)	1 (16.7)	0 (0.0)	1 (8.3)	1 (10.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
[18.5-25[	4 (40.0)	2 (33.3)	2 (50.0)	5 (41.7)	3 (30.0)	2 (100.0)	1 (50.0)	1 (50.0)	0 (0.0)	3 (75.0)	1 (50.0)	2 (100.0)
[25-30[	3 (30.0)	3 (50.0)	0 (0.0)	3 (25.0)	3 (30.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (50.0)	0 (0.0)
≥30	2 (20.0)	0 (0.0)	2 (50.0)	3 (25.0)	3 (30.0)	0 (0.0)	1 (50.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
≥65	**6 (6.3)**	**4 (5.6)**	**2 (8.3)**	**16 (15.5)**	**11 (13.8)**	**5 (21.7)**	**2 (9.5)**	**1 (6.7)**	**1 (16.7)**	**1 (9.1)**	**1 (12.5)**	**0 (0.0)**
BMI (kg/m2) (in categories), n (%)												
<18.5	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)	0 (0.0)	0 (0.0)	0 (0.0)
[18.5-25[	2 (33.3)	2 (50.0)	0 (0.0)	6 (37.5)	4 (36.4)	2 (40.0)	1 (50.0)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
[25-30[	4 (66.7)	2 (50.0)	2 (100.0)	8 (50.0)	5 (45.5)	3 (60.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)	0 (0.0)
≥30	0 (0.0)	0 (0.0)	0 (0.0)	2 (12.5)	2 (18.2)	0 (0.0)	1 (50.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 8. Description of Body Mass Index (BMI) among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and according to age at the date of initiation of the considered drug, whatever the rank of treatment line

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	Women n = 4	Men n = 1	ALL n = 21	Women n = 16	Men n = 5	ALL n = 20	Women n = 17	Men n = 3
Total									
BMI (kg/m2)									
Size (missing)	5 (0)	4 (0)	1 (0)	21 (0)	16 (0)	5 (0)	20 (0)	17 (0)	3 (0)
Mean (± SD)	28.4 (6.6)	25.6 (2.2)	39.8	26.2 (3.5)	26.6 (3.3)	24.7 (4.0)	24.3 (4.7)	24.5 (4.9)	22.9 (3.5)
Median	26.7	26.1	39.8	25.6	26.0	24.6	23.7	23.7	22.9
[p25% - p75%]	[25.5;27.5]	[24.0;27.1]	[39.8;39.8]	[24.4;28.7]	[24.4;29.2]	[22.0;27.0]	[21.8;26.1]	[22.2;25.8]	[19.4;26.4]
[Min - Max]	[22.5;39.8]	[22.5;27.5]	[39.8;39.8]	[19.9;32.0]	[21.3;32.0]	[19.9;30.1]	[16.4;35.2]	[16.4;35.2]	[19.4;26.4]
[18-30[	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**1 (4.8)**	**1 (6.3)**	**0 (0.0)**	**4 (20.0)**	**4 (23.5)**	**0 (0.0)**
BMI (kg/m2)									
Size (missing)				1 (0)	1 (0)		4 (0)	4 (0)	
Mean (± SD)				24.4	24.4		22.5 (5.7)	22.5 (5.7)	
Median				24.4	24.4		22.5	22.5	
[p25% - p75%]				[24.4;24.4]	[24.4;24.4]		[17.8;27.2]	[17.8;27.2]	
[Min - Max]				[24.4;24.4]	[24.4;24.4]		[16.4;28.6]	[16.4;28.6]	
[30-40[	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**2 (9.5)**	**0 (0.0)**	**2 (40.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
BMI (kg/m2)									
Size (missing)				2 (0)		2 (0)			
Mean (± SD)				25.0 (7.2)		25.0 (7.2)			
Median				25.0		25.0			
[p25% - p75%]				[19.9;30.1]		[19.9;30.1]			
[Min - Max]				[19.9;30.1]		[19.9;30.1]			
[40-50[	**2 (40.0)**	**1 (25.0)**	**1 (100.0)**	**1 (4.8)**	**1 (6.3)**	**0 (0.0)**	**2 (10.0)**	**2 (11.8)**	**0 (0.0)**
BMI (kg/m2)									
Size (missing)	2 (0)	1 (0)	1 (0)	1 (0)	1 (0)		2 (0)	2 (0)	
Mean (± SD)	32.6 (10.1)	25.5	39.8	26.3	26.3		22.5 (1.6)	22.5 (1.6)	
Median	32.6	25.5	39.8	26.3	26.3		22.5	22.5	
[p25% - p75%]	[25.5;39.8]	[25.5;25.5]	[39.8;39.8]	[26.3;26.3]	[26.3;26.3]		[21.4;23.7]	[21.4;23.7]	
[Min - Max]	[25.5;39.8]	[25.5;25.5]	[39.8;39.8]	[26.3;26.3]	[26.3;26.3]		[21.4;23.7]	[21.4;23.7]	

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	**Women n = 4**	**Men n = 1**	**ALL n = 21**	**Women n = 16**	**Men n = 5**	**ALL n = 20**	**Women n = 17**	**Men n = 3**
[50-60[	**1 (20.0)**	**1 (25.0)**	**0 (0.0)**	**7 (33.3)**	**6 (37.5)**	**1 (20.0)**	**6 (30.0)**	**5 (29.4)**	**1 (33.3)**
BMI (kg/m2)									
Size (missing)	1 (0)	1 (0)		7 (0)	6 (0)	1 (0)	6 (0)	5 (0)	1 (0)
Mean (± SD)	27.5	27.5		25.3 (2.6)	25.4 (2.8)	24.6	28.1 (5.6)	28.5 (6.1)	26.4
Median	27.5	27.5		24.6	25.0	24.6	27.0	27.5	26.4
[p25% - p75%]	[27.5;27.5]	[27.5;27.5]		[23.1;27.5]	[23.1;27.5]	[24.6;24.6]	[23.1;34.5]	[23.1;34.5]	[26.4;26.4]
[Min - Max]	[27.5;27.5]	[27.5;27.5]		[22.2;29.7]	[22.2;29.7]	[24.6;24.6]	[22.2;35.2]	[22.2;35.2]	[26.4;26.4]
[60-65[	**1 (20.0)**	**1 (25.0)**	**0 (0.0)**	**4 (19.0)**	**2 (12.5)**	**2 (40.0)**	**4 (20.0)**	**3 (17.6)**	**1 (33.3)**
BMI (kg/m2)									
Size (missing)	1 (0)	1 (0)		4 (0)	2 (0)	2 (0)	4 (0)	3 (0)	1 (0)
Mean (± SD)	26.7	26.7		26.1 (2.9)	27.7 (1.4)	24.5 (3.5)	24.1 (1.0)	24.5 (0.7)	22.9
Median	26.7	26.7		26.8	27.7	24.5	24.1	24.5	22.9
[p25% - p75%]	[26.7;26.7]	[26.7;26.7]		[24.3;27.8]	[26.7;28.7]	[22.0;27.0]	[23.3;24.8]	[23.7;25.1]	[22.9;22.9]
[Min - Max]	[26.7;26.7]	[26.7;26.7]		[22.0;28.7]	[26.7;28.7]	[22.0;27.0]	[22.9;25.1]	[23.7;25.1]	[22.9;22.9]
≥65	**1 (20.0)**	**1 (25.0)**	**0 (0.0)**	**6 (28.6)**	**6 (37.5)**	**0 (0.0)**	**4 (20.0)**	**3 (17.6)**	**1 (33.3)**
BMI (kg/m2)									
Size (missing)	1 (0)	1 (0)		6 (0)	6 (0)		4 (0)	3 (0)	1 (0)
Mean (± SD)	22.5	22.5		27.8 (4.4)	27.8 (4.4)		21.4 (2.7)	22.1 (2.9)	19.4
Median	22.5	22.5		28.4	28.4		20.8	22.2	19.4
[p25% - p75%]	[22.5;22.5]	[22.5;22.5]		[25.5;31.5]	[25.5;31.5]		[19.3;23.6]	[19.1;25.0]	[19.4;19.4]
[Min - Max]	[22.5;22.5]	[22.5;22.5]		[21.3;32.0]	[21.3;32.0]		[19.1;25.0]	[19.1;25.0]	[19.4;19.4]

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 9. Description of Body Mass Index (BMI) in categories among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and according to age at the date of initiation of the considered drug, whatever the rank of treatment line

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	Women n = 4	Men n = 1	ALL n = 21	Women n = 16	Men n = 5	ALL n = 20	Women n = 17	Men n = 3
Total									
BMI (kg/m2) (in categories), n (%)									
<18.5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.0)	1 (5.9)	0 (0.0)
[18.5-25[	1 (20.0)	1 (25.0)	0 (0.0)	8 (38.1)	5 (31.3)	3 (60.0)	12 (60.0)	10 (58.8)	2 (66.7)
[25-30[	3 (60.0)	3 (75.0)	0 (0.0)	9 (42.9)	8 (50.0)	1 (20.0)	5 (25.0)	4 (23.5)	1 (33.3)
≥30	1 (20.0)	0 (0.0)	1 (100.0)	4 (19.0)	3 (18.8)	1 (20.0)	2 (10.0)	2 (11.8)	0 (0.0)
[18-30[	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**1 (4.8)**	**1 (6.3)**	**0 (0.0)**	**4 (20.0)**	**4 (23.5)**	**0 (0.0)**
BMI (kg/m2) (in categories), n (%)									
<18.5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (25.0)	0 (0.0)
[18.5-25[	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)	0 (0.0)	1 (25.0)	1 (25.0)	0 (0.0)
[25-30[	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (50.0)	2 (50.0)	0 (0.0)
≥30	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)
[30-40[	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**2 (9.5)**	**0 (0.0)**	**2 (40.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
BMI (kg/m2) (in categories), n (%)									
<18.5	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)
[18.5-25[	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	0 (0.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)
[25-30[	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)
≥30	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	0 (0.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)
[40-50[	**2 (40.0)**	**1 (25.0)**	**1 (100.0)**	**1 (4.8)**	**1 (6.3)**	**0 (0.0)**	**2 (10.0)**	**2 (11.8)**	**0 (0.0)**
BMI (kg/m2) (in categories), n (%)									
<18.5	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)
[18.5-25[	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)	2 (100.0)	0 (0.0)
[25-30[	1 (50.0)	1 (100.0)	0 (0.0)	1 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
≥30	1 (50.0)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	Women n = 4	Men n = 1	ALL n = 21	Women n = 16	Men n = 5	ALL n = 20	Women n = 17	Men n = 3
[50-60[	**1 (20.0)**	**1 (25.0)**	**0 (0.0)**	**7 (33.3)**	**6 (37.5)**	**1 (20.0)**	**6 (30.0)**	**5 (29.4)**	**1 (33.3)**
BMI (kg/m2) (in categories), n (%)									
<18.5	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)
[18.5-25[	0 (0.0)	0 (0.0)	0 (0.0)	4 (57.1)	3 (50.0)	1 (100.0)	2 (33.3)	2 (40.0)	0 (0.0)
[25-30[	1 (100.0)	1 (100.0)	0 (0.0)	3 (42.9)	3 (50.0)	0 (0.0)	2 (33.3)	1 (20.0)	1 (100.0)
≥30	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (33.3)	2 (40.0)	0 (0.0)
[60-65[	**1 (20.0)**	**1 (25.0)**	**0 (0.0)**	**4 (19.0)**	**2 (12.5)**	**2 (40.0)**	**4 (20.0)**	**3 (17.6)**	**1 (33.3)**
BMI (kg/m2) (in categories), n (%)									
<18.5	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)
[18.5-25[	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	1 (50.0)	3 (75.0)	2 (66.7)	1 (100.0)
[25-30[	1 (100.0)	1 (100.0)	0 (0.0)	3 (75.0)	2 (100.0)	1 (50.0)	1 (25.0)	1 (33.3)	0 (0.0)
≥30	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)
≥65	**1 (20.0)**	**1 (25.0)**	**0 (0.0)**	**6 (28.6)**	**6 (37.5)**	**0 (0.0)**	**4 (20.0)**	**3 (17.6)**	**1 (33.3)**
BMI (kg/m2) (in categories), n (%)									
<18.5	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)
[18.5-25[	1 (100.0)	1 (100.0)	0 (0.0)	1 (16.7)	1 (16.7)	0 (0.0)	4 (100.0)	3 (100.0)	1 (100.0)
[25-30[	0 (0.0)	0 (0.0)	0 (0.0)	2 (33.3)	2 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
≥30	0 (0.0)	0 (0.0)	0 (0.0)	3 (50.0)	3 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

3.2.2 SMOKING STATUS

Table 10. Description of smoking status among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and according to age at the date of initiation of the considered drug, whatever the rank of treatment line

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	Women n = 72	Men n = 24	ALL n = 103	Women n = 80	Men n = 23	ALL n = 21	Women n = 15	Men n = 6	ALL n = 11	Women n = 8	Men n = 3
Total												
Smoking status, n (%)												
Never smoker	50 (52.1)	40 (55.6)	10 (41.7)	60 (58.3)	51 (63.8)	9 (39.1)	12 (57.1)	9 (60.0)	3 (50.0)	5 (45.5)	5 (62.5)	0 (0.0)
Former smoker	27 (28.1)	19 (26.4)	8 (33.3)	22 (21.4)	13 (16.3)	9 (39.1)	5 (23.8)	3 (20.0)	2 (33.3)	4 (36.4)	2 (25.0)	2 (66.7)
Current smoker	19 (19.8)	13 (18.1)	6 (25.0)	21 (20.4)	16 (20.0)	5 (21.7)	4 (19.0)	3 (20.0)	1 (16.7)	2 (18.2)	1 (12.5)	1 (33.3)
[18-30[	**5 (5.2)**	**3 (4.2)**	**2 (8.3)**	**8 (7.8)**	**7 (8.8)**	**1 (4.3)**	**3 (14.3)**	**2 (13.3)**	**1 (16.7)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Smoking status, n (%)												
Never smoker	3 (60.0)	1 (33.3)	2 (100.0)	6 (75.0)	5 (71.4)	1 (100.0)	3 (100.0)	2 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
Former smoker	1 (20.0)	1 (33.3)	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)	0 (0.0)
Current smoker	1 (20.0)	1 (33.3)	0 (0.0)	2 (25.0)	2 (28.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
[30-40[	**18 (18.8)**	**14 (19.4)**	**4 (16.7)**	**8 (7.8)**	**6 (7.5)**	**2 (8.7)**	**3 (14.3)**	**3 (20.0)**	**0 (0.0)**	**1 (9.1)**	**1 (12.5)**	**0 (0.0)**
Smoking status, n (%)												
Never smoker	8 (44.4)	7 (50.0)	1 (25.0)	5 (62.5)	4 (66.7)	1 (50.0)	1 (33.3)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Former smoker	4 (22.2)	4 (28.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (66.7)	2 (66.7)	0 (0.0)	1 (100.0)	1 (100.0)	0 (0.0)
Current smoker	6 (33.3)	3 (21.4)	3 (75.0)	3 (37.5)	2 (33.3)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
[40-50[	**26 (27.1)**	**23 (31.9)**	**3 (12.5)**	**20 (19.4)**	**17 (21.3)**	**3 (13.0)**	**7 (33.3)**	**4 (26.7)**	**3 (50.0)**	**3 (27.3)**	**2 (25.0)**	**1 (33.3)**
Smoking status, n (%)												
Never smoker	17 (65.4)	15 (65.2)	2 (66.7)	12 (60.0)	11 (64.7)	1 (33.3)	3 (42.9)	3 (75.0)	0 (0.0)	1 (33.3)	1 (50.0)	0 (0.0)
Former smoker	7 (26.9)	6 (26.1)	1 (33.3)	6 (30.0)	4 (23.5)	2 (66.7)	2 (28.6)	0 (0.0)	2 (66.7)	2 (66.7)	1 (50.0)	1 (100.0)
Current smoker	2 (7.7)	2 (8.7)	0 (0.0)	2 (10.0)	2 (11.8)	0 (0.0)	2 (28.6)	1 (25.0)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)
[50-60[	**31 (32.3)**	**22 (30.6)**	**9 (37.5)**	**39 (37.9)**	**29 (36.3)**	**10 (43.5)**	**4 (19.0)**	**3 (20.0)**	**1 (16.7)**	**2 (18.2)**	**2 (25.0)**	**0 (0.0)**
Smoking status, n (%)												
Never smoker	15 (48.4)	11 (50.0)	4 (44.4)	21 (53.8)	19 (65.5)	2 (20.0)	3 (75.0)	2 (66.7)	1 (100.0)	2 (100.0)	2 (100.0)	0 (0.0)
Former smoker	10 (32.3)	7 (31.8)	3 (33.3)	11 (28.2)	5 (17.2)	6 (60.0)	1 (25.0)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Current smoker	6 (19.4)	4 (18.2)	2 (22.2)	7 (17.9)	5 (17.2)	2 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	Women n = 72	Men n = 24	ALL n = 103	Women n = 80	Men n = 23	ALL n = 21	Women n = 15	Men n = 6	ALL n = 11	Women n = 8	Men n = 3
[60-65[	**10 (10.4)**	**6 (8.3)**	**4 (16.7)**	**12 (11.7)**	**10 (12.5)**	**2 (8.7)**	**2 (9.5)**	**2 (13.3)**	**0 (0.0)**	**4 (36.4)**	**2 (25.0)**	**2 (66.7)**
Smoking status, n (%)												
Never smoker	4 (40.0)	3 (50.0)	1 (25.0)	4 (33.3)	3 (30.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (50.0)	0 (0.0)
Former smoker	4 (40.0)	1 (16.7)	3 (75.0)	3 (25.0)	2 (20.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	1 (50.0)
Current smoker	2 (20.0)	2 (33.3)	0 (0.0)	5 (41.7)	5 (50.0)	0 (0.0)	2 (100.0)	2 (100.0)	0 (0.0)	2 (50.0)	1 (50.0)	1 (50.0)
≥65	**6 (6.3)**	**4 (5.6)**	**2 (8.3)**	**16 (15.5)**	**11 (13.8)**	**5 (21.7)**	**2 (9.5)**	**1 (6.7)**	**1 (16.7)**	**1 (9.1)**	**1 (12.5)**	**0 (0.0)**
Smoking status, n (%)												
Never smoker	3 (50.0)	3 (75.0)	0 (0.0)	12 (75.0)	9 (81.8)	3 (60.0)	2 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	0 (0.0)
Former smoker	1 (16.7)	0 (0.0)	1 (50.0)	2 (12.5)	2 (18.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Current smoker	2 (33.3)	1 (25.0)	1 (50.0)	2 (12.5)	0 (0.0)	2 (40.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 11. Description of smoking status among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and according to age at the date of initiation of the considered drug, whatever the rank of treatment line

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	Women n = 4	Men n = 1	ALL n = 21	Women n = 16	Men n = 5	ALL n = 20	Women n = 17	Men n = 3
Total									
Smoking status, n (%)									
Never smoker	3 (60.0)	3 (75.0)	0 (0.0)	13 (61.9)	10 (62.5)	3 (60.0)	13 (65.0)	12 (70.6)	1 (33.3)
Former smoker	1 (20.0)	0 (0.0)	1 (100.0)	5 (23.8)	3 (18.8)	2 (40.0)	6 (30.0)	5 (29.4)	1 (33.3)
Current smoker	1 (20.0)	1 (25.0)	0 (0.0)	3 (14.3)	3 (18.8)	0 (0.0)	1 (5.0)	0 (0.0)	1 (33.3)
[18-30[	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**1 (4.8)**	**1 (6.3)**	**0 (0.0)**	**4 (20.0)**	**4 (23.5)**	**0 (0.0)**
Smoking status, n (%)									
Never smoker	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)	0 (0.0)	4 (100.0)	4 (100.0)	0 (0.0)
Former smoker	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)
Current smoker	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)
[30-40[	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**2 (9.5)**	**0 (0.0)**	**2 (40.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Smoking status, n (%)									
Never smoker	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)	0 (0.0)	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
Former smoker	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)
Current smoker	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)
[40-50[	**2 (40.0)**	**1 (25.0)**	**1 (100.0)**	**1 (4.8)**	**1 (6.3)**	**0 (0.0)**	**2 (10.0)**	**2 (11.8)**	**0 (0.0)**
Smoking status, n (%)									
Never smoker	1 (50.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	1 (50.0)	0 (0.0)
Former smoker	1 (50.0)	0 (0.0)	1 (100.0)	1 (100.0)	1 (100.0)	0 (0.0)	1 (50.0)	1 (50.0)	0 (0.0)
Current smoker	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)
[50-60[	**1 (20.0)**	**1 (25.0)**	**0 (0.0)**	**7 (33.3)**	**6 (37.5)**	**1 (20.0)**	**6 (30.0)**	**5 (29.4)**	**1 (33.3)**
Smoking status, n (%)									
Never smoker	1 (100.0)	1 (100.0)	0 (0.0)	6 (85.7)	5 (83.3)	1 (100.0)	2 (33.3)	2 (40.0)	0 (0.0)
Former smoker	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	1 (16.7)	0 (0.0)	4 (66.7)	3 (60.0)	1 (100.0)
Current smoker	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)

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	**Women n = 4**	**Men n = 1**	**ALL n = 21**	**Women n = 16**	**Men n = 5**	**ALL n = 20**	**Women n = 17**	**Men n = 3**
[60-65[	**1 (20.0)**	**1 (25.0)**	**0 (0.0)**	**4 (19.0)**	**2 (12.5)**	**2 (40.0)**	**4 (20.0)**	**3 (17.6)**	**1 (33.3)**
Smoking status, n (%)									
Never smoker	1 (100.0)	1 (100.0)	0 (0.0)	2 (50.0)	2 (100.0)	0 (0.0)	3 (75.0)	3 (100.0)	0 (0.0)
Former smoker	0 (0.0)	0 (0.0)	0 (0.0)	2 (50.0)	0 (0.0)	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
Current smoker	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	1 (100.0)
≥65	**1 (20.0)**	**1 (25.0)**	**0 (0.0)**	**6 (28.6)**	**6 (37.5)**	**0 (0.0)**	**4 (20.0)**	**3 (17.6)**	**1 (33.3)**
Smoking status, n (%)									
Never smoker	0 (0.0)	0 (0.0)	0 (0.0)	2 (33.3)	2 (33.3)	0 (0.0)	3 (75.0)	2 (66.7)	1 (100.0)
Former smoker	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	1 (16.7)	0 (0.0)	1 (25.0)	1 (33.3)	0 (0.0)
Current smoker	1 (100.0)	1 (100.0)	0 (0.0)	3 (50.0)	3 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

3.2.3 HAQ

Table 12. Description of the Health Assessment Questionnaire functional disability index (HAQ) among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and according to age at the date of initiation of the considered drug, whatever the rank of treatment line

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	**Women n = 72**	**Men n = 24**	**ALL n = 103**	**Women n = 80**	**Men n = 23**	**ALL n = 21**	**Women n = 15**	**Men n = 6**	**ALL n = 11**	**Women n = 8**	**Men n = 3**
Total												
HAQ [0-3]												
Size (missing)	96 (0)	72 (0)	24 (0)	103 (0)	80 (0)	23 (0)	21 (0)	15 (0)	6 (0)	11 (0)	8 (0)	3 (0)
Mean (± SD)	0.9 (0.7)	1.0 (0.7)	0.7 (0.6)	0.9 (0.7)	1.0 (0.7)	0.8 (0.6)	1.0 (0.7)	1.1 (0.8)	0.7 (0.4)	1.2 (0.7)	1.4 (0.7)	0.5 (0.6)
Median	0.9	0.9	0.8	1.0	1.0	1.0	0.9	1.0	0.8	1.3	1.3	0.3
[p25% - p75%]	[0.3;1.5]	[0.3;1.5]	[0.2;1.1]	[0.4;1.4]	[0.5;1.4]	[0.1;1.4]	[0.5;1.3]	[0.4;1.4]	[0.5;1.1]	[0.3;1.8]	[1.3;1.9]	[0.1;1.3]
[Min - Max]	[0.0;2.5]	[0.0;2.5]	[0.0;2.4]	[0.0;2.5]	[0.0;2.5]	[0.0;1.6]	[0.0;2.6]	[0.3;2.6]	[0.0;1.1]	[0.0;2.1]	[0.0;2.1]	[0.1;1.3]
[18-30[	**5 (5.2)**	**3 (4.2)**	**2 (8.3)**	**8 (7.8)**	**7 (8.8)**	**1 (4.3)**	**3 (14.3)**	**2 (13.3)**	**1 (16.7)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
HAQ [0-3]												
Size (missing)	5 (0)	3 (0)	2 (0)	8 (0)	7 (0)	1 (0)	3 (0)	2 (0)	1 (0)			
Mean (± SD)	0.6 (0.8)	0.9 (0.9)	0.0 (0.0)	0.5 (0.5)	0.6 (0.5)	0.0	0.8 (0.5)	0.6 (0.4)	1.1			
Median	0.0	1.0	0.0	0.4	0.5	0.0	0.9	0.6	1.1			
[p25% - p75%]	[0.0;1.0]	[0.0;1.8]	[0.0;0.0]	[0.1;1.1]	[0.1;1.1]	[0.0;0.0]	[0.3;1.1]	[0.3;0.9]	[1.1;1.1]			
[Min - Max]	[0.0;1.8]	[0.0;1.8]	[0.0;0.0]	[0.0;1.1]	[0.0;1.1]	[0.0;0.0]	[0.3;1.1]	[0.3;0.9]	[1.1;1.1]			
[30-40[	**18 (18.8)**	**14 (19.4)**	**4 (16.7)**	**8 (7.8)**	**6 (7.5)**	**2 (8.7)**	**3 (14.3)**	**3 (20.0)**	**0 (0.0)**	**1 (9.1)**	**1 (12.5)**	**0 (0.0)**
HAQ [0-3]												
Size (missing)	18 (0)	14 (0)	4 (0)	8 (0)	6 (0)	2 (0)	3 (0)	3 (0)		1 (0)	1 (0)	
Mean (± SD)	0.7 (0.6)	0.6 (0.5)	1.0 (1.0)	0.8 (0.5)	0.8 (0.5)	0.8 (0.4)	0.6 (0.6)	0.6 (0.6)		0.0	0.0	
Median	0.5	0.4	0.8	0.8	0.8	0.8	0.3	0.3		0.0	0.0	
[p25% - p75%]	[0.3;1.0]	[0.3;1.0]	[0.3;1.7]	[0.4;1.1]	[0.4;1.1]	[0.5;1.1]	[0.3;1.4]	[0.3;1.4]		[0.0;0.0]	[0.0;0.0]	
[Min - Max]	[0.0;2.4]	[0.0;1.5]	[0.1;2.4]	[0.0;1.4]	[0.0;1.4]	[0.5;1.1]	[0.3;1.4]	[0.3;1.4]		[0.0;0.0]	[0.0;0.0]	
[40-50[	**26 (27.1)**	**23 (31.9)**	**3 (12.5)**	**20 (19.4)**	**17 (21.3)**	**3 (13.0)**	**7 (33.3)**	**4 (26.7)**	**3 (50.0)**	**3 (27.3)**	**2 (25.0)**	**1 (33.3)**
HAQ [0-3]												
Size (missing)	26 (0)	23 (0)	3 (0)	20 (0)	17 (0)	3 (0)	7 (0)	4 (0)	3 (0)	3 (0)	2 (0)	1 (0)
Mean (± SD)	0.9 (0.6)	1.0 (0.6)	0.6 (0.4)	0.8 (0.7)	1.0 (0.7)	0.0 (0.1)	1.0 (0.5)	1.3 (0.2)	0.5 (0.5)	0.9 (0.6)	1.3 (0.0)	0.1
Median	0.8	0.9	0.6	0.8	0.9	0.0	1.1	1.3	0.6	1.3	1.3	0.1
[p25% - p75%]	[0.4;1.5]	[0.4;1.5]	[0.3;1.0]	[0.1;1.1]	[0.6;1.1]	[0.0;0.1]	[0.6;1.4]	[1.2;1.4]	[0.0;0.9]	[0.1;1.3]	[1.3;1.3]	[0.1;0.1]
[Min - Max]	[0.0;2.3]	[0.0;2.3]	[0.3;1.0]	[0.0;2.4]	[0.0;2.4]	[0.0;0.1]	[0.0;1.5]	[1.1;1.5]	[0.0;0.9]	[0.1;1.3]	[1.3;1.3]	[0.1;0.1]

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	**Women n = 72**	**Men n = 24**	**ALL n = 103**	**Women n = 80**	**Men n = 23**	**ALL n = 21**	**Women n = 15**	**Men n = 6**	**ALL n = 11**	**Women n = 8**	**Men n = 3**
[50-60[	**31 (32.3)**	**22 (30.6)**	**9 (37.5)**	**39 (37.9)**	**29 (36.3)**	**10 (43.5)**	**4 (19.0)**	**3 (20.0)**	**1 (16.7)**	**2 (18.2)**	**2 (25.0)**	**0 (0.0)**
HAQ [0-3]												
Size (missing)	31 (0)	22 (0)	9 (0)	39 (0)	29 (0)	10 (0)	4 (0)	3 (0)	1 (0)	2 (0)	2 (0)	
Mean (± SD)	1.0 (0.7)	1.1 (0.7)	0.8 (0.6)	1.0 (0.6)	1.0 (0.6)	1.0 (0.6)	0.7 (0.2)	0.8 (0.3)	0.5	1.8 (0.5)	1.8 (0.5)	
Median	1.1	1.3	0.9	1.3	1.1	1.3	0.6	0.8	0.5	1.8	1.8	
[p25% - p75%]	[0.3;1.5]	[0.3;1.8]	[0.4;1.3]	[0.5;1.4]	[0.5;1.4]	[0.3;1.4]	[0.5;0.9]	[0.5;1.0]	[0.5;0.5]	[1.4;2.1]	[1.4;2.1]	
[Min - Max]	[0.0;2.5]	[0.1;2.5]	[0.0;1.8]	[0.0;2.5]	[0.0;2.5]	[0.0;1.6]	[0.5;1.0]	[0.5;1.0]	[0.5;0.5]	[1.4;2.1]	[1.4;2.1]	
[60-65[	**10 (10.4)**	**6 (8.3)**	**4 (16.7)**	**12 (11.7)**	**10 (12.5)**	**2 (8.7)**	**2 (9.5)**	**2 (13.3)**	**0 (0.0)**	**4 (36.4)**	**2 (25.0)**	**2 (66.7)**
HAQ [0-3]												
Size (missing)	10 (0)	6 (0)	4 (0)	12 (0)	10 (0)	2 (0)	2 (0)	2 (0)		4 (0)	2 (0)	2 (0)
Mean (± SD)	1.1 (0.7)	1.3 (0.7)	0.9 (0.7)	1.1 (0.6)	1.1 (0.7)	1.2 (0.3)	1.5 (1.6)	1.5 (1.6)		1.2 (0.8)	1.7 (0.6)	0.8 (0.7)
Median	1.4	1.6	0.9	1.3	1.3	1.2	1.5	1.5		1.3	1.7	0.8
[p25% - p75%]	[0.9;1.6]	[1.3;1.8]	[0.4;1.3]	[0.8;1.5]	[0.6;1.5]	[1.0;1.4]	[0.4;2.6]	[0.4;2.6]		[0.8;1.7]	[1.3;2.1]	[0.3;1.3]
[Min - Max]	[0.0;1.8]	[0.0;1.8]	[0.0;1.6]	[0.0;2.0]	[0.0;2.0]	[1.0;1.4]	[0.4;2.6]	[0.4;2.6]		[0.3;2.1]	[1.3;2.1]	[0.3;1.3]
≥65	**6 (6.3)**	**4 (5.6)**	**2 (8.3)**	**16 (15.5)**	**11 (13.8)**	**5 (21.7)**	**2 (9.5)**	**1 (6.7)**	**1 (16.7)**	**1 (9.1)**	**1 (12.5)**	**0 (0.0)**
HAQ [0-3]												
Size (missing)	6 (0)	4 (0)	2 (0)	16 (0)	11 (0)	5 (0)	2 (0)	1 (0)	1 (0)	1 (0)	1 (0)	
Mean (± SD)	1.1 (0.8)	1.4 (0.8)	0.6 (0.7)	1.2 (0.8)	1.3 (0.9)	0.8 (0.5)	1.9 (1.1)	2.6	1.1	1.8	1.8	
Median	0.9	1.4	0.6	1.3	1.5	0.8	1.9	2.6	1.1	1.8	1.8	
[p25% - p75%]	[0.6;2.0]	[0.7;2.1]	[0.1;1.1]	[0.5;1.7]	[0.4;2.1]	[0.6;1.1]	[1.1;2.6]	[2.6;2.6]	[1.1;1.1]	[1.8;1.8]	[1.8;1.8]	
[Min - Max]	[0.1;2.1]	[0.6;2.1]	[0.1;1.1]	[0.1;2.5]	[0.1;2.5]	[0.1;1.5]	[1.1;2.6]	[2.6;2.6]	[1.1;1.1]	[1.8;1.8]	[1.8;1.8]	

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 13. Description of the Health Assessment Questionnaire functional disability index (HAQ) among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and according to age at the date of initiation of the considered drug, whatever the rank of treatment line

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	**Women n = 4**	**Men n = 1**	**ALL n = 21**	**Women n = 16**	**Men n = 5**	**ALL n = 20**	**Women n = 17**	**Men n = 3**
Total									
HAQ [0-3]									
Size (missing)	5 (0)	4 (0)	1 (0)	21 (0)	16 (0)	5 (0)	20 (0)	17 (0)	3 (0)
Mean (± SD)	0.6 (0.7)	0.8 (0.7)	0.0	1.1 (0.7)	1.2 (0.7)	0.9 (0.9)	1.0 (0.7)	1.1 (0.7)	0.8 (0.8)
Median	0.4	0.9	0.0	1.3	1.3	0.6	0.9	1.0	0.8
[p25% - p75%]	[0.0;1.4]	[0.2;1.4]	[0.0;0.0]	[0.6;1.5]	[0.8;1.5]	[0.3;1.3]	[0.6;1.4]	[0.6;1.4]	[0.0;1.6]
[Min - Max]	[0.0;1.4]	[0.0;1.4]	[0.0;0.0]	[0.0;2.5]	[0.0;2.5]	[0.0;2.1]	[0.0;2.8]	[0.3;2.8]	[0.0;1.6]
[18-30[	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**1 (4.8)**	**1 (6.3)**	**0 (0.0)**	**4 (20.0)**	**4 (23.5)**	**0 (0.0)**
HAQ [0-3]									
Size (missing)				1 (0)	1 (0)		4 (0)	4 (0)	
Mean (± SD)				1.4	1.4		1.0 (0.5)	1.0 (0.5)	
Median				1.4	1.4		1.1	1.1	
[p25% - p75%]				[1.4;1.4]	[1.4;1.4]		[0.6;1.4]	[0.6;1.4]	
[Min - Max]				[1.4;1.4]	[1.4;1.4]		[0.3;1.5]	[0.3;1.5]	
[30-40[	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**2 (9.5)**	**0 (0.0)**	**2 (40.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
HAQ [0-3]									
Size (missing)				2 (0)		2 (0)			
Mean (± SD)				0.6 (0.9)		0.6 (0.9)			
Median				0.6		0.6			
[p25% - p75%]				[0.0;1.3]		[0.0;1.3]			
[Min - Max]				[0.0;1.3]		[0.0;1.3]			
[40-50[	**2 (40.0)**	**1 (25.0)**	**1 (100.0)**	**1 (4.8)**	**1 (6.3)**	**0 (0.0)**	**2 (10.0)**	**2 (11.8)**	**0 (0.0)**
HAQ [0-3]									
Size (missing)	2 (0)	1 (0)	1 (0)	1 (0)	1 (0)		2 (0)	2 (0)	
Mean (± SD)	0.0 (0.0)	0.0	0.0	0.0	0.0		0.3 (0.0)	0.3 (0.0)	
Median	0.0	0.0	0.0	0.0	0.0		0.3	0.3	
[p25% - p75%]	[0.0;0.0]	[0.0;0.0]	[0.0;0.0]	[0.0;0.0]	[0.0;0.0]		[0.3;0.3]	[0.3;0.3]	
[Min - Max]	[0.0;0.0]	[0.0;0.0]	[0.0;0.0]	[0.0;0.0]	[0.0;0.0]		[0.3;0.3]	[0.3;0.3]	

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	**Women n = 4**	**Men n = 1**	**ALL n = 21**	**Women n = 16**	**Men n = 5**	**ALL n = 20**	**Women n = 17**	**Men n = 3**
[50-60[	**1 (20.0)**	**1 (25.0)**	**0 (0.0)**	**7 (33.3)**	**6 (37.5)**	**1 (20.0)**	**6 (30.0)**	**5 (29.4)**	**1 (33.3)**
HAQ [0-3]									
Size (missing)	1 (0)	1 (0)		7 (0)	6 (0)	1 (0)	6 (0)	5 (0)	1 (0)
Mean (± SD)	1.4	1.4		1.0 (0.5)	1.1 (0.4)	0.3	1.1 (0.5)	1.2 (0.6)	0.8
Median	1.4	1.4		0.9	1.1	0.3	0.9	1.0	0.8
[p25% - p75%]	[1.4;1.4]	[1.4;1.4]		[0.6;1.5]	[0.8;1.5]	[0.3;0.3]	[0.8;1.5]	[0.8;1.5]	[0.8;0.8]
[Min - Max]	[1.4;1.4]	[1.4;1.4]		[0.3;1.5]	[0.6;1.5]	[0.3;0.3]	[0.6;2.0]	[0.6;2.0]	[0.8;0.8]
[60-65[	**1 (20.0)**	**1 (25.0)**	**0 (0.0)**	**4 (19.0)**	**2 (12.5)**	**2 (40.0)**	**4 (20.0)**	**3 (17.6)**	**1 (33.3)**
HAQ [0-3]									
Size (missing)	1 (0)	1 (0)		4 (0)	2 (0)	2 (0)	4 (0)	3 (0)	1 (0)
Mean (± SD)	1.4	1.4		1.4 (0.6)	1.4 (0.2)	1.4 (1.1)	0.7 (0.5)	0.9 (0.4)	0.0
Median	1.4	1.4		1.4	1.4	1.4	0.7	0.9	0.0
[p25% - p75%]	[1.4;1.4]	[1.4;1.4]		[0.9;1.8]	[1.3;1.5]	[0.6;2.1]	[0.3;1.1]	[0.5;1.3]	[0.0;0.0]
[Min - Max]	[1.4;1.4]	[1.4;1.4]		[0.6;2.1]	[1.3;1.5]	[0.6;2.1]	[0.0;1.3]	[0.5;1.3]	[0.0;0.0]
≥65	**1 (20.0)**	**1 (25.0)**	**0 (0.0)**	**6 (28.6)**	**6 (37.5)**	**0 (0.0)**	**4 (20.0)**	**3 (17.6)**	**1 (33.3)**
HAQ [0-3]									
Size (missing)	1 (0)	1 (0)		6 (0)	6 (0)		4 (0)	3 (0)	1 (0)
Mean (± SD)	0.4	0.4		1.5 (0.9)	1.5 (0.9)		1.7 (0.7)	1.8 (0.9)	1.6
Median	0.4	0.4		1.6	1.6		1.5	1.4	1.6
[p25% - p75%]	[0.4;0.4]	[0.4;0.4]		[1.1;2.1]	[1.1;2.1]		[1.3;2.2]	[1.1;2.8]	[1.6;1.6]
[Min - Max]	[0.4;0.4]	[0.4;0.4]		[0.0;2.5]	[0.0;2.5]		[1.1;2.8]	[1.1;2.8]	[1.6;1.6]

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 14. Description of RA severity among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and according to age at the date of initiation of the considered drug, whatever the rank of treatment line

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	Women n = 72	Men n = 24	ALL n = 103	Women n = 80	Men n = 23	ALL n = 21	Women n = 15	Men n = 6	ALL n = 11	Women n = 8	Men n = 3
Total												
RA severity, n (%)												
Not severe RA	30 (31.3)	21 (29.2)	9 (37.5)	26 (25.2)	18 (22.5)	8 (34.8)	5 (23.8)	4 (26.7)	1 (16.7)	3 (27.3)	1 (12.5)	2 (66.7)
Severe RA	66 (68.8)	51 (70.8)	15 (62.5)	77 (74.8)	62 (77.5)	15 (65.2)	16 (76.2)	11 (73.3)	5 (83.3)	8 (72.7)	7 (87.5)	1 (33.3)
[18-30[	**5 (5.2)**	**3 (4.2)**	**2 (8.3)**	**8 (7.8)**	**7 (8.8)**	**1 (4.3)**	**3 (14.3)**	**2 (13.3)**	**1 (16.7)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
RA severity, n (%)												
Not severe RA	3 (60.0)	1 (33.3)	2 (100.0)	4 (50.0)	3 (42.9)	1 (100.0)	1 (33.3)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe RA	2 (40.0)	2 (66.7)	0 (0.0)	4 (50.0)	4 (57.1)	0 (0.0)	2 (66.7)	1 (50.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
[30-40[	**18 (18.8)**	**14 (19.4)**	**4 (16.7)**	**8 (7.8)**	**6 (7.5)**	**2 (8.7)**	**3 (14.3)**	**3 (20.0)**	**0 (0.0)**	**1 (9.1)**	**1 (12.5)**	**0 (0.0)**
RA severity, n (%)												
Not severe RA	8 (44.4)	7 (50.0)	1 (25.0)	2 (25.0)	2 (33.3)	0 (0.0)	2 (66.7)	2 (66.7)	0 (0.0)	1 (100.0)	1 (100.0)	0 (0.0)
Severe RA	10 (55.6)	7 (50.0)	3 (75.0)	6 (75.0)	4 (66.7)	2 (100.0)	1 (33.3)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
[40-50[	**26 (27.1)**	**23 (31.9)**	**3 (12.5)**	**20 (19.4)**	**17 (21.3)**	**3 (13.0)**	**7 (33.3)**	**4 (26.7)**	**3 (50.0)**	**3 (27.3)**	**2 (25.0)**	**1 (33.3)**
RA severity, n (%)												
Not severe RA	7 (26.9)	6 (26.1)	1 (33.3)	6 (30.0)	3 (17.6)	3 (100.0)	1 (14.3)	0 (0.0)	1 (33.3)	1 (33.3)	0 (0.0)	1 (100.0)
Severe RA	19 (73.1)	17 (73.9)	2 (66.7)	14 (70.0)	14 (82.4)	0 (0.0)	6 (85.7)	4 (100.0)	2 (66.7)	2 (66.7)	2 (100.0)	0 (0.0)
[50-60[	**31 (32.3)**	**22 (30.6)**	**9 (37.5)**	**39 (37.9)**	**29 (36.3)**	**10 (43.5)**	**4 (19.0)**	**3 (20.0)**	**1 (16.7)**	**2 (18.2)**	**2 (25.0)**	**0 (0.0)**
RA severity, n (%)												
Not severe RA	9 (29.0)	6 (27.3)	3 (33.3)	8 (20.5)	5 (17.2)	3 (30.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe RA	22 (71.0)	16 (72.7)	6 (66.7)	31 (79.5)	24 (82.8)	7 (70.0)	4 (100.0)	3 (100.0)	1 (100.0)	2 (100.0)	2 (100.0)	0 (0.0)

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	Women n = 72	Men n = 24	ALL n = 103	Women n = 80	Men n = 23	ALL n = 21	Women n = 15	Men n = 6	ALL n = 11	Women n = 8	Men n = 3
[60-65[	**10 (10.4)**	**6 (8.3)**	**4 (16.7)**	**12 (11.7)**	**10 (12.5)**	**2 (8.7)**	**2 (9.5)**	**2 (13.3)**	**0 (0.0)**	**4 (36.4)**	**2 (25.0)**	**2 (66.7)**
RA severity, n (%)												
Not severe RA	2 (20.0)	1 (16.7)	1 (25.0)	2 (16.7)	2 (20.0)	0 (0.0)	1 (50.0)	1 (50.0)	0 (0.0)	1 (25.0)	0 (0.0)	1 (50.0)
Severe RA	8 (80.0)	5 (83.3)	3 (75.0)	10 (83.3)	8 (80.0)	2 (100.0)	1 (50.0)	1 (50.0)	0 (0.0)	3 (75.0)	2 (100.0)	1 (50.0)
≥65	**6 (6.3)**	**4 (5.6)**	**2 (8.3)**	**16 (15.5)**	**11 (13.8)**	**5 (21.7)**	**2 (9.5)**	**1 (6.7)**	**1 (16.7)**	**1 (9.1)**	**1 (12.5)**	**0 (0.0)**
RA severity, n (%)												
Not severe RA	1 (16.7)	0 (0.0)	1 (50.0)	4 (25.0)	3 (27.3)	1 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe RA	5 (83.3)	4 (100.0)	1 (50.0)	12 (75.0)	8 (72.7)	4 (80.0)	2 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	0 (0.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 15. Description of RA severity among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and according to age at the date of initiation of the considered drug, whatever the rank of treatment line

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	Women n = 4	Men n = 1	ALL n = 21	Women n = 16	Men n = 5	ALL n = 20	Women n = 17	Men n = 3
Total									
RA severity, n (%)									
Not severe RA	3 (60.0)	2 (50.0)	1 (100.0)	4 (19.0)	2 (12.5)	2 (40.0)	4 (20.0)	3 (17.6)	1 (33.3)
Severe RA	2 (40.0)	2 (50.0)	0 (0.0)	17 (81.0)	14 (87.5)	3 (60.0)	16 (80.0)	14 (82.4)	2 (66.7)
[18-30[	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**1 (4.8)**	**1 (6.3)**	**0 (0.0)**	**4 (20.0)**	**4 (23.5)**	**0 (0.0)**
RA severity, n (%)									
Not severe RA	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (25.0)	0 (0.0)
Severe RA	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)	0 (0.0)	3 (75.0)	3 (75.0)	0 (0.0)
[30-40[	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**2 (9.5)**	**0 (0.0)**	**2 (40.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
RA severity, n (%)									
Not severe RA	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	0 (0.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe RA	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	0 (0.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)
[40-50[	**2 (40.0)**	**1 (25.0)**	**1 (100.0)**	**1 (4.8)**	**1 (6.3)**	**0 (0.0)**	**2 (10.0)**	**2 (11.8)**	**0 (0.0)**
RA severity, n (%)									
Not severe RA	2 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	0 (0.0)	2 (100.0)	2 (100.0)	0 (0.0)
Severe RA	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)
[50-60[	**1 (20.0)**	**1 (25.0)**	**0 (0.0)**	**7 (33.3)**	**6 (37.5)**	**1 (20.0)**	**6 (30.0)**	**5 (29.4)**	**1 (33.3)**
RA severity, n (%)									
Not severe RA	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe RA	1 (100.0)	1 (100.0)	0 (0.0)	6 (85.7)	6 (100.0)	0 (0.0)	6 (100.0)	5 (100.0)	1 (100.0)
[60-65[	**1 (20.0)**	**1 (25.0)**	**0 (0.0)**	**4 (19.0)**	**2 (12.5)**	**2 (40.0)**	**4 (20.0)**	**3 (17.6)**	**1 (33.3)**
RA severity, n (%)									
Not severe RA	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	1 (100.0)
Severe RA	1 (100.0)	1 (100.0)	0 (0.0)	4 (100.0)	2 (100.0)	2 (100.0)	3 (75.0)	3 (100.0)	0 (0.0)

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	**Women n = 4**	**Men n = 1**	**ALL n = 21**	**Women n = 16**	**Men n = 5**	**ALL n = 20**	**Women n = 17**	**Men n = 3**
≥65	**1 (20.0)**	**1 (25.0)**	**0 (0.0)**	**6 (28.6)**	**6 (37.5)**	**0 (0.0)**	**4 (20.0)**	**3 (17.6)**	**1 (33.3)**
RA severity, n (%)									
Not severe RA	1 (100.0)	1 (100.0)	0 (0.0)	1 (16.7)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe RA	0 (0.0)	0 (0.0)	0 (0.0)	5 (83.3)	5 (83.3)	0 (0.0)	4 (100.0)	3 (100.0)	1 (100.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

3.3 BY RA SEVERITY

3.3.1 BMI

Table 16. Description of Body Mass Index (BMI) among patients with Rheumatoid Arthritis aged ≥ 18 years for overall population and by RA severity according to age at the date of initiation of the first treatment line among the drugs of interest[1]

	All drugs of interest[1]			TNFi[2]		
	All n = 180	Severe RA n = 123	Not Severe RA n = 57	All n = 172	Severe RA n = 117	Not Severe RA n = 55
Total						
BMI (kg/m2)						
Size (missing)	180 (0)	123 (0)	57 (0)	172 (0)	117 (0)	55 (0)
Mean (± SD)	25.3 (4.8)	25.7 (5.1)	24.4 (4.0)	25.2 (4.9)	25.7 (5.2)	24.3 (4.0)
Median	24.4	24.4	24.4	24.3	24.4	23.5
[p25% - p75%]	[21.7;27.8]	[21.9;29.0]	[21.6;26.3]	[21.6;27.8]	[21.9;29.0]	[21.5;26.0]
[Min - Max]	[16.4;43.5]	[17.2;43.5]	[16.4;35.8]	[16.4;43.5]	[17.2;43.5]	[16.4;35.8]
[18-30[	**14 (7.8)**	**6 (4.9)**	**8 (14.0)**	**14 (8.1)**	**6 (5.1)**	**8 (14.5)**
BMI (kg/m2)						
Size (missing)	14 (0)	6 (0)	8 (0)	14 (0)	6 (0)	8 (0)
Mean (± SD)	21.8 (2.8)	21.0 (2.1)	22.4 (3.2)	21.8 (2.8)	21.0 (2.1)	22.4 (3.2)
Median	21.9	20.6	22.4	21.9	20.6	22.4
[p25% - p75%]	[19.8;24.0]	[19.1;22.8]	[20.8;25.3]	[19.8;24.0]	[19.1;22.8]	[20.8;25.3]
[Min - Max]	[16.4;25.8]	[18.9;24.0]	[16.4;25.8]	[16.4;25.8]	[18.9;24.0]	[16.4;25.8]
[30-40[	**22 (12.2)**	**14 (11.4)**	**8 (14.0)**	**22 (12.8)**	**14 (12.0)**	**8 (14.5)**
BMI (kg/m2)						
Size (missing)	22 (0)	14 (0)	8 (0)	22 (0)	14 (0)	8 (0)
Mean (± SD)	23.3 (3.2)	23.6 (3.2)	22.9 (3.3)	23.3 (3.2)	23.6 (3.2)	22.9 (3.3)
Median	22.6	23.4	21.3	22.6	23.4	21.3
[p25% - p75%]	[20.8;25.7]	[20.9;25.7]	[20.3;25.8]	[20.8;25.7]	[20.9;25.7]	[20.3;25.8]
[Min - Max]	[19.6;29.6]	[20.1;29.6]	[19.6;28.3]	[19.6;29.6]	[20.1;29.6]	[19.6;28.3]

	All drugs of interest[1]			TNFi[2]		
	All	Severe RA	Not Severe RA	All	Severe RA	Not Severe RA
	n = 180	n = 123	n = 57	n = 172	n = 117	n = 55
[40-50[	**45 (25.0)**	**31 (25.2)**	**14 (24.6)**	**44 (25.6)**	**31 (26.5)**	**13 (23.6)**
BMI (kg/m2)						
Size (missing)	45 (0)	31 (0)	14 (0)	44 (0)	31 (0)	13 (0)
Mean (± SD)	24.8 (4.9)	25.2 (5.5)	24.0 (3.4)	24.8 (5.0)	25.2 (5.5)	23.8 (3.5)
Median	23.8	23.8	24.0	23.8	23.8	23.1
[p25% - p75%]	[21.5;26.3]	[21.6;26.8]	[21.1;26.3]	[21.3;26.4]	[21.6;26.8]	[21.1;25.5]
[Min - Max]	[18.6;39.8]	[18.6;39.8]	[19.1;31.4]	[18.6;39.8]	[18.6;39.8]	[19.1;31.4]
[50-60[	**56 (31.1)**	**41 (33.3)**	**15 (26.3)**	**55 (32.0)**	**40 (34.2)**	**15 (27.3)**
BMI (kg/m2)						
Size (missing)	56 (0)	41 (0)	15 (0)	55 (0)	40 (0)	15 (0)
Mean (± SD)	26.4 (5.2)	26.9 (5.6)	24.8 (4.0)	26.4 (5.3)	27.0 (5.6)	24.8 (4.0)
Median	25.3	26.2	24.8	25.5	26.2	24.8
[p25% - p75%]	[22.8;29.0]	[23.0;29.7]	[22.2;26.5]	[22.7;29.1]	[22.9;29.9]	[22.2;26.5]
[Min - Max]	[17.2;43.5]	[17.2;43.5]	[18.1;33.2]	[17.2;43.5]	[17.2;43.5]	[18.1;33.2]
[60-65[	**22 (12.2)**	**17 (13.8)**	**5 (8.8)**	**19 (11.0)**	**14 (12.0)**	**5 (9.1)**
BMI (kg/m2)						
Size (missing)	22 (0)	17 (0)	5 (0)	19 (0)	14 (0)	5 (0)
Mean (± SD)	26.9 (4.9)	27.4 (4.9)	25.3 (4.9)	27.0 (5.2)	27.6 (5.4)	25.3 (4.9)
Median	27.4	28.6	24.4	27.7	28.8	24.4
[p25% - p75%]	[23.3;30.0]	[23.7;30.0]	[23.3;25.8]	[22.9;30.5]	[22.9;30.5]	[23.3;25.8]
[Min - Max]	[17.9;36.8]	[17.9;36.8]	[20.1;33.2]	[17.9;36.8]	[17.9;36.8]	[20.1;33.2]
≥65	**21 (11.7)**	**14 (11.4)**	**7 (12.3)**	**18 (10.5)**	**12 (10.3)**	**6 (10.9)**
BMI (kg/m2)						
Size (missing)	21 (0)	14 (0)	7 (0)	18 (0)	12 (0)	6 (0)
Mean (± SD)	26.0 (4.4)	24.9 (3.8)	28.0 (4.9)	25.9 (4.3)	25.2 (4.0)	27.3 (5.1)
Median	26.7	25.0	27.7	26.8	25.9	27.3
[p25% - p75%]	[21.9;29.2]	[21.3;28.0]	[22.5;32.0]	[21.9;29.2]	[21.4;28.7]	[22.5;29.2]
[Min - Max]	[19.7;35.8]	[19.7;30.1]	[21.9;35.8]	[19.7;35.8]	[19.7;30.1]	[21.9;35.8]

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB
2. TNFi: ADALIMUMAB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB
   JAK inhibitors: BARICITINIB, TOFACITINIB (not available in the database)

Table 17. Description of Body Mass Index (BMI) in categories among patients with Rheumatoid Arthritis aged ≥ 18 years for overall population and by RA severity according to age at the date of initiation of the first treatment line among the drugs of interest[1]

	All drugs of interest[1]						TNFi[2]					
	All n = 180		Severe RA n = 123		Not Severe RA n = 57		All n = 172		Severe RA n = 117		Not Severe RA n = 55	
Total												
BMI (kg/m2) (in categories), n (%)												
<18.5	4	(2.2)	2	(1.6)	2	(3.5)	4	(2.3)	2	(1.7)	2	(3.6)
[18.5-25[	93	(51.7)	62	(50.4)	31	(54.4)	89	(51.7)	58	(49.6)	31	(56.4)
[25-30[	54	(30.0)	36	(29.3)	18	(31.6)	51	(29.7)	34	(29.1)	17	(30.9)
≥30	29	(16.1)	23	(18.7)	6	(10.5)	28	(16.3)	23	(19.7)	5	(9.1)
[18-30[	**14**	**(7.8)**	**6**	**(4.9)**	**8**	**(14.0)**	**14**	**(8.1)**	**6**	**(5.1)**	**8**	**(14.5)**
BMI (kg/m2) (in categories), n (%)												
<18.5	1	(7.1)	0	(0.0)	1	(12.5)	1	(7.1)	0	(0.0)	1	(12.5)
[18.5-25[	11	(78.6)	6	(100.0)	5	(62.5)	11	(78.6)	6	(100.0)	5	(62.5)
[25-30[	2	(14.3)	0	(0.0)	2	(25.0)	2	(14.3)	0	(0.0)	2	(25.0)
≥30	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
[30-40[	**22**	**(12.2)**	**14**	**(11.4)**	**8**	**(14.0)**	**22**	**(12.8)**	**14**	**(12.0)**	**8**	**(14.5)**
BMI (kg/m2) (in categories), n (%)												
<18.5	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
[18.5-25[	14	(63.6)	9	(64.3)	5	(62.5)	14	(63.6)	9	(64.3)	5	(62.5)
[25-30[	8	(36.4)	5	(35.7)	3	(37.5)	8	(36.4)	5	(35.7)	3	(37.5)
≥30	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
[40-50[	**45**	**(25.0)**	**31**	**(25.2)**	**14**	**(24.6)**	**44**	**(25.6)**	**31**	**(26.5)**	**13**	**(23.6)**
BMI (kg/m2) (in categories), n (%)												
<18.5	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
[18.5-25[	29	(64.4)	20	(64.5)	9	(64.3)	29	(65.9)	20	(64.5)	9	(69.2)
[25-30[	9	(20.0)	5	(16.1)	4	(28.6)	8	(18.2)	5	(16.1)	3	(23.1)
≥30	7	(15.6)	6	(19.4)	1	(7.1)	7	(15.9)	6	(19.4)	1	(7.7)

	All drugs of interest[1]						TNFi[2]					
	All n = 180		Severe RA n = 123		Not Severe RA n = 57		All n = 172		Severe RA n = 117		Not Severe RA n = 55	
[50-60[	**56**	**(31.1)**	**41**	**(33.3)**	**15**	**(26.3)**	**55**	**(32.0)**	**40**	**(34.2)**	**15**	**(27.3)**
BMI (kg/m2) (in categories), n (%)												
<18.5	2	(3.6)	1	(2.4)	1	(6.7)	2	(3.6)	1	(2.5)	1	(6.7)
[18.5-25[	23	(41.1)	16	(39.0)	7	(46.7)	22	(40.0)	15	(37.5)	7	(46.7)
[25-30[	19	(33.9)	14	(34.1)	5	(33.3)	19	(34.5)	14	(35.0)	5	(33.3)
≥30	12	(21.4)	10	(24.4)	2	(13.3)	12	(21.8)	10	(25.0)	2	(13.3)
[60-65[	**22**	**(12.2)**	**17**	**(13.8)**	**5**	**(8.8)**	**19**	**(11.0)**	**14**	**(12.0)**	**5**	**(9.1)**
BMI (kg/m2) (in categories), n (%)												
<18.5	1	(4.5)	1	(5.9)	0	(0.0)	1	(5.3)	1	(7.1)	0	(0.0)
[18.5-25[	7	(31.8)	4	(23.5)	3	(60.0)	6	(31.6)	3	(21.4)	3	(60.0)
[25-30[	8	(36.4)	7	(41.2)	1	(20.0)	6	(31.6)	5	(35.7)	1	(20.0)
≥30	6	(27.3)	5	(29.4)	1	(20.0)	6	(31.6)	5	(35.7)	1	(20.0)
≥65	**21**	**(11.7)**	**14**	**(11.4)**	**7**	**(12.3)**	**18**	**(10.5)**	**12**	**(10.3)**	**6**	**(10.9)**
BMI (kg/m2) (in categories), n (%)												
<18.5	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
[18.5-25[	9	(42.9)	7	(50.0)	2	(28.6)	7	(38.9)	5	(41.7)	2	(33.3)
[25-30[	8	(38.1)	5	(35.7)	3	(42.9)	8	(44.4)	5	(41.7)	3	(50.0)
≥30	4	(19.0)	2	(14.3)	2	(28.6)	3	(16.7)	2	(16.7)	1	(16.7)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB
2. TNFi: ADALIMUMAB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB
   JAK inhibitors: BARICITINIB, TOFACITINIB (not available in the database)

Table 18. Description of Body Mass Index (BMI) among patients with Rheumatoid Arthritis aged ≥ 18 years for overall population and by RA severity according to gender at the date of initiation of the first treatment line among the drugs of interest[1]

	All drugs of interest[1]			TNFi[2]		
	All n = 180	**Severe RA n = 123**	**Not Severe RA n = 57**	**All n = 172**	**Severe RA n = 117**	**Not Severe RA n = 55**
Total						
BMI (kg/m2)						
Size (missing)	180 (0)	123 (0)	57 (0)	172 (0)	117 (0)	55 (0)
Mean (± SD)	25.3 (4.8)	25.7 (5.1)	24.4 (4.0)	25.2 (4.9)	25.7 (5.2)	24.3 (4.0)
Median	24.4	24.4	24.4	24.3	24.4	23.5
[p25% - p75%]	[21.7;27.8]	[21.9;29.0]	[21.6;26.3]	[21.6;27.8]	[21.9;29.0]	[21.5;26.0]
[Min - Max]	[16.4;43.5]	[17.2;43.5]	[16.4;35.8]	[16.4;43.5]	[17.2;43.5]	[16.4;35.8]
Women	**134 (74.4)**	**95 (77.2)**	**39 (68.4)**	**127 (73.8)**	**90 (76.9)**	**37 (67.3)**
BMI (kg/m2)						
Size (missing)	134 (0)	95 (0)	39 (0)	127 (0)	90 (0)	37 (0)
Mean (± SD)	25.0 (4.9)	25.4 (5.2)	23.9 (3.9)	24.9 (5.0)	25.5 (5.3)	23.6 (3.8)
Median	24.0	24.0	23.3	23.9	24.1	23.1
[p25% - p75%]	[21.6;27.7]	[21.7;29.0]	[21.1;25.5]	[21.3;27.7]	[21.7;29.1]	[21.1;25.2]
[Min - Max]	[16.4;43.5]	[17.2;43.5]	[16.4;35.8]	[16.4;43.5]	[17.2;43.5]	[16.4;35.8]
Men	**46 (25.6)**	**28 (22.8)**	**18 (31.6)**	**45 (26.2)**	**27 (23.1)**	**18 (32.7)**
BMI (kg/m2)						
Size (missing)	46 (0)	28 (0)	18 (0)	45 (0)	27 (0)	18 (0)
Mean (± SD)	26.1 (4.6)	26.4 (4.9)	25.6 (4.1)	26.1 (4.6)	26.4 (5.0)	25.6 (4.1)
Median	25.9	26.1	25.8	25.9	26.0	25.8
[p25% - p75%]	[22.2;28.0]	[22.6;28.4]	[21.8;28.0]	[22.2;28.0]	[22.3;29.0]	[21.8;28.0]
[Min - Max]	[19.0;38.2]	[19.0;38.2]	[19.1;33.2]	[19.0;38.2]	[19.0;38.2]	[19.1;33.2]

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB
2. TNFi: ADALIMUMAB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB
   JAK inhibitors: BARICITINIB, TOFACITINIB (not available in the database)

Table 19. Description of Body Mass Index (BMI) in categories among patients with Rheumatoid Arthritis aged ≥ 18 years for overall population and by RA severity according to gender at the date of initiation of the first treatment line among the drugs of interest[1]

	All drugs of interest[1]						TNFi[2]					
	All n = 180		Severe RA n = 123		Not Severe RA n = 57		All n = 172		Severe RA n = 117		Not Severe RA n = 55	
Total												
BMI (kg/m2) (in categories), n (%)												
<18.5	4	(2.2)	2	(1.6)	2	(3.5)	4	(2.3)	2	(1.7)	2	(3.6)
[18.5-25[	93	(51.7)	62	(50.4)	31	(54.4)	89	(51.7)	58	(49.6)	31	(56.4)
[25-30[	54	(30.0)	36	(29.3)	18	(31.6)	51	(29.7)	34	(29.1)	17	(30.9)
≥30	29	(16.1)	23	(18.7)	6	(10.5)	28	(16.3)	23	(19.7)	5	(9.1)
Women	**134**	**(74.4)**	**95**	**(77.2)**	**39**	**(68.4)**	**127**	**(73.8)**	**90**	**(76.9)**	**37**	**(67.3)**
BMI (kg/m2) (in categories), n (%)												
<18.5	4	(3.0)	2	(2.1)	2	(5.1)	4	(3.1)	2	(2.2)	2	(5.4)
[18.5-25[	74	(55.2)	51	(53.7)	23	(59.0)	70	(55.1)	47	(52.2)	23	(62.2)
[25-30[	35	(26.1)	24	(25.3)	11	(28.2)	33	(26.0)	23	(25.6)	10	(27.0)
≥30	21	(15.7)	18	(18.9)	3	(7.7)	20	(15.7)	18	(20.0)	2	(5.4)
Men	**46**	**(25.6)**	**28**	**(22.8)**	**18**	**(31.6)**	**45**	**(26.2)**	**27**	**(23.1)**	**18**	**(32.7)**
BMI (kg/m2) (in categories), n (%)												
<18.5	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
[18.5-25[	19	(41.3)	11	(39.3)	8	(44.4)	19	(42.2)	11	(40.7)	8	(44.4)
[25-30[	19	(41.3)	12	(42.9)	7	(38.9)	18	(40.0)	11	(40.7)	7	(38.9)
≥30	8	(17.4)	5	(17.9)	3	(16.7)	8	(17.8)	5	(18.5)	3	(16.7)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB
2. TNFi: ADALIMUMAB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB
   JAK inhibitors: BARICITINIB, TOFACITINIB (not available in the database)

Table 20. Description of Body Mass Index (BMI) among patients with Rheumatoid Arthritis aged ≥ 18 years for overall population and according to calendar year at the date of initiation of the first treatment line among the drugs of interest[1]

	All drugs of interest[1]			TNFi[2]		
	All n = 180	**Severe RA n = 123**	**Not Severe RA n = 57**	**All n = 172**	**Severe RA n = 117**	**Not Severe RA n = 55**
Total						
BMI (kg/m2)						
Size (missing)	180 (0)	123 (0)	57 (0)	172 (0)	117 (0)	55 (0)
Mean (± SD)	25.3 (4.8)	25.7 (5.1)	24.4 (4.0)	25.2 (4.9)	25.7 (5.2)	24.3 (4.0)
Median	24.4	24.4	24.4	24.3	24.4	23.5
[p25% - p75%]	[21.7;27.8]	[21.9;29.0]	[21.6;26.3]	[21.6;27.8]	[21.9;29.0]	[21.5;26.0]
[Min - Max]	[16.4;43.5]	[17.2;43.5]	[16.4;35.8]	[16.4;43.5]	[17.2;43.5]	[16.4;35.8]
[2003-2009]	**131 (72.8)**	**94 (76.4)**	**37 (64.9)**	**129 (75.0)**	**92 (78.6)**	**37 (67.3)**
BMI (kg/m2)						
Size (missing)	131 (0)	94 (0)	37 (0)	129 (0)	92 (0)	37 (0)
Mean (± SD)	24.9 (4.8)	25.2 (5.2)	24.1 (3.7)	24.9 (4.9)	25.2 (5.2)	24.1 (3.7)
Median	23.9	24.0	23.1	23.8	23.9	23.1
[p25% - p75%]	[21.5;27.7]	[21.6;28.6]	[21.5;25.7]	[21.5;27.3]	[21.5;28.2]	[21.5;25.7]
[Min - Max]	[17.2;43.5]	[17.2;43.5]	[18.1;33.2]	[17.2;43.5]	[17.2;43.5]	[18.1;33.2]
[2010-2016]	**49 (27.2)**	**29 (23.6)**	**20 (35.1)**	**43 (25.0)**	**25 (21.4)**	**18 (32.7)**
BMI (kg/m2)						
Size (missing)	49 (0)	29 (0)	20 (0)	43 (0)	25 (0)	18 (0)
Mean (± SD)	26.3 (4.7)	27.1 (4.6)	25.1 (4.6)	26.4 (4.8)	27.7 (4.7)	24.7 (4.5)
Median	26.3	26.7	25.2	26.5	27.4	24.6
[p25% - p75%]	[23.1;28.5]	[23.4;29.4]	[21.9;27.3]	[22.9;29.0]	[25.1;30.0]	[21.6;26.8]
[Min - Max]	[16.4;38.2]	[20.8;38.2]	[16.4;35.8]	[16.4;38.2]	[20.8;38.2]	[16.4;35.8]

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB
2. TNFi: ADALIMUMAB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB
   JAK inhibitors: BARICITINIB, TOFACITINIB (not available in the database)

Table 21. Description of Body Mass Index (BMI) in categories among patients with Rheumatoid Arthritis aged ≥ 18 years for overall population and by RA severity according to calendar year at the date of initiation of the first treatment line among the drugs of interest[1]

	All drugs of interest[1]						TNFi[2]					
	All n = 180		Severe RA n = 123		Not Severe RA n = 57		All n = 172		Severe RA n = 117		Not Severe RA n = 55	
Total												
BMI (kg/m2) (in categories), n (%)												
<18.5	4	(2.2)	2	(1.6)	2	(3.5)	4	(2.3)	2	(1.7)	2	(3.6)
[18.5-25[	93	(51.7)	62	(50.4)	31	(54.4)	89	(51.7)	58	(49.6)	31	(56.4)
[25-30[	54	(30.0)	36	(29.3)	18	(31.6)	51	(29.7)	34	(29.1)	17	(30.9)
≥30	29	(16.1)	23	(18.7)	6	(10.5)	28	(16.3)	23	(19.7)	5	(9.1)
[2003-2009]	**131**	**(72.8)**	**94**	**(76.4)**	**37**	**(64.9)**	**129**	**(75.0)**	**92**	**(78.6)**	**37**	**(67.3)**
BMI (kg/m2) (in categories), n (%)												
<18.5	3	(2.3)	2	(2.1)	1	(2.7)	3	(2.3)	2	(2.2)	1	(2.7)
[18.5-25[	74	(56.5)	52	(55.3)	22	(59.5)	74	(57.4)	52	(56.5)	22	(59.5)
[25-30[	35	(26.7)	24	(25.5)	11	(29.7)	33	(25.6)	22	(23.9)	11	(29.7)
≥30	19	(14.5)	16	(17.0)	3	(8.1)	19	(14.7)	16	(17.4)	3	(8.1)
[2010-2016]	**49**	**(27.2)**	**29**	**(23.6)**	**20**	**(35.1)**	**43**	**(25.0)**	**25**	**(21.4)**	**18**	**(32.7)**
BMI (kg/m2) (in categories), n (%)												
<18.5	1	(2.0)	0	(0.0)	1	(5.0)	1	(2.3)	0	(0.0)	1	(5.6)
[18.5-25[	19	(38.8)	10	(34.5)	9	(45.0)	15	(34.9)	6	(24.0)	9	(50.0)
[25-30[	19	(38.8)	12	(41.4)	7	(35.0)	18	(41.9)	12	(48.0)	6	(33.3)
≥30	10	(20.4)	7	(24.1)	3	(15.0)	9	(20.9)	7	(28.0)	2	(11.1)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB
2. TNFi: ADALIMUMAB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB
   JAK inhibitors: BARICITINIB, TOFACITINIB (not available in the database)

Table 22. Description of Body Mass Index (BMI) among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and by RA severity according to age at the date of initiation of the considered drug, whatever the rank of treatment line

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	Severe RA n = 66	Not Severe RA n = 30	ALL n = 103	Severe RA n = 77	Not Severe RA n = 26	ALL n = 21	Severe RA n = 16	Not Severe RA n = 5	ALL n = 11	Severe RA n = 8	Not Severe RA n = 3
Total												
BMI (kg/m2)												
Size (missing)	96 (0)	66 (0)	30 (0)	103 (0)	77 (0)	26 (0)	21 (0)	16 (0)	5 (0)	11 (0)	8 (0)	3 (0)
Mean (± SD)	25.2 (5.0)	25.9 (5.4)	23.8 (3.8)	25.2 (4.6)	25.3 (4.8)	24.8 (3.8)	25.6 (6.6)	26.5 (6.9)	22.6 (4.9)	25.4 (6.3)	24.5 (4.5)	27.7 (10.8)
Median	24.7	25.4	22.7	24.2	24.1	24.4	23.8	24.1	23.3	22.6	23.9	21.8
[p25% - p75%]	[21.6;27.4]	[22.2;28.6]	[21.0;25.8]	[21.8;27.9]	[21.3;28.5]	[21.9;27.3]	[21.5;28.3]	[21.6;30.4]	[19.1;26.0]	[20.9;29.0]	[20.5;28.2]	[21.1;40.1]
[Min - Max]	[17.2;43.5]	[17.2;43.5]	[18.1;33.2]	[17.6;39.8]	[17.6;39.8]	[20.1;35.8]	[16.4;46.6]	[19.1;46.6]	[16.4;28.3]	[19.4;40.1]	[19.4;31.6]	[21.1;40.1]
[18-30[	**5 (5.2)**	**2 (3.0)**	**3 (10.0)**	**8 (7.8)**	**4 (5.2)**	**4 (15.4)**	**3 (14.3)**	**2 (12.5)**	**1 (20.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
BMI (kg/m2)												
Size (missing)	5 (0)	2 (0)	3 (0)	8 (0)	4 (0)	4 (0)	3 (0)	2 (0)	1 (0)			
Mean (± SD)	23.3 (2.5)	24.3 (2.1)	22.7 (2.9)	22.3 (2.4)	20.9 (2.2)	23.7 (1.9)	19.0 (2.6)	20.3 (1.7)	16.4			
Median	22.8	24.3	22.2	22.1	20.4	23.7	19.1	20.3	16.4			
[p25% - p75%]	[22.2;25.8]	[22.8;25.8]	[20.0;25.8]	[20.4;24.4]	[19.4;22.5]	[22.1;25.3]	[16.4;21.5]	[19.1;21.5]	[16.4;16.4]			
[Min - Max]	[20.0;25.8]	[22.8;25.8]	[20.0;25.8]	[18.9;25.7]	[18.9;24.0]	[21.6;25.7]	[16.4;21.5]	[19.1;21.5]	[16.4;16.4]			
[30-40[	**18 (18.8)**	**10 (15.2)**	**8 (26.7)**	**8 (7.8)**	**6 (7.8)**	**2 (7.7)**	**3 (14.3)**	**1 (6.3)**	**2 (40.0)**	**1 (9.1)**	**0 (0.0)**	**1 (33.3)**
BMI (kg/m2)												
Size (missing)	18 (0)	10 (0)	8 (0)	8 (0)	6 (0)	2 (0)	3 (0)	1 (0)	2 (0)	1 (0)		1 (0)
Mean (± SD)	22.6 (2.8)	23.5 (3.0)	21.4 (2.0)	23.0 (3.0)	23.5 (3.3)	21.6 (0.7)	25.4 (3.4)	21.7	27.2 (1.6)	21.8		21.8
Median	21.8	23.5	21.2	22.7	23.5	21.6	26.0	21.7	27.2	21.8		21.8
[p25% - p75%]	[20.2;25.3]	[20.9;25.7]	[19.7;22.1]	[21.0;23.5]	[20.9;23.6]	[21.1;22.0]	[21.7;28.3]	[21.7;21.7]	[26.0;28.3]	[21.8;21.8]		[21.8;21.8]
[Min - Max]	[19.6;29.0]	[20.1;29.0]	[19.6;25.5]	[20.2;29.6]	[20.2;29.6]	[21.1;22.0]	[21.7;28.3]	[21.7;21.7]	[26.0;28.3]	[21.8;21.8]		[21.8;21.8]
[40-50[	**26 (27.1)**	**19 (28.8)**	**7 (23.3)**	**20 (19.4)**	**14 (18.2)**	**6 (23.1)**	**7 (33.3)**	**6 (37.5)**	**1 (20.0)**	**3 (27.3)**	**2 (25.0)**	**1 (33.3)**
BMI (kg/m2)												
Size (missing)	26 (0)	19 (0)	7 (0)	20 (0)	14 (0)	6 (0)	7 (0)	6 (0)	1 (0)	3 (0)	2 (0)	1 (0)
Mean (± SD)	24.8 (5.0)	24.8 (5.4)	24.5 (3.9)	24.8 (5.0)	25.3 (5.8)	23.4 (2.3)	29.3 (9.1)	31.0 (8.6)	19.1	26.8 (11.5)	20.2 (1.0)	40.1
Median	24.0	23.8	24.9	23.3	23.7	23.0	26.0	28.8	19.1	20.9	20.2	40.1
[p25% - p75%]	[21.6;26.8]	[21.6;26.8]	[21.0;27.2]	[21.3;26.5]	[21.2;27.2]	[21.5;24.8]	[23.8;33.7]	[24.3;33.7]	[19.1;19.1]	[19.4;40.1]	[19.4;20.9]	[40.1;40.1]
[Min - Max]	[18.7;38.2]	[18.7;38.2]	[20.0;31.4]	[18.6;39.8]	[18.6;39.8]	[21.1;27.3]	[19.1;46.6]	[23.8;46.6]	[19.1;19.1]	[19.4;40.1]	[19.4;20.9]	[40.1;40.1]

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	**Severe RA n = 66**	**Not Severe RA n = 30**	**ALL n = 103**	**Severe RA n = 77**	**Not Severe RA n = 26**	**ALL n = 21**	**Severe RA n = 16**	**Not Severe RA n = 5**	**ALL n = 11**	**Severe RA n = 8**	**Not Severe RA n = 3**
[50-60[	31 (32.3)	22 (33.3)	9 (30.0)	39 (37.9)	31 (40.3)	8 (30.8)	4 (19.0)	4 (25.0)	0 (0.0)	2 (18.2)	2 (25.0)	0 (0.0)
BMI (kg/m2)												
Size (missing)	31 (0)	22 (0)	9 (0)	39 (0)	31 (0)	8 (0)	4 (0)	4 (0)		2 (0)	2 (0)	
Mean (± SD)	27.3 (5.7)	28.6 (5.8)	24.1 (3.9)	26.1 (4.6)	26.2 (4.9)	26.0 (3.6)	23.5 (2.8)	23.5 (2.8)		29.6 (2.9)	29.6 (2.9)	
Median	26.2	27.6	23.5	25.0	26.2	24.9	22.6	22.6		29.6	29.6	
[p25% - p75%]	[23.5;30.1]	[25.5;31.2]	[22.2;25.2]	[22.3;29.0]	[22.2;29.7]	[23.6;27.9]	[21.7;25.3]	[21.7;25.3]		[27.5;31.6]	[27.5;31.6]	
[Min - Max]	[17.2;43.5]	[17.2;43.5]	[18.1;32.0]	[19.0;38.2]	[19.0;38.2]	[21.8;33.2]	[21.3;27.5]	[21.3;27.5]		[27.5;31.6]	[27.5;31.6]	
[60-65[	**10 (10.4)**	**8 (12.1)**	**2 (6.7)**	**12 (11.7)**	**10 (13.0)**	**2 (7.7)**	**2 (9.5)**	**1 (6.3)**	**1 (20.0)**	**4 (36.4)**	**3 (37.5)**	**1 (33.3)**
BMI (kg/m2)												
Size (missing)	10 (0)	8 (0)	2 (0)	12 (0)	10 (0)	2 (0)	2 (0)	1 (0)	1 (0)	4 (0)	3 (0)	1 (0)
Mean (± SD)	25.7 (6.1)	24.7 (6.2)	29.5 (5.3)	25.9 (4.9)	26.6 (5.0)	22.2 (3.0)	27.0 (5.2)	30.6	23.3	23.2 (4.0)	23.9 (4.6)	21.1
Median	24.7	23.3	29.5	26.0	28.2	22.2	27.0	30.6	23.3	21.9	22.6	21.1
[p25% - p75%]	[21.3;28.6]	[20.1;28.0]	[25.8;33.2]	[22.1;29.7]	[22.9;30.0]	[20.1;24.4]	[23.3;30.6]	[30.6;30.6]	[23.3;23.3]	[20.6;25.8]	[20.1;29.0]	[21.1;21.1]
[Min - Max]	[17.9;36.8]	[17.9;36.8]	[25.8;33.2]	[17.6;34.3]	[17.6;34.3]	[20.1;24.4]	[23.3;30.6]	[30.6;30.6]	[23.3;23.3]	[20.1;29.0]	[20.1;29.0]	[21.1;21.1]
≥65	**6 (6.3)**	**5 (7.6)**	**1 (3.3)**	**16 (15.5)**	**12 (15.6)**	**4 (15.4)**	**2 (9.5)**	**2 (12.5)**	**0 (0.0)**	**1 (9.1)**	**1 (12.5)**	**0 (0.0)**
BMI (kg/m2)												
Size (missing)	6 (0)	5 (0)	1 (0)	16 (0)	12 (0)	4 (0)	2 (0)	2 (0)		1 (0)	1 (0)	
Mean (± SD)	25.4 (3.3)	25.1 (3.6)	26.8	25.5 (4.6)	24.5 (3.9)	28.7 (5.7)	25.5 (6.6)	25.5 (6.6)		25.2	25.2	
Median	26.8	26.7	26.8	25.5	25.1	28.5	25.5	25.5		25.2	25.2	
[p25% - p75%]	[23.3;27.8]	[23.3;27.8]	[26.8;26.8]	[21.4;28.8]	[20.5;28.0]	[24.8;32.5]	[20.8;30.1]	[20.8;30.1]		[25.2;25.2]	[25.2;25.2]	
[Min - Max]	[19.7;28.0]	[19.7;28.0]	[26.8;26.8]	[19.4;35.8]	[19.4;30.1]	[21.9;35.8]	[20.8;30.1]	[20.8;30.1]		[25.2;25.2]	[25.2;25.2]	

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 23. Description of Body Mass Index (BMI) in categories among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and by RA severity according to age at the date of initiation of the considered drug, whatever the rank of treatment line

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	Severe RA n = 66	Not Severe RA n = 30	ALL n = 103	Severe RA n = 77	Not Severe RA n = 26	ALL n = 21	Severe RA n = 16	Not Severe RA n = 5	ALL n = 11	Severe RA n = 8	Not Severe RA n = 3
Total												
BMI (kg/m2) (in categories), n (%)												
<18.5	3 (3.1)	2 (3.0)	1 (3.3)	1 (1.0)	1 (1.3)	0 (0.0)	1 (4.8)	0 (0.0)	1 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)
[18.5-25[	48 (50.0)	30 (45.5)	18 (60.0)	57 (55.3)	40 (51.9)	17 (65.4)	11 (52.4)	9 (56.3)	2 (40.0)	6 (54.5)	4 (50.0)	2 (66.7)
[25-30[	30 (31.3)	22 (33.3)	8 (26.7)	30 (29.1)	23 (29.9)	7 (26.9)	4 (19.0)	2 (12.5)	2 (40.0)	3 (27.3)	3 (37.5)	0 (0.0)
≥30	15 (15.6)	12 (18.2)	3 (10.0)	15 (14.6)	13 (16.9)	2 (7.7)	5 (23.8)	5 (31.3)	0 (0.0)	2 (18.2)	1 (12.5)	1 (33.3)
[18-30[	**5 (5.2)**	**2 (3.0)**	**3 (10.0)**	**8 (7.8)**	**4 (5.2)**	**4 (15.4)**	**3 (14.3)**	**2 (12.5)**	**1 (20.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
BMI (kg/m2) (in categories), n (%)												
<18.5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
[18.5-25[	3 (60.0)	1 (50.0)	2 (66.7)	7 (87.5)	4 (100.0)	3 (75.0)	2 (66.7)	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
[25-30[	2 (40.0)	1 (50.0)	1 (33.3)	1 (12.5)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
≥30	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)	0 (0.0)	0 (0.0)	0 (0.0)
[30-40[	**18 (18.8)**	**10 (15.2)**	**8 (26.7)**	**8 (7.8)**	**6 (7.8)**	**2 (7.7)**	**3 (14.3)**	**1 (6.3)**	**2 (40.0)**	**1 (9.1)**	**0 (0.0)**	**1 (33.3)**
BMI (kg/m2) (in categories), n (%)												
<18.5	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)	0 (0.0)	0 (0.0)	0 (0.0)
[18.5-25[	13 (72.2)	6 (60.0)	7 (87.5)	7 (87.5)	5 (83.3)	2 (100.0)	1 (33.3)	1 (100.0)	0 (0.0)	1 (100.0)	0 (0.0)	1 (100.0)
[25-30[	5 (27.8)	4 (40.0)	1 (12.5)	1 (12.5)	1 (16.7)	0 (0.0)	2 (66.7)	0 (0.0)	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
≥30	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)	0 (0.0)	0 (0.0)	0 (0.0)
[40-50[	**26 (27.1)**	**19 (28.8)**	**7 (23.3)**	**20 (19.4)**	**14 (18.2)**	**6 (23.1)**	**7 (33.3)**	**6 (37.5)**	**1 (20.0)**	**3 (27.3)**	**2 (25.0)**	**1 (33.3)**
BMI (kg/m2) (in categories), n (%)												
<18.5	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)	0 (0.0)	0 (0.0)	0 (0.0)
[18.5-25[	18 (69.2)	13 (68.4)	5 (71.4)	13 (65.0)	8 (57.1)	5 (83.3)	3 (42.9)	2 (33.3)	1 (100.0)	2 (66.7)	2 (100.0)	0 (0.0)
[25-30[	3 (11.5)	2 (10.5)	1 (14.3)	5 (25.0)	4 (28.6)	1 (16.7)	1 (14.3)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
≥30	5 (19.2)	4 (21.1)	1 (14.3)	2 (10.0)	2 (14.3)	0 (0.0)	3 (42.9)	3 (50.0)	0 (0.0)	1 (33.3)	0 (0.0)	1 (100.0)

	Adalimumab						Etanercept						Infliximab						Certolizumab					
	ALL n = 96		Severe RA n = 66		Not Severe RA n = 30		ALL n = 103		Severe RA n = 77		Not Severe RA n = 26		ALL n = 21		Severe RA n = 16		Not Severe RA n = 5		ALL n = 11		Severe RA n = 8		Not Severe RA n = 3	
[50-60[	**31**	**(32.3)**	**22**	**(33.3)**	**9**	**(30.0)**	**39**	**(37.9)**	**31**	**(40.3)**	**8**	**(30.8)**	**4**	**(19.0)**	**4**	**(25.0)**	**0**	**(0.0)**	**2**	**(18.2)**	**2**	**(25.0)**	**0**	**(0.0)**
BMI (kg/m2) (in categories), n (%)																								
<18.5	2	(6.5)	1	(4.5)	1	(11.1)	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)
[18.5-25[	8	(25.8)	4	(18.2)	4	(44.4)	19	(48.7)	15	(48.4)	4	(50.0)	3	(75.0)	3	(75.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
[25-30[	13	(41.9)	10	(45.5)	3	(33.3)	12	(30.8)	9	(29.0)	3	(37.5)	1	(25.0)	1	(25.0)	0	(0.0)	1	(50.0)	1	(50.0)	0	(0.0)
≥30	8	(25.8)	7	(31.8)	1	(11.1)	8	(20.5)	7	(22.6)	1	(12.5)	0	(0.0)	0	(0.0)	0	(0.0)	1	(50.0)	1	(50.0)	0	(0.0)
[60-65[	**10**	**(10.4)**	**8**	**(12.1)**	**2**	**(6.7)**	**12**	**(11.7)**	**10**	**(13.0)**	**2**	**(7.7)**	**2**	**(9.5)**	**1**	**(6.3)**	**1**	**(20.0)**	**4**	**(36.4)**	**3**	**(37.5)**	**1**	**(33.3)**
BMI (kg/m2) (in categories), n (%)																								
<18.5	1	(10.0)	1	(12.5)	0	(0.0)	1	(8.3)	1	(10.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
[18.5-25[	4	(40.0)	4	(50.0)	0	(0.0)	5	(41.7)	3	(30.0)	2	(100.0)	1	(50.0)	0	(0.0)	1	(100.0)	3	(75.0)	2	(66.7)	1	(100.0)
[25-30[	3	(30.0)	2	(25.0)	1	(50.0)	3	(25.0)	3	(30.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(25.0)	1	(33.3)	0	(0.0)
≥30	2	(20.0)	1	(12.5)	1	(50.0)	3	(25.0)	3	(30.0)	0	(0.0)	1	(50.0)	1	(100.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
≥65	**6**	**(6.3)**	**5**	**(7.6)**	**1**	**(3.3)**	**16**	**(15.5)**	**12**	**(15.6)**	**4**	**(15.4)**	**2**	**(9.5)**	**2**	**(12.5)**	**0**	**(0.0)**	**1**	**(9.1)**	**1**	**(12.5)**	**0**	**(0.0)**
BMI (kg/m2) (in categories), n (%)																								
<18.5	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)	0	(0.0)	0	(0.0)	0	(0.0)
[18.5-25[	2	(33.3)	2	(40.0)	0	(0.0)	6	(37.5)	5	(41.7)	1	(25.0)	1	(50.0)	1	(50.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
[25-30[	4	(66.7)	3	(60.0)	1	(100.0)	8	(50.0)	6	(50.0)	2	(50.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(100.0)	1	(100.0)	0	(0.0)
≥30	0	(0.0)	0	(0.0)	0	(0.0)	2	(12.5)	1	(8.3)	1	(25.0)	1	(50.0)	1	(50.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 24. Description of Body Mass Index (BMI) among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and by RA severity according to age at the date of initiation of the considered drug, whatever the rank of treatment line

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	**Severe RA n = 2**	**Not Severe RA n = 3**	**ALL n = 21**	**Severe RA n = 17**	**Not Severe RA n = 4**	**ALL n = 20**	**Severe RA n = 16**	**Not Severe RA n = 4**
Total									
BMI (kg/m2)									
Size (missing)	5 (0)	2 (0)	3 (0)	21 (0)	17 (0)	4 (0)	20 (0)	16 (0)	4 (0)
Mean (± SD)	28.4 (6.6)	27.1 (0.6)	29.3 (9.2)	26.2 (3.5)	25.7 (3.4)	28.3 (3.4)	24.3 (4.7)	25.1 (4.7)	21.1 (3.3)
Median	26.7	27.1	25.5	25.6	25.6	28.2	23.7	24.7	22.1
[p25% - p75%]	[25.5;27.5]	[26.7;27.5]	[22.5;39.8]	[24.4;28.7]	[23.1;27.5]	[25.5;31.0]	[21.8;26.1]	[22.2;27.0]	[18.9;23.3]
[Min - Max]	[22.5;39.8]	[26.7;27.5]	[22.5;39.8]	[19.9;32.0]	[19.9;31.5]	[24.6;32.0]	[16.4;35.2]	[19.1;35.2]	[16.4;23.7]
[18-30[	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**1 (4.8)**	**1 (5.9)**	**0 (0.0)**	**4 (20.0)**	**3 (18.8)**	**1 (25.0)**
BMI (kg/m2)									
Size (missing)				1 (0)	1 (0)		4 (0)	3 (0)	1 (0)
Mean (± SD)				24.4	24.4		22.5 (5.7)	24.5 (4.8)	16.4
Median				24.4	24.4		22.5	25.8	16.4
[p25% - p75%]				[24.4;24.4]	[24.4;24.4]		[17.8;27.2]	[19.3;28.6]	[16.4;16.4]
[Min - Max]				[24.4;24.4]	[24.4;24.4]		[16.4;28.6]	[19.3;28.6]	[16.4;16.4]
[30-40[	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**2 (9.5)**	**1 (5.9)**	**1 (25.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
BMI (kg/m2)									
Size (missing)				2 (0)	1 (0)	1 (0)			
Mean (± SD)				25.0 (7.2)	19.9	30.1			
Median				25.0	19.9	30.1			
[p25% - p75%]				[19.9;30.1]	[19.9;19.9]	[30.1;30.1]			
[Min - Max]				[19.9;30.1]	[19.9;19.9]	[30.1;30.1]			
[40-50[	**2 (40.0)**	**0 (0.0)**	**2 (66.7)**	**1 (4.8)**	**0 (0.0)**	**1 (25.0)**	**2 (10.0)**	**0 (0.0)**	**2 (50.0)**
BMI (kg/m2)									
Size (missing)	2 (0)		2 (0)	1 (0)		1 (0)	2 (0)		2 (0)
Mean (± SD)	32.6 (10.1)		32.6 (10.1)	26.3		26.3	22.5 (1.6)		22.5 (1.6)
Median	32.6		32.6	26.3		26.3	22.5		22.5
[p25% - p75%]	[25.5;39.8]		[25.5;39.8]	[26.3;26.3]		[26.3;26.3]	[21.4;23.7]		[21.4;23.7]
[Min - Max]	[25.5;39.8]		[25.5;39.8]	[26.3;26.3]		[26.3;26.3]	[21.4;23.7]		[21.4;23.7]

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	**Severe RA n = 2**	**Not Severe RA n = 3**	**ALL n = 21**	**Severe RA n = 17**	**Not Severe RA n = 4**	**ALL n = 20**	**Severe RA n = 16**	**Not Severe RA n = 4**
[50-60[	**1 (20.0)**	**1 (50.0)**	**0 (0.0)**	**7 (33.3)**	**6 (35.3)**	**1 (25.0)**	**6 (30.0)**	**6 (37.5)**	**0 (0.0)**
BMI (kg/m2)									
Size (missing)	1 (0)	1 (0)		7 (0)	6 (0)	1 (0)	6 (0)	6 (0)	
Mean (± SD)	27.5	27.5		25.3 (2.6)	25.4 (2.8)	24.6	28.1 (5.6)	28.1 (5.6)	
Median	27.5	27.5		24.6	25.0	24.6	27.0	27.0	
[p25% - p75%]	[27.5;27.5]	[27.5;27.5]		[23.1;27.5]	[23.1;27.5]	[24.6;24.6]	[23.1;34.5]	[23.1;34.5]	
[Min - Max]	[27.5;27.5]	[27.5;27.5]		[22.2;29.7]	[22.2;29.7]	[24.6;24.6]	[22.2;35.2]	[22.2;35.2]	
[60-65[	**1 (20.0)**	**1 (50.0)**	**0 (0.0)**	**4 (19.0)**	**4 (23.5)**	**0 (0.0)**	**4 (20.0)**	**3 (18.8)**	**1 (25.0)**
BMI (kg/m2)									
Size (missing)	1 (0)	1 (0)		4 (0)	4 (0)		4 (0)	3 (0)	1 (0)
Mean (± SD)	26.7	26.7		26.1 (2.9)	26.1 (2.9)		24.1 (1.0)	24.5 (0.7)	22.9
Median	26.7	26.7		26.8	26.8		24.1	24.5	22.9
[p25% - p75%]	[26.7;26.7]	[26.7;26.7]		[24.3;27.8]	[24.3;27.8]		[23.3;24.8]	[23.7;25.1]	[22.9;22.9]
[Min - Max]	[26.7;26.7]	[26.7;26.7]		[22.0;28.7]	[22.0;28.7]		[22.9;25.1]	[23.7;25.1]	[22.9;22.9]
≥65	**1 (20.0)**	**0 (0.0)**	**1 (33.3)**	**6 (28.6)**	**5 (29.4)**	**1 (25.0)**	**4 (20.0)**	**4 (25.0)**	**0 (0.0)**
BMI (kg/m2)									
Size (missing)	1 (0)		1 (0)	6 (0)	5 (0)	1 (0)	4 (0)	4 (0)	
Mean (± SD)	22.5		22.5	27.8 (4.4)	27.0 (4.4)	32.0	21.4 (2.7)	21.4 (2.7)	
Median	22.5		22.5	28.4	25.6	32.0	20.8	20.8	
[p25% - p75%]	[22.5;22.5]		[22.5;22.5]	[25.5;31.5]	[25.5;31.2]	[32.0;32.0]	[19.3;23.6]	[19.3;23.6]	
[Min - Max]	[22.5;22.5]		[22.5;22.5]	[21.3;32.0]	[21.3;31.5]	[32.0;32.0]	[19.1;25.0]	[19.1;25.0]	

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 25. Description of Body Mass Index (BMI) in categories among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and by RA severity according to age at the date of initiation of the considered drug, whatever the rank of treatment line

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	Severe RA n = 2	Not Severe RA n = 3	ALL n = 21	Severe RA n = 17	Not Severe RA n = 4	ALL n = 20	Severe RA n = 16	Not Severe RA n = 4
Total									
BMI (kg/m2) (in categories), n (%)									
<18.5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.0)	0 (0.0)	1 (25.0)
[18.5-25[	1 (20.0)	0 (0.0)	1 (33.3)	8 (38.1)	7 (41.2)	1 (25.0)	12 (60.0)	9 (56.3)	3 (75.0)
[25-30[	3 (60.0)	2 (100.0)	1 (33.3)	9 (42.9)	8 (47.1)	1 (25.0)	5 (25.0)	5 (31.3)	0 (0.0)
≥30	1 (20.0)	0 (0.0)	1 (33.3)	4 (19.0)	2 (11.8)	2 (50.0)	2 (10.0)	2 (12.5)	0 (0.0)
[18-30[	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**1 (4.8)**	**1 (5.9)**	**0 (0.0)**	**4 (20.0)**	**3 (18.8)**	**1 (25.0)**
BMI (kg/m2) (in categories), n (%)									
<18.5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	1 (100.0)
[18.5-25[	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)	0 (0.0)	1 (25.0)	1 (33.3)	0 (0.0)
[25-30[	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (50.0)	2 (66.7)	0 (0.0)
≥30	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)
[30-40[	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**2 (9.5)**	**1 (5.9)**	**1 (25.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
BMI (kg/m2) (in categories), n (%)									
<18.5	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)
[18.5-25[	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
[25-30[	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)
≥30	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
[40-50[	**2 (40.0)**	**0 (0.0)**	**2 (66.7)**	**1 (4.8)**	**0 (0.0)**	**1 (25.0)**	**2 (10.0)**	**0 (0.0)**	**2 (50.0)**
BMI (kg/m2) (in categories), n (%)									
<18.5	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)
[18.5-25[	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)	0 (0.0)	2 (100.0)
[25-30[	1 (50.0)	0 (0.0)	1 (50.0)	1 (100.0)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
≥30	1 (50.0)	0 (0.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	Severe RA n = 2	Not Severe RA n = 3	ALL n = 21	Severe RA n = 17	Not Severe RA n = 4	ALL n = 20	Severe RA n = 16	Not Severe RA n = 4
[50-60[	**1 (20.0)**	**1 (50.0)**	**0 (0.0)**	**7 (33.3)**	**6 (35.3)**	**1 (25.0)**	**6 (30.0)**	**6 (37.5)**	**0 (0.0)**
BMI (kg/m2) (in categories), n (%)									
<18.5	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)
[18.5-25[	0 (0.0)	0 (0.0)	0 (0.0)	4 (57.1)	3 (50.0)	1 (100.0)	2 (33.3)	2 (33.3)	0 (0.0)
[25-30[	1 (100.0)	1 (100.0)	0 (0.0)	3 (42.9)	3 (50.0)	0 (0.0)	2 (33.3)	2 (33.3)	0 (0.0)
≥30	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (33.3)	2 (33.3)	0 (0.0)
[60-65[	**1 (20.0)**	**1 (50.0)**	**0 (0.0)**	**4 (19.0)**	**4 (23.5)**	**0 (0.0)**	**4 (20.0)**	**3 (18.8)**	**1 (25.0)**
BMI (kg/m2) (in categories), n (%)									
<18.5	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)
[18.5-25[	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (25.0)	0 (0.0)	3 (75.0)	2 (66.7)	1 (100.0)
[25-30[	1 (100.0)	1 (100.0)	0 (0.0)	3 (75.0)	3 (75.0)	0 (0.0)	1 (25.0)	1 (33.3)	0 (0.0)
≥30	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)
≥65	**1 (20.0)**	**0 (0.0)**	**1 (33.3)**	**6 (28.6)**	**5 (29.4)**	**1 (25.0)**	**4 (20.0)**	**4 (25.0)**	**0 (0.0)**
BMI (kg/m2) (in categories), n (%)									
<18.5	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)
[18.5-25[	1 (100.0)	0 (0.0)	1 (100.0)	1 (16.7)	1 (20.0)	0 (0.0)	4 (100.0)	4 (100.0)	0 (0.0)
[25-30[	0 (0.0)	0 (0.0)	0 (0.0)	2 (33.3)	2 (40.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
≥30	0 (0.0)	0 (0.0)	0 (0.0)	3 (50.0)	2 (40.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 26. Description of Body Mass Index (BMI) among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and by RA severity according to gender at the date of initiation of the considered drug, whatever the rank of treatment line

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	**Severe RA n = 66**	**Not Severe RA n = 30**	**ALL n = 103**	**Severe RA n = 77**	**Not Severe RA n = 26**	**ALL n = 21**	**Severe RA n = 16**	**Not Severe RA n = 5**	**ALL n = 11**	**Severe RA n = 8**	**Not Severe RA n = 3**
Total												
BMI (kg/m2)												
Size (missing)	96 (0)	66 (0)	30 (0)	103 (0)	77 (0)	26 (0)	21 (0)	16 (0)	5 (0)	11 (0)	8 (0)	3 (0)
Mean (± SD)	25.2 (5.0)	25.9 (5.4)	23.8 (3.8)	25.2 (4.6)	25.3 (4.8)	24.8 (3.8)	25.6 (6.6)	26.5 (6.9)	22.6 (4.9)	25.4 (6.3)	24.5 (4.5)	27.7 (10.8)
Median	24.7	25.4	22.7	24.2	24.1	24.4	23.8	24.1	23.3	22.6	23.9	21.8
[p25% - p75%]	[21.6;27.4]	[22.2;28.6]	[21.0;25.8]	[21.8;27.9]	[21.3;28.5]	[21.9;27.3]	[21.5;28.3]	[21.6;30.4]	[19.1;26.0]	[20.9;29.0]	[20.5;28.2]	[21.1;40.1]
[Min - Max]	[17.2;43.5]	[17.2;43.5]	[18.1;33.2]	[17.6;39.8]	[17.6;39.8]	[20.1;35.8]	[16.4;46.6]	[19.1;46.6]	[16.4;28.3]	[19.4;40.1]	[19.4;31.6]	[21.1;40.1]
Women	**72 (75.0)**	**51 (77.3)**	**21 (70.0)**	**80 (77.7)**	**62 (80.5)**	**18 (69.2)**	**15 (71.4)**	**11 (68.8)**	**4 (80.0)**	**8 (72.7)**	**7 (87.5)**	**1 (33.3)**
BMI (kg/m2)												
Size (missing)	72 (0)	51 (0)	21 (0)	80 (0)	62 (0)	18 (0)	15 (0)	11 (0)	4 (0)	8 (0)	7 (0)	1 (0)
Mean (± SD)	24.6 (4.8)	25.4 (5.3)	22.4 (2.6)	25.4 (4.9)	25.5 (5.1)	24.8 (4.1)	26.3 (7.1)	27.2 (7.6)	23.5 (5.2)	24.4 (4.6)	24.8 (4.8)	21.8
Median	23.8	24.4	22.2	24.1	24.1	23.7	24.3	24.3	24.7	23.5	25.2	21.8
[p25% - p75%]	[21.1;26.2]	[21.7;28.0]	[20.0;24.9]	[21.7;28.4]	[21.3;29.4]	[22.0;25.0]	[21.7;30.1]	[21.7;30.6]	[19.8;27.2]	[20.5;28.2]	[20.1;29.0]	[21.8;21.8]
[Min - Max]	[17.2;43.5]	[17.2;43.5]	[18.1;27.2]	[17.6;39.8]	[17.6;39.8]	[20.1;35.8]	[16.4;46.6]	[19.1;46.6]	[16.4;28.3]	[19.4;31.6]	[19.4;31.6]	[21.8;21.8]
Men	**24 (25.0)**	**15 (22.7)**	**9 (30.0)**	**23 (22.3)**	**15 (19.5)**	**8 (30.8)**	**6 (28.6)**	**5 (31.3)**	**1 (20.0)**	**3 (27.3)**	**1 (12.5)**	**2 (66.7)**
BMI (kg/m2)												
Size (missing)	24 (0)	15 (0)	9 (0)	23 (0)	15 (0)	8 (0)	6 (0)	5 (0)	1 (0)	3 (0)	1 (0)	2 (0)
Mean (± SD)	27.2 (5.1)	27.3 (5.7)	26.9 (4.4)	24.6 (3.1)	24.5 (3.1)	24.9 (3.2)	23.9 (5.3)	24.8 (5.4)	19.1	28.0 (10.5)	22.6	30.6 (13.4)
Median	26.8	27.4	26.5	24.5	24.2	25.3	21.8	22.1	19.1	22.6	22.6	30.6
[p25% - p75%]	[22.9;30.2]	[22.9;29.0]	[22.9;31.4]	[21.8;27.3]	[22.3;26.2]	[21.6;27.7]	[20.8;26.0]	[21.5;26.0]	[19.1;19.1]	[21.1;40.1]	[22.6;22.6]	[21.1;40.1]
[Min - Max]	[19.0;38.2]	[19.0;38.2]	[21.6;33.2]	[19.4;30.9]	[19.4;30.9]	[21.1;29.2]	[19.1;33.7]	[20.8;33.7]	[19.1;19.1]	[21.1;40.1]	[22.6;22.6]	[21.1;40.1]

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 27. Description of Body Mass Index (BMI) in categories among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and by RA severity according to gender at the date of initiation of the considered drug, whatever the rank of treatment line

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	Severe RA n = 66	Not Severe RA n = 30	ALL n = 103	Severe RA n = 77	Not Severe RA n = 26	ALL n = 21	Severe RA n = 16	Not Severe RA n = 5	ALL n = 11	Severe RA n = 8	Not Severe RA n = 3
Total												
BMI (kg/m2) (in categories), n (%)												
<18.5	3 (3.1)	2 (3.0)	1 (3.3)	1 (1.0)	1 (1.3)	0 (0.0)	1 (4.8)	0 (0.0)	1 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)
[18.5-25[	48 (50.0)	30 (45.5)	18 (60.0)	57 (55.3)	40 (51.9)	17 (65.4)	11 (52.4)	9 (56.3)	2 (40.0)	6 (54.5)	4 (50.0)	2 (66.7)
[25-30[	30 (31.3)	22 (33.3)	8 (26.7)	30 (29.1)	23 (29.9)	7 (26.9)	4 (19.0)	2 (12.5)	2 (40.0)	3 (27.3)	3 (37.5)	0 (0.0)
≥30	15 (15.6)	12 (18.2)	3 (10.0)	15 (14.6)	13 (16.9)	2 (7.7)	5 (23.8)	5 (31.3)	0 (0.0)	2 (18.2)	1 (12.5)	1 (33.3)
Women	**72 (75.0)**	**51 (77.3)**	**21 (70.0)**	**80 (77.7)**	**62 (80.5)**	**18 (69.2)**	**15 (71.4)**	**11 (68.8)**	**4 (80.0)**	**8 (72.7)**	**7 (87.5)**	**1 (33.3)**
BMI (kg/m2) (in categories), n (%)												
<18.5	3 (4.2)	2 (3.9)	1 (4.8)	1 (1.3)	1 (1.6)	0 (0.0)	1 (6.7)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)
[18.5-25[	40 (55.6)	25 (49.0)	15 (71.4)	44 (55.0)	31 (50.0)	13 (72.2)	7 (46.7)	6 (54.5)	1 (25.0)	4 (50.0)	3 (42.9)	1 (100.0)
[25-30[	20 (27.8)	15 (29.4)	5 (23.8)	21 (26.3)	18 (29.0)	3 (16.7)	3 (20.0)	1 (9.1)	2 (50.0)	3 (37.5)	3 (42.9)	0 (0.0)
≥30	9 (12.5)	9 (17.6)	0 (0.0)	14 (17.5)	12 (19.4)	2 (11.1)	4 (26.7)	4 (36.4)	0 (0.0)	1 (12.5)	1 (14.3)	0 (0.0)
Men	**24 (25.0)**	**15 (22.7)**	**9 (30.0)**	**23 (22.3)**	**15 (19.5)**	**8 (30.8)**	**6 (28.6)**	**5 (31.3)**	**1 (20.0)**	**3 (27.3)**	**1 (12.5)**	**2 (66.7)**
BMI (kg/m2) (in categories), n (%)												
<18.5	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)	0 (0.0)	0 (0.0)	0 (0.0)
[18.5-25[	8 (33.3)	5 (33.3)	3 (33.3)	13 (56.5)	9 (60.0)	4 (50.0)	4 (66.7)	3 (60.0)	1 (100.0)	2 (66.7)	1 (100.0)	1 (50.0)
[25-30[	10 (41.7)	7 (46.7)	3 (33.3)	9 (39.1)	5 (33.3)	4 (50.0)	1 (16.7)	1 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
≥30	6 (25.0)	3 (20.0)	3 (33.3)	1 (4.3)	1 (6.7)	0 (0.0)	1 (16.7)	1 (20.0)	0 (0.0)	1 (33.3)	0 (0.0)	1 (50.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 28. Description of Body Mass Index (BMI) among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and by RA severity according to gender at the date of initiation of the considered drug, whatever the rank of treatment line

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	**Severe RA n = 2**	**Not Severe RA n = 3**	**ALL n = 21**	**Severe RA n = 17**	**Not Severe RA n = 4**	**ALL n = 20**	**Severe RA n = 16**	**Not Severe RA n = 4**
Total									
BMI (kg/m2)									
Size (missing)	5 (0)	2 (0)	3 (0)	21 (0)	17 (0)	4 (0)	20 (0)	16 (0)	4 (0)
Mean (± SD)	28.4 (6.6)	27.1 (0.6)	29.3 (9.2)	26.2 (3.5)	25.7 (3.4)	28.3 (3.4)	24.3 (4.7)	25.1 (4.7)	21.1 (3.3)
Median	26.7	27.1	25.5	25.6	25.6	28.2	23.7	24.7	22.1
[p25% - p75%]	[25.5;27.5]	[26.7;27.5]	[22.5;39.8]	[24.4;28.7]	[23.1;27.5]	[25.5;31.0]	[21.8;26.1]	[22.2;27.0]	[18.9;23.3]
[Min - Max]	[22.5;39.8]	[26.7;27.5]	[22.5;39.8]	[19.9;32.0]	[19.9;31.5]	[24.6;32.0]	[16.4;35.2]	[19.1;35.2]	[16.4;23.7]
Women	**4 (80.0)**	**2 (100.0)**	**2 (66.7)**	**16 (76.2)**	**14 (82.4)**	**2 (50.0)**	**17 (85.0)**	**14 (87.5)**	**3 (75.0)**
BMI (kg/m2)									
Size (missing)	4 (0)	2 (0)	2 (0)	16 (0)	14 (0)	2 (0)	17 (0)	14 (0)	3 (0)
Mean (± SD)	25.6 (2.2)	27.1 (0.6)	24.0 (2.1)	26.6 (3.3)	26.3 (3.2)	29.2 (4.0)	24.5 (4.9)	25.4 (4.8)	20.5 (3.7)
Median	26.1	27.1	24.0	26.0	25.6	29.2	23.7	24.7	21.4
[p25% - p75%]	[24.0;27.1]	[26.7;27.5]	[22.5;25.5]	[24.4;29.2]	[24.4;28.7]	[26.3;32.0]	[22.2;25.8]	[22.2;27.5]	[16.4;23.7]
[Min - Max]	[22.5;27.5]	[26.7;27.5]	[22.5;25.5]	[21.3;32.0]	[21.3;31.5]	[26.3;32.0]	[16.4;35.2]	[19.1;35.2]	[16.4;23.7]
Men	**1 (20.0)**	**0 (0.0)**	**1 (33.3)**	**5 (23.8)**	**3 (17.6)**	**2 (50.0)**	**3 (15.0)**	**2 (12.5)**	**1 (25.0)**
BMI (kg/m2)									
Size (missing)	1 (0)		1 (0)	5 (0)	3 (0)	2 (0)	3 (0)	2 (0)	1 (0)
Mean (± SD)	39.8		39.8	24.7 (4.0)	23.0 (3.6)	27.4 (3.9)	22.9 (3.5)	22.9 (5.0)	22.9
Median	39.8		39.8	24.6	22.0	27.4	22.9	22.9	22.9
[p25% - p75%]	[39.8;39.8]		[39.8;39.8]	[22.0;27.0]	[19.9;27.0]	[24.6;30.1]	[19.4;26.4]	[19.4;26.4]	[22.9;22.9]
[Min - Max]	[39.8;39.8]		[39.8;39.8]	[19.9;30.1]	[19.9;27.0]	[24.6;30.1]	[19.4;26.4]	[19.4;26.4]	[22.9;22.9]

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 29. Description of Body Mass Index (BMI) in categories among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and by RA severity according to gender at the date of initiation of the considered drug, whatever the rank of treatment line

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	Severe RA n = 2	Not Severe RA n = 3	ALL n = 21	Severe RA n = 17	Not Severe RA n = 4	ALL n = 20	Severe RA n = 16	Not Severe RA n = 4
Total									
BMI (kg/m2) (in categories), n (%)									
<18.5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.0)	0 (0.0)	1 (25.0)
[18.5-25[	1 (20.0)	0 (0.0)	1 (33.3)	8 (38.1)	7 (41.2)	1 (25.0)	12 (60.0)	9 (56.3)	3 (75.0)
[25-30[	3 (60.0)	2 (100.0)	1 (33.3)	9 (42.9)	8 (47.1)	1 (25.0)	5 (25.0)	5 (31.3)	0 (0.0)
≥30	1 (20.0)	0 (0.0)	1 (33.3)	4 (19.0)	2 (11.8)	2 (50.0)	2 (10.0)	2 (12.5)	0 (0.0)
Women	**4 (80.0)**	**2 (100.0)**	**2 (66.7)**	**16 (76.2)**	**14 (82.4)**	**2 (50.0)**	**17 (85.0)**	**14 (87.5)**	**3 (75.0)**
BMI (kg/m2) (in categories), n (%)									
<18.5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.9)	0 (0.0)	1 (33.3)
[18.5-25[	1 (25.0)	0 (0.0)	1 (50.0)	5 (31.3)	5 (35.7)	0 (0.0)	10 (58.8)	8 (57.1)	2 (66.7)
[25-30[	3 (75.0)	2 (100.0)	1 (50.0)	8 (50.0)	7 (50.0)	1 (50.0)	4 (23.5)	4 (28.6)	0 (0.0)
≥30	0 (0.0)	0 (0.0)	0 (0.0)	3 (18.8)	2 (14.3)	1 (50.0)	2 (11.8)	2 (14.3)	0 (0.0)
Men	**1 (20.0)**	**0 (0.0)**	**1 (33.3)**	**5 (23.8)**	**3 (17.6)**	**2 (50.0)**	**3 (15.0)**	**2 (12.5)**	**1 (25.0)**
BMI (kg/m2) (in categories), n (%)									
<18.5	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)
[18.5-25[	0 (0.0)	0 (0.0)	0 (0.0)	3 (60.0)	2 (66.7)	1 (50.0)	2 (66.7)	1 (50.0)	1 (100.0)
[25-30[	0 (0.0)	0 (0.0)	0 (0.0)	1 (20.0)	1 (33.3)	0 (0.0)	1 (33.3)	1 (50.0)	0 (0.0)
≥30	1 (100.0)	0 (0.0)	1 (100.0)	1 (20.0)	0 (0.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 30. Description of Body Mass Index (BMI) among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and by RA severity according to calendar year at the date of initiation of the considered drug, whatever the rank of treatment line

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	**Severe RA n = 66**	**Not Severe RA n = 30**	**ALL n = 103**	**Severe RA n = 77**	**Not Severe RA n = 26**	**ALL n = 21**	**Severe RA n = 16**	**Not Severe RA n = 5**	**ALL n = 11**	**Severe RA n = 8**	**Not Severe RA n = 3**
Total												
BMI (kg/m2)												
Size (missing)	96 (0)	66 (0)	30 (0)	103 (0)	77 (0)	26 (0)	21 (0)	16 (0)	5 (0)	11 (0)	8 (0)	3 (0)
Mean (± SD)	25.2 (5.0)	25.9 (5.4)	23.8 (3.8)	25.2 (4.6)	25.3 (4.8)	24.8 (3.8)	25.6 (6.6)	26.5 (6.9)	22.6 (4.9)	25.4 (6.3)	24.5 (4.5)	27.7 (10.8)
Median	24.7	25.4	22.7	24.2	24.1	24.4	23.8	24.1	23.3	22.6	23.9	21.8
[p25% - p75%]	[21.6;27.4]	[22.2;28.6]	[21.0;25.8]	[21.8;27.9]	[21.3;28.5]	[21.9;27.3]	[21.5;28.3]	[21.6;30.4]	[19.1;26.0]	[20.9;29.0]	[20.5;28.2]	[21.1;40.1]
[Min - Max]	[17.2;43.5]	[17.2;43.5]	[18.1;33.2]	[17.6;39.8]	[17.6;39.8]	[20.1;35.8]	[16.4;46.6]	[19.1;46.6]	[16.4;28.3]	[19.4;40.1]	[19.4;31.6]	[21.1;40.1]
[2003-2009]	**77 (80.2)**	**56 (84.8)**	**21 (70.0)**	**70 (68.0)**	**52 (67.5)**	**18 (69.2)**	**16 (76.2)**	**13 (81.3)**	**3 (60.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
BMI (kg/m2)												
Size (missing)	77 (0)	56 (0)	21 (0)	70 (0)	52 (0)	18 (0)	16 (0)	13 (0)	3 (0)			
Mean (± SD)	25.0 (5.1)	25.4 (5.4)	23.6 (3.9)	24.8 (4.7)	25.0 (5.1)	24.3 (3.3)	26.2 (7.0)	26.6 (7.5)	24.5 (4.8)			
Median	24.2	24.3	22.9	23.7	23.9	23.0	24.1	23.8	26.0			
[p25% - p75%]	[21.3;26.7]	[21.6;28.2]	[20.8;25.2]	[21.5;27.7]	[20.9;28.8]	[21.8;25.7]	[21.6;29.5]	[21.7;30.6]	[19.1;28.3]			
[Min - Max]	[17.2;43.5]	[17.2;43.5]	[18.1;33.2]	[17.6;39.8]	[17.6;39.8]	[21.1;33.2]	[19.1;46.6]	[19.1;46.6]	[19.1;28.3]			
[2010-2016]	**19 (19.8)**	**10 (15.2)**	**9 (30.0)**	**33 (32.0)**	**25 (32.5)**	**8 (30.8)**	**5 (23.8)**	**3 (18.8)**	**2 (40.0)**	**11 (100.0)**	**8 (100.0)**	**3 (100.0)**
BMI (kg/m2)												
Size (missing)	19 (0)	10 (0)	9 (0)	33 (0)	25 (0)	8 (0)	5 (0)	3 (0)	2 (0)	11 (0)	8 (0)	3 (0)
Mean (± SD)	26.3 (4.8)	28.2 (5.1)	24.1 (3.7)	26.0 (4.1)	26.0 (4.1)	26.1 (4.7)	23.6 (5.4)	26.2 (4.8)	19.8 (4.9)	25.4 (6.3)	24.5 (4.5)	27.7 (10.8)
Median	26.5	27.4	22.2	25.8	25.9	24.8	23.3	27.5	19.8	22.6	23.9	21.8
[p25% - p75%]	[21.9;28.0]	[25.8;29.0]	[21.6;26.5]	[22.9;28.0]	[22.9;28.4]	[23.6;27.9]	[20.8;27.5]	[20.8;30.1]	[16.4;23.3]	[20.9;29.0]	[20.5;28.2]	[21.1;40.1]
[Min - Max]	[19.9;38.2]	[21.3;38.2]	[19.9;31.4]	[20.1;38.2]	[20.8;38.2]	[20.1;35.8]	[16.4;30.1]	[20.8;30.1]	[16.4;23.3]	[19.4;40.1]	[19.4;31.6]	[21.1;40.1]

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 31. Description of Body Mass Index (BMI) in categories among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest1 and by RA severity according to calendar year at the date of initiation of the considered drug, whatever the rank of treatment line

	Adalimumab						Etanercept						Infliximab						Certolizumab					
	ALL n = 96		Severe RA n = 66		Not Severe RA n = 30		ALL n = 103		Severe RA n = 77		Not Severe RA n = 26		ALL n = 21		Severe RA n = 16		Not Severe RA n = 5		ALL n = 11		Severe RA n = 8		Not Severe RA n = 3	
Total																								
BMI (kg/m2) (in categories), n (%)																								
<18.5	3	(3.1)	2	(3.0)	1	(3.3)	1	(1.0)	1	(1.3)	0	(0.0)	1	(4.8)	0	(0.0)	1	(20.0)	0	(0.0)	0	(0.0)	0	(0.0)
[18.5-25[	48	(50.0)	30	(45.5)	18	(60.0)	57	(55.3)	40	(51.9)	17	(65.4)	11	(52.4)	9	(56.3)	2	(40.0)	6	(54.5)	4	(50.0)	2	(66.7)
[25-30[	30	(31.3)	22	(33.3)	8	(26.7)	30	(29.1)	23	(29.9)	7	(26.9)	4	(19.0)	2	(12.5)	2	(40.0)	3	(27.3)	3	(37.5)	0	(0.0)
≥30	15	(15.6)	12	(18.2)	3	(10.0)	15	(14.6)	13	(16.9)	2	(7.7)	5	(23.8)	5	(31.3)	0	(0.0)	2	(18.2)	1	(12.5)	1	(33.3)
[2003-2009]	**77**	**(80.2)**	**56**	**(84.8)**	**21**	**(70.0)**	**70**	**(68.0)**	**52**	**(67.5)**	**18**	**(69.2)**	**16**	**(76.2)**	**13**	**(81.3)**	**3**	**(60.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
BMI (kg/m2) (in categories), n (%)																								
<18.5	3	(3.9)	2	(3.6)	1	(4.8)	1	(1.4)	1	(1.9)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
[18.5-25[	41	(53.2)	28	(50.0)	13	(61.9)	43	(61.4)	31	(59.6)	12	(66.7)	9	(56.3)	8	(61.5)	1	(33.3)	0	(0.0)	0	(0.0)	0	(0.0)
[25-30[	21	(27.3)	16	(28.6)	5	(23.8)	16	(22.9)	11	(21.2)	5	(27.8)	3	(18.8)	1	(7.7)	2	(66.7)	0	(0.0)	0	(0.0)	0	(0.0)
≥30	12	(15.6)	10	(17.9)	2	(9.5)	10	(14.3)	9	(17.3)	1	(5.6)	4	(25.0)	4	(30.8)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
[2010-2016]	**19**	**(19.8)**	**10**	**(15.2)**	**9**	**(30.0)**	**33**	**(32.0)**	**25**	**(32.5)**	**8**	**(30.8)**	**5**	**(23.8)**	**3**	**(18.8)**	**2**	**(40.0)**	**11**	**(100.0)**	**8**	**(100.0)**	**3**	**(100.0)**
BMI (kg/m2) (in categories), n (%)																								
<18.5	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(20.0)	0	(0.0)	1	(50.0)	0	(0.0)	0	(0.0)	0	(0.0)
[18.5-25[	7	(36.8)	2	(20.0)	5	(55.6)	14	(42.4)	9	(36.0)	5	(62.5)	2	(40.0)	1	(33.3)	1	(50.0)	6	(54.5)	4	(50.0)	2	(66.7)
[25-30[	9	(47.4)	6	(60.0)	3	(33.3)	14	(42.4)	12	(48.0)	2	(25.0)	1	(20.0)	1	(33.3)	0	(0.0)	3	(27.3)	3	(37.5)	0	(0.0)
≥30	3	(15.8)	2	(20.0)	1	(11.1)	5	(15.2)	4	(16.0)	1	(12.5)	1	(20.0)	1	(33.3)	0	(0.0)	2	(18.2)	1	(12.5)	1	(33.3)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 32. Description of Body Mass Index (BMI) among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and by RA severity according to calendar year at the date of initiation of the considered drug, whatever the rank of treatment line

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	Severe RA n = 2	Not Severe RA n = 3	ALL n = 21	Severe RA n = 17	Not Severe RA n = 4	ALL n = 20	Severe RA n = 16	Not Severe RA n = 4
Total									
BMI (kg/m2)									
Size (missing)	5 (0)	2 (0)	3 (0)	21 (0)	17 (0)	4 (0)	20 (0)	16 (0)	4 (0)
Mean (± SD)	28.4 (6.6)	27.1 (0.6)	29.3 (9.2)	26.2 (3.5)	25.7 (3.4)	28.3 (3.4)	24.3 (4.7)	25.1 (4.7)	21.1 (3.3)
Median	26.7	27.1	25.5	25.6	25.6	28.2	23.7	24.7	22.1
[p25% - p75%]	[25.5;27.5]	[26.7;27.5]	[22.5;39.8]	[24.4;28.7]	[23.1;27.5]	[25.5;31.0]	[21.8;26.1]	[22.2;27.0]	[18.9;23.3]
[Min - Max]	[22.5;39.8]	[26.7;27.5]	[22.5;39.8]	[19.9;32.0]	[19.9;31.5]	[24.6;32.0]	[16.4;35.2]	[19.1;35.2]	[16.4;23.7]
[2003-2009]	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**8 (38.1)**	**8 (47.1)**	**0 (0.0)**	**1 (5.0)**	**1 (6.3)**	**0 (0.0)**
BMI (kg/m2)									
Size (missing)				8 (0)	8 (0)		1 (0)	1 (0)	
Mean (± SD)				26.1 (3.8)	26.1 (3.8)		22.2	22.2	
Median				25.7	25.7		22.2	22.2	
[p25% - p75%]				[23.8;29.2]	[23.8;29.2]		[22.2;22.2]	[22.2;22.2]	
[Min - Max]				[19.9;31.5]	[19.9;31.5]		[22.2;22.2]	[22.2;22.2]	
[2010-2016]	**5 (100.0)**	**2 (100.0)**	**3 (100.0)**	**13 (61.9)**	**9 (52.9)**	**4 (100.0)**	**19 (95.0)**	**15 (93.8)**	**4 (100.0)**
BMI (kg/m2)									
Size (missing)	5 (0)	2 (0)	3 (0)	13 (0)	9 (0)	4 (0)	19 (0)	15 (0)	4 (0)
Mean (± SD)	28.4 (6.6)	27.1 (0.6)	29.3 (9.2)	26.2 (3.4)	25.3 (3.1)	28.3 (3.4)	24.4 (4.8)	25.3 (4.8)	21.1 (3.3)
Median	26.7	27.1	25.5	25.6	25.6	28.2	23.7	25.0	22.1
[p25% - p75%]	[25.5;27.5]	[26.7;27.5]	[22.5;39.8]	[24.6;27.5]	[22.2;26.7]	[25.5;31.0]	[21.4;26.4]	[22.2;27.5]	[18.9;23.3]
[Min - Max]	[22.5;39.8]	[26.7;27.5]	[22.5;39.8]	[21.3;32.0]	[21.3;31.2]	[24.6;32.0]	[16.4;35.2]	[19.1;35.2]	[16.4;23.7]

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 33. Description of Body Mass Index (BMI) in categories among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and by RA severity according to calendar year at the date of initiation of the considered drug, whatever the rank of treatment line

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	Severe RA n = 2	Not Severe RA n = 3	ALL n = 21	Severe RA n = 17	Not Severe RA n = 4	ALL n = 20	Severe RA n = 16	Not Severe RA n = 4
Total									
BMI (kg/m2) (in categories), n (%)									
<18.5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.0)	0 (0.0)	1 (25.0)
[18.5-25[	1 (20.0)	0 (0.0)	1 (33.3)	8 (38.1)	7 (41.2)	1 (25.0)	12 (60.0)	9 (56.3)	3 (75.0)
[25-30[	3 (60.0)	2 (100.0)	1 (33.3)	9 (42.9)	8 (47.1)	1 (25.0)	5 (25.0)	5 (31.3)	0 (0.0)
≥30	1 (20.0)	0 (0.0)	1 (33.3)	4 (19.0)	2 (11.8)	2 (50.0)	2 (10.0)	2 (12.5)	0 (0.0)
[2003-2009]	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**8 (38.1)**	**8 (47.1)**	**0 (0.0)**	**1 (5.0)**	**1 (6.3)**	**0 (0.0)**
BMI (kg/m2) (in categories), n (%)									
<18.5	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)
[18.5-25[	0 (0.0)	0 (0.0)	0 (0.0)	4 (50.0)	4 (50.0)	0 (0.0)	1 (100.0)	1 (100.0)	0 (0.0)
[25-30[	0 (0.0)	0 (0.0)	0 (0.0)	3 (37.5)	3 (37.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
≥30	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
[2010-2016]	**5 (100.0)**	**2 (100.0)**	**3 (100.0)**	**13 (61.9)**	**9 (52.9)**	**4 (100.0)**	**19 (95.0)**	**15 (93.8)**	**4 (100.0)**
BMI (kg/m2) (in categories), n (%)									
<18.5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.3)	0 (0.0)	1 (25.0)
[18.5-25[	1 (20.0)	0 (0.0)	1 (33.3)	4 (30.8)	3 (33.3)	1 (25.0)	11 (57.9)	8 (53.3)	3 (75.0)
[25-30[	3 (60.0)	2 (100.0)	1 (33.3)	6 (46.2)	5 (55.6)	1 (25.0)	5 (26.3)	5 (33.3)	0 (0.0)
≥30	1 (20.0)	0 (0.0)	1 (33.3)	3 (23.1)	1 (11.1)	2 (50.0)	2 (10.5)	2 (13.3)	0 (0.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

3.3.2 SMOKING STATUS

Table 34. Description of smoking status among patients with Rheumatoid Arthritis aged ≥ 18 years for overall population and by RA severity according to age at the date of initiation of the first treatment line among the drugs of interest[1] and by group of patients treated by therapeutic class (TNFi and JAK inhibitors)

	All drugs of interest[1]						TNFi[2]					
	All n = 180		Severe RA n = 123		Not Severe RA n = 57		All n = 172		Severe RA n = 117		Not Severe RA n = 55	
Total												
Smoking status, n (%)												
Never smoker	96	(53.3)	66	(53.7)	30	(52.6)	93	(54.1)	63	(53.8)	30	(54.5)
Former smoker	49	(27.2)	36	(29.3)	13	(22.8)	45	(26.2)	34	(29.1)	11	(20.0)
Current smoker	35	(19.4)	21	(17.1)	14	(24.6)	34	(19.8)	20	(17.1)	14	(25.5)
[18-30[	**14**	**(7.8)**	**6**	**(4.9)**	**8**	**(14.0)**	**14**	**(8.1)**	**6**	**(5.1)**	**8**	**(14.5)**
Smoking status, n (%)												
Never smoker	11	(78.6)	5	(83.3)	6	(75.0)	11	(78.6)	5	(83.3)	6	(75.0)
Former smoker	1	(7.1)	1	(16.7)	0	(0.0)	1	(7.1)	1	(16.7)	0	(0.0)
Current smoker	2	(14.3)	0	(0.0)	2	(25.0)	2	(14.3)	0	(0.0)	2	(25.0)
[30-40[	**22**	**(12.2)**	**14**	**(11.4)**	**8**	**(14.0)**	**22**	**(12.8)**	**14**	**(12.0)**	**8**	**(14.5)**
Smoking status, n (%)												
Never smoker	11	(50.0)	8	(57.1)	3	(37.5)	11	(50.0)	8	(57.1)	3	(37.5)
Former smoker	5	(22.7)	2	(14.3)	3	(37.5)	5	(22.7)	2	(14.3)	3	(37.5)
Current smoker	6	(27.3)	4	(28.6)	2	(25.0)	6	(27.3)	4	(28.6)	2	(25.0)
[40-50[	**45**	**(25.0)**	**31**	**(25.2)**	**14**	**(24.6)**	**44**	**(25.6)**	**31**	**(26.5)**	**13**	**(23.6)**
Smoking status, n (%)												
Never smoker	24	(53.3)	16	(51.6)	8	(57.1)	24	(54.5)	16	(51.6)	8	(61.5)
Former smoker	15	(33.3)	11	(35.5)	4	(28.6)	14	(31.8)	11	(35.5)	3	(23.1)
Current smoker	6	(13.3)	4	(12.9)	2	(14.3)	6	(13.6)	4	(12.9)	2	(15.4)
[50-60[	**56**	**(31.1)**	**41**	**(33.3)**	**15**	**(26.3)**	**55**	**(32.0)**	**40**	**(34.2)**	**15**	**(27.3)**
Smoking status, n (%)												
Never smoker	27	(48.2)	18	(43.9)	9	(60.0)	27	(49.1)	18	(45.0)	9	(60.0)
Former smoker	18	(32.1)	15	(36.6)	3	(20.0)	17	(30.9)	14	(35.0)	3	(20.0)
Current smoker	11	(19.6)	8	(19.5)	3	(20.0)	11	(20.0)	8	(20.0)	3	(20.0)

	All drugs of interest[1]						TNFi[2]					
	All n = 180		Severe RA n = 123		Not Severe RA n = 57		All n = 172		Severe RA n = 117		Not Severe RA n = 55	
[60-65[	**22**	**(12.2)**	**17**	**(13.8)**	**5**	**(8.8)**	**19**	**(11.0)**	**14**	**(12.0)**	**5**	**(9.1)**
Smoking status, n (%)												
Never smoker	10	(45.5)	8	(47.1)	2	(40.0)	8	(42.1)	6	(42.9)	2	(40.0)
Former smoker	7	(31.8)	6	(35.3)	1	(20.0)	6	(31.6)	5	(35.7)	1	(20.0)
Current smoker	5	(22.7)	3	(17.6)	2	(40.0)	5	(26.3)	3	(21.4)	2	(40.0)
≥65	**21**	**(11.7)**	**14**	**(11.4)**	**7**	**(12.3)**	**18**	**(10.5)**	**12**	**(10.3)**	**6**	**(10.9)**
Smoking status, n (%)												
Never smoker	13	(61.9)	11	(78.6)	2	(28.6)	12	(66.7)	10	(83.3)	2	(33.3)
Former smoker	3	(14.3)	1	(7.1)	2	(28.6)	2	(11.1)	1	(8.3)	1	(16.7)
Current smoker	5	(23.8)	2	(14.3)	3	(42.9)	4	(22.2)	1	(8.3)	3	(50.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 35. Description of smoking status among patients with Rheumatoid Arthritis aged ≥ 18 years for overall population and according to gender at the date of initiation of the first treatment line among the drugs of interest[1] and by group of patients treated by therapeutic class (TNFi and JAK inhibitors)

	All drugs of interest[1]						TNFi[2]					
	All n = 180		Severe RA n = 123		Not Severe RA n = 57		All n = 172		Severe RA n = 117		Not Severe RA n = 55	
Total												
Smoking status, n (%)												
Never smoker	96	(53.3)	66	(53.7)	30	(52.6)	93	(54.1)	63	(53.8)	30	(54.5)
Former smoker	49	(27.2)	36	(29.3)	13	(22.8)	45	(26.2)	34	(29.1)	11	(20.0)
Current smoker	35	(19.4)	21	(17.1)	14	(24.6)	34	(19.8)	20	(17.1)	14	(25.5)
Women	**134**	**(74.4)**	**95**	**(77.2)**	**39**	**(68.4)**	**127**	**(73.8)**	**90**	**(76.9)**	**37**	**(67.3)**
Smoking status, n (%)												
Never smoker	77	(57.5)	55	(57.9)	22	(56.4)	74	(58.3)	52	(57.8)	22	(59.5)
Former smoker	32	(23.9)	23	(24.2)	9	(23.1)	29	(22.8)	22	(24.4)	7	(18.9)
Current smoker	25	(18.7)	17	(17.9)	8	(20.5)	24	(18.9)	16	(17.8)	8	(21.6)
Men	**46**	**(25.6)**	**28**	**(22.8)**	**18**	**(31.6)**	**45**	**(26.2)**	**27**	**(23.1)**	**18**	**(32.7)**
Smoking status, n (%)												
Never smoker	19	(41.3)	11	(39.3)	8	(44.4)	19	(42.2)	11	(40.7)	8	(44.4)
Former smoker	17	(37.0)	13	(46.4)	4	(22.2)	16	(35.6)	12	(44.4)	4	(22.2)
Current smoker	10	(21.7)	4	(14.3)	6	(33.3)	10	(22.2)	4	(14.8)	6	(33.3)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 36. Description of smoking status among patients with Rheumatoid Arthritis aged ≥ 18 years for overall population and bu RA severity according to calendar year at the date of initiation of the first treatment line among the drugs of interest[1] and by group of patients treated by therapeutic class (TNFi and JAK inhibitors)

	All drugs of interest[1]						TNFi[2]					
	All n = 180		Severe RA n = 123		Not Severe RA n = 57		All n = 172		Severe RA n = 117		Not Severe RA n = 55	
Total												
Smoking status, n (%)												
Never smoker	96	(53.3)	66	(53.7)	30	(52.6)	93	(54.1)	63	(53.8)	30	(54.5)
Former smoker	49	(27.2)	36	(29.3)	13	(22.8)	45	(26.2)	34	(29.1)	11	(20.0)
Current smoker	35	(19.4)	21	(17.1)	14	(24.6)	34	(19.8)	20	(17.1)	14	(25.5)
[2003-2009]	**131**	**(72.8)**	**94**	**(76.4)**	**37**	**(64.9)**	**129**	**(75.0)**	**92**	**(78.6)**	**37**	**(67.3)**
Smoking status, n (%)												
Never smoker	64	(48.9)	44	(46.8)	20	(54.1)	63	(48.8)	43	(46.7)	20	(54.1)
Former smoker	41	(31.3)	31	(33.0)	10	(27.0)	40	(31.0)	30	(32.6)	10	(27.0)
Current smoker	26	(19.8)	19	(20.2)	7	(18.9)	26	(20.2)	19	(20.7)	7	(18.9)
[2010-2016]	**49**	**(27.2)**	**29**	**(23.6)**	**20**	**(35.1)**	**43**	**(25.0)**	**25**	**(21.4)**	**18**	**(32.7)**
Smoking status, n (%)												
Never smoker	32	(65.3)	22	(75.9)	10	(50.0)	30	(69.8)	20	(80.0)	10	(55.6)
Former smoker	8	(16.3)	5	(17.2)	3	(15.0)	5	(11.6)	4	(16.0)	1	(5.6)
Current smoker	9	(18.4)	2	(6.9)	7	(35.0)	8	(18.6)	1	(4.0)	7	(38.9)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 37. Description of smoking status among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and by RA severity according to age at the date of initiation of the considered drug, whatever the rank of treatment line

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	Severe RA n = 66	Not Severe RA n = 30	ALL n = 103	Severe RA n = 77	Not Severe RA n = 26	ALL n = 21	Severe RA n = 16	Not Severe RA n = 5	ALL n = 11	Severe RA n = 8	Not Severe RA n = 3
Total												
Smoking status, n (%)												
Never smoker	50 (52.1)	33 (50.0)	17 (56.7)	60 (58.3)	44 (57.1)	16 (61.5)	12 (57.1)	11 (68.8)	1 (20.0)	5 (45.5)	5 (62.5)	0 (0.0)
Former smoker	27 (28.1)	22 (33.3)	5 (16.7)	22 (21.4)	17 (22.1)	5 (19.2)	5 (23.8)	3 (18.8)	2 (40.0)	4 (36.4)	2 (25.0)	2 (66.7)
Current smoker	19 (19.8)	11 (16.7)	8 (26.7)	21 (20.4)	16 (20.8)	5 (19.2)	4 (19.0)	2 (12.5)	2 (40.0)	2 (18.2)	1 (12.5)	1 (33.3)
[18-30[	**5 (5.2)**	**2 (3.0)**	**3 (10.0)**	**8 (7.8)**	**4 (5.2)**	**4 (15.4)**	**3 (14.3)**	**2 (12.5)**	**1 (20.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Smoking status, n (%)												
Never smoker	3 (60.0)	1 (50.0)	2 (66.7)	6 (75.0)	3 (75.0)	3 (75.0)	3 (100.0)	2 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
Former smoker	1 (20.0)	1 (50.0)	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 (0.0)	0 (0.0)
Current smoker	1 (20.0)	0 (0.0)	1 (33.3)	2 (25.0)	1 (25.0)	1 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
[30-40[	**18 (18.8)**	**10 (15.2)**	**8 (26.7)**	**8 (7.8)**	**6 (7.8)**	**2 (7.7)**	**3 (14.3)**	**1 (6.3)**	**2 (40.0)**	**1 (9.1)**	**0 (0.0)**	**1 (33.3)**
Smoking status, n (%)												
Never smoker	8 (44.4)	5 (50.0)	3 (37.5)	5 (62.5)	4 (66.7)	1 (50.0)	1 (33.3)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Former smoker	4 (22.2)	2 (20.0)	2 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (66.7)	0 (0.0)	2 (100.0)	1 (100.0)	0 (0.0)	1 (100.0)
Current smoker	6 (33.3)	3 (30.0)	3 (37.5)	3 (37.5)	2 (33.3)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
[40-50[	**26 (27.1)**	**19 (28.8)**	**7 (23.3)**	**20 (19.4)**	**14 (18.2)**	**6 (23.1)**	**7 (33.3)**	**6 (37.5)**	**1 (20.0)**	**3 (27.3)**	**2 (25.0)**	**1 (33.3)**
Smoking status, n (%)												
Never smoker	17 (65.4)	12 (63.2)	5 (71.4)	12 (60.0)	8 (57.1)	4 (66.7)	3 (42.9)	3 (50.0)	0 (0.0)	1 (33.3)	1 (50.0)	0 (0.0)
Former smoker	7 (26.9)	6 (31.6)	1 (14.3)	6 (30.0)	4 (28.6)	2 (33.3)	2 (28.6)	2 (33.3)	0 (0.0)	2 (66.7)	1 (50.0)	1 (100.0)
Current smoker	2 (7.7)	1 (5.3)	1 (14.3)	2 (10.0)	2 (14.3)	0 (0.0)	2 (28.6)	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
[50-60[	**31 (32.3)**	**22 (33.3)**	**9 (30.0)**	**39 (37.9)**	**31 (40.3)**	**8 (30.8)**	**4 (19.0)**	**4 (25.0)**	**0 (0.0)**	**2 (18.2)**	**2 (25.0)**	**0 (0.0)**
Smoking status, n (%)												
Never smoker	15 (48.4)	9 (40.9)	6 (66.7)	21 (53.8)	16 (51.6)	5 (62.5)	3 (75.0)	3 (75.0)	0 (0.0)	2 (100.0)	2 (100.0)	0 (0.0)
Former smoker	10 (32.3)	9 (40.9)	1 (11.1)	11 (28.2)	9 (29.0)	2 (25.0)	1 (25.0)	1 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Current smoker	6 (19.4)	4 (18.2)	2 (22.2)	7 (17.9)	6 (19.4)	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	Severe RA n = 66	Not Severe RA n = 30	ALL n = 103	Severe RA n = 77	Not Severe RA n = 26	ALL n = 21	Severe RA n = 16	Not Severe RA n = 5	ALL n = 11	Severe RA n = 8	Not Severe RA n = 3
[60-65[	**10 (10.4)**	**8 (12.1)**	**2 (6.7)**	**12 (11.7)**	**10 (13.0)**	**2 (7.7)**	**2 (9.5)**	**1 (6.3)**	**1 (20.0)**	**4 (36.4)**	**3 (37.5)**	**1 (33.3)**
Smoking status, n (%)												
Never smoker	4 (40.0)	3 (37.5)	1 (50.0)	4 (33.3)	3 (30.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (33.3)	0 (0.0)
Former smoker	4 (40.0)	3 (37.5)	1 (50.0)	3 (25.0)	3 (30.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (33.3)	0 (0.0)
Current smoker	2 (20.0)	2 (25.0)	0 (0.0)	5 (41.7)	4 (40.0)	1 (50.0)	2 (100.0)	1 (100.0)	1 (100.0)	2 (50.0)	1 (33.3)	1 (100.0)
≥65	**6 (6.3)**	**5 (7.6)**	**1 (3.3)**	**16 (15.5)**	**12 (15.6)**	**4 (15.4)**	**2 (9.5)**	**2 (12.5)**	**0 (0.0)**	**1 (9.1)**	**1 (12.5)**	**0 (0.0)**
Smoking status, n (%)												
Never smoker	3 (50.0)	3 (60.0)	0 (0.0)	12 (75.0)	10 (83.3)	2 (50.0)	2 (100.0)	2 (100.0)	0 (0.0)	1 (100.0)	1 (100.0)	0 (0.0)
Former smoker	1 (16.7)	1 (20.0)	0 (0.0)	2 (12.5)	1 (8.3)	1 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Current smoker	2 (33.3)	1 (20.0)	1 (100.0)	2 (12.5)	1 (8.3)	1 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 38. Description of smoking status among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and by RA severity according to age at the date of initiation of the considered drug, whatever the rank of treatment line

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	Severe RA n = 2	Not Severe RA n = 3	ALL n = 21	Severe RA n = 17	Not Severe RA n = 4	ALL n = 20	Severe RA n = 16	Not Severe RA n = 4
Total									
Smoking status, n (%)									
Never smoker	3 (60.0)	2 (100.0)	1 (33.3)	13 (61.9)	11 (64.7)	2 (50.0)	13 (65.0)	11 (68.8)	2 (50.0)
Former smoker	1 (20.0)	0 (0.0)	1 (33.3)	5 (23.8)	3 (17.6)	2 (50.0)	6 (30.0)	5 (31.3)	1 (25.0)
Current smoker	1 (20.0)	0 (0.0)	1 (33.3)	3 (14.3)	3 (17.6)	0 (0.0)	1 (5.0)	0 (0.0)	1 (25.0)
[18-30[	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**1 (4.8)**	**1 (5.9)**	**0 (0.0)**	**4 (20.0)**	**3 (18.8)**	**1 (25.0)**
Smoking status, n (%)									
Never smoker	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)	0 (0.0)	4 (100.0)	3 (100.0)	1 (100.0)
Former smoker	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)
Current smoker	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)
[30-40[	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**2 (9.5)**	**1 (5.9)**	**1 (25.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Smoking status, n (%)									
Never smoker	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)	1 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
Former smoker	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)
Current smoker	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)
[40-50[	**2 (40.0)**	**0 (0.0)**	**2 (66.7)**	**1 (4.8)**	**0 (0.0)**	**1 (25.0)**	**2 (10.0)**	**0 (0.0)**	**2 (50.0)**
Smoking status, n (%)									
Never smoker	1 (50.0)	0 (0.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	0 (0.0)	1 (50.0)
Former smoker	1 (50.0)	0 (0.0)	1 (50.0)	1 (100.0)	0 (0.0)	1 (100.0)	1 (50.0)	0 (0.0)	1 (50.0)
Current smoker	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)
[50-60[	**1 (20.0)**	**1 (50.0)**	**0 (0.0)**	**7 (33.3)**	**6 (35.3)**	**1 (25.0)**	**6 (30.0)**	**6 (37.5)**	**0 (0.0)**
Smoking status, n (%)									
Never smoker	1 (100.0)	1 (100.0)	0 (0.0)	6 (85.7)	5 (83.3)	1 (100.0)	2 (33.3)	2 (33.3)	0 (0.0)
Former smoker	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	1 (16.7)	0 (0.0)	4 (66.7)	4 (66.7)	0 (0.0)
Current smoker	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)

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	Severe RA n = 2	Not Severe RA n = 3	ALL n = 21	Severe RA n = 17	Not Severe RA n = 4	ALL n = 20	Severe RA n = 16	Not Severe RA n = 4
[60-65[	**1 (20.0)**	**1 (50.0)**	**0 (0.0)**	**4 (19.0)**	**4 (23.5)**	**0 (0.0)**	**4 (20.0)**	**3 (18.8)**	**1 (25.0)**
Smoking status, n (%)									
Never smoker	1 (100.0)	1 (100.0)	0 (0.0)	2 (50.0)	2 (50.0)	0 (0.0)	3 (75.0)	3 (100.0)	0 (0.0)
Former smoker	0 (0.0)	0 (0.0)	0 (0.0)	2 (50.0)	2 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Current smoker	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	1 (100.0)
≥65	**1 (20.0)**	**0 (0.0)**	**1 (33.3)**	**6 (28.6)**	**5 (29.4)**	**1 (25.0)**	**4 (20.0)**	**4 (25.0)**	**0 (0.0)**
Smoking status, n (%)									
Never smoker	0 (0.0)	0 (0.0)	0 (0.0)	2 (33.3)	2 (40.0)	0 (0.0)	3 (75.0)	3 (75.0)	0 (0.0)
Former smoker	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (100.0)	1 (25.0)	1 (25.0)	0 (0.0)
Current smoker	1 (100.0)	0 (0.0)	1 (100.0)	3 (50.0)	3 (60.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 39. Description of smoking status among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and by RA severity according to gender at the date of initiation of the considered drug, whatever the rank of treatment line

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	Severe RA n = 66	Not Severe RA n = 30	ALL n = 103	Severe RA n = 77	Not Severe RA n = 26	ALL n = 21	Severe RA n = 16	Not Severe RA n = 5	ALL n = 11	Severe RA n = 8	Not Severe RA n = 3
Total												
Smoking status, n (%)												
Never smoker	50 (52.1)	33 (50.0)	17 (56.7)	60 (58.3)	44 (57.1)	16 (61.5)	12 (57.1)	11 (68.8)	1 (20.0)	5 (45.5)	5 (62.5)	0 (0.0)
Former smoker	27 (28.1)	22 (33.3)	5 (16.7)	22 (21.4)	17 (22.1)	5 (19.2)	5 (23.8)	3 (18.8)	2 (40.0)	4 (36.4)	2 (25.0)	2 (66.7)
Current smoker	19 (19.8)	11 (16.7)	8 (26.7)	21 (20.4)	16 (20.8)	5 (19.2)	4 (19.0)	2 (12.5)	2 (40.0)	2 (18.2)	1 (12.5)	1 (33.3)
Women	**72 (75.0)**	**51 (77.3)**	**21 (70.0)**	**80 (77.7)**	**62 (80.5)**	**18 (69.2)**	**15 (71.4)**	**11 (68.8)**	**4 (80.0)**	**8 (72.7)**	**7 (87.5)**	**1 (33.3)**
Smoking status, n (%)												
Never smoker	40 (55.6)	28 (54.9)	12 (57.1)	51 (63.8)	38 (61.3)	13 (72.2)	9 (60.0)	8 (72.7)	1 (25.0)	5 (62.5)	5 (71.4)	0 (0.0)
Former smoker	19 (26.4)	15 (29.4)	4 (19.0)	13 (16.3)	11 (17.7)	2 (11.1)	3 (20.0)	1 (9.1)	2 (50.0)	2 (25.0)	1 (14.3)	1 (100.0)
Current smoker	13 (18.1)	8 (15.7)	5 (23.8)	16 (20.0)	13 (21.0)	3 (16.7)	3 (20.0)	2 (18.2)	1 (25.0)	1 (12.5)	1 (14.3)	0 (0.0)
Men	**24 (25.0)**	**15 (22.7)**	**9 (30.0)**	**23 (22.3)**	**15 (19.5)**	**8 (30.8)**	**6 (28.6)**	**5 (31.3)**	**1 (20.0)**	**3 (27.3)**	**1 (12.5)**	**2 (66.7)**
Smoking status, n (%)												
Never smoker	10 (41.7)	5 (33.3)	5 (55.6)	9 (39.1)	6 (40.0)	3 (37.5)	3 (50.0)	3 (60.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Former smoker	8 (33.3)	7 (46.7)	1 (11.1)	9 (39.1)	6 (40.0)	3 (37.5)	2 (33.3)	2 (40.0)	0 (0.0)	2 (66.7)	1 (100.0)	1 (50.0)
Current smoker	6 (25.0)	3 (20.0)	3 (33.3)	5 (21.7)	3 (20.0)	2 (25.0)	1 (16.7)	0 (0.0)	1 (100.0)	1 (33.3)	0 (0.0)	1 (50.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 40. Description of smoking status among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and by RA severity according to gender at the date of initiation of the considered drug, whatever the rank of treatment line

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	Severe RA n = 2	Not Severe RA n = 3	ALL n = 21	Severe RA n = 17	Not Severe RA n = 4	ALL n = 20	Severe RA n = 16	Not Severe RA n = 4
Total									
Smoking status, n (%)									
Never smoker	3 (60.0)	2 (100.0)	1 (33.3)	13 (61.9)	11 (64.7)	2 (50.0)	13 (65.0)	11 (68.8)	2 (50.0)
Former smoker	1 (20.0)	0 (0.0)	1 (33.3)	5 (23.8)	3 (17.6)	2 (50.0)	6 (30.0)	5 (31.3)	1 (25.0)
Current smoker	1 (20.0)	0 (0.0)	1 (33.3)	3 (14.3)	3 (17.6)	0 (0.0)	1 (5.0)	0 (0.0)	1 (25.0)
Women	**4 (80.0)**	**2 (100.0)**	**2 (66.7)**	**16 (76.2)**	**14 (82.4)**	**2 (50.0)**	**17 (85.0)**	**14 (87.5)**	**3 (75.0)**
Smoking status, n (%)									
Never smoker	3 (75.0)	2 (100.0)	1 (50.0)	10 (62.5)	10 (71.4)	0 (0.0)	12 (70.6)	10 (71.4)	2 (66.7)
Former smoker	0 (0.0)	0 (0.0)	0 (0.0)	3 (18.8)	1 (7.1)	2 (100.0)	5 (29.4)	4 (28.6)	1 (33.3)
Current smoker	1 (25.0)	0 (0.0)	1 (50.0)	3 (18.8)	3 (21.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Men	**1 (20.0)**	**0 (0.0)**	**1 (33.3)**	**5 (23.8)**	**3 (17.6)**	**2 (50.0)**	**3 (15.0)**	**2 (12.5)**	**1 (25.0)**
Smoking status, n (%)									
Never smoker	0 (0.0)	0 (0.0)	0 (0.0)	3 (60.0)	1 (33.3)	2 (100.0)	1 (33.3)	1 (50.0)	0 (0.0)
Former smoker	1 (100.0)	0 (0.0)	1 (100.0)	2 (40.0)	2 (66.7)	0 (0.0)	1 (33.3)	1 (50.0)	0 (0.0)
Current smoker	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)	0 (0.0)	1 (100.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 41. Description of smoking status among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and by RA severity according to calendar year at the date of initiation of the considered drug, whatever the rank of treatment line

	Adalimumab			Etanercept			Infliximab			Certolizumab		
	ALL n = 96	Severe RA n = 66	Not Severe RA n = 30	ALL n = 103	Severe RA n = 77	Not Severe RA n = 26	ALL n = 21	Severe RA n = 16	Not Severe RA n = 5	ALL n = 11	Severe RA n = 8	Not Severe RA n = 3
Total												
Smoking status, n (%)												
Never smoker	50 (52.1)	33 (50.0)	17 (56.7)	60 (58.3)	44 (57.1)	16 (61.5)	12 (57.1)	11 (68.8)	1 (20.0)	5 (45.5)	5 (62.5)	0 (0.0)
Former smoker	27 (28.1)	22 (33.3)	5 (16.7)	22 (21.4)	17 (22.1)	5 (19.2)	5 (23.8)	3 (18.8)	2 (40.0)	4 (36.4)	2 (25.0)	2 (66.7)
Current smoker	19 (19.8)	11 (16.7)	8 (26.7)	21 (20.4)	16 (20.8)	5 (19.2)	4 (19.0)	2 (12.5)	2 (40.0)	2 (18.2)	1 (12.5)	1 (33.3)
[2003-2009]	**77 (80.2)**	**56 (84.8)**	**21 (70.0)**	**70 (68.0)**	**52 (67.5)**	**18 (69.2)**	**16 (76.2)**	**13 (81.3)**	**3 (60.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Smoking status, n (%)												
Never smoker	40 (51.9)	28 (50.0)	12 (57.1)	35 (50.0)	24 (46.2)	11 (61.1)	8 (50.0)	8 (61.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Former smoker	23 (29.9)	19 (33.9)	4 (19.0)	19 (27.1)	15 (28.8)	4 (22.2)	5 (31.3)	3 (23.1)	2 (66.7)	0 (0.0)	0 (0.0)	0 (0.0)
Current smoker	14 (18.2)	9 (16.1)	5 (23.8)	16 (22.9)	13 (25.0)	3 (16.7)	3 (18.8)	2 (15.4)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)
[2010-2016]	**19 (19.8)**	**10 (15.2)**	**9 (30.0)**	**33 (32.0)**	**25 (32.5)**	**8 (30.8)**	**5 (23.8)**	**3 (18.8)**	**2 (40.0)**	**11 (100.0)**	**8 (100.0)**	**3 (100.0)**
Smoking status, n (%)												
Never smoker	10 (52.6)	5 (50.0)	5 (55.6)	25 (75.8)	20 (80.0)	5 (62.5)	4 (80.0)	3 (100.0)	1 (50.0)	5 (45.5)	5 (62.5)	0 (0.0)
Former smoker	4 (21.1)	3 (30.0)	1 (11.1)	3 (9.1)	2 (8.0)	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	4 (36.4)	2 (25.0)	2 (66.7)
Current smoker	5 (26.3)	2 (20.0)	3 (33.3)	5 (15.2)	3 (12.0)	2 (25.0)	1 (20.0)	0 (0.0)	1 (50.0)	2 (18.2)	1 (12.5)	1 (33.3)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Table 42. Description of smoking status among patients with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and by RA severity according to calendar year at the date of initiation of the considered drug, whatever the rank of treatment line

	Golimumab			Abatacept			Tocizilumab		
	ALL n = 5	Severe RA n = 2	Not Severe RA n = 3	ALL n = 21	Severe RA n = 17	Not Severe RA n = 4	ALL n = 20	Severe RA n = 16	Not Severe RA n = 4
Total									
Smoking status, n (%)									
Never smoker	3 (60.0)	2 (100.0)	1 (33.3)	13 (61.9)	11 (64.7)	2 (50.0)	13 (65.0)	11 (68.8)	2 (50.0)
Former smoker	1 (20.0)	0 (0.0)	1 (33.3)	5 (23.8)	3 (17.6)	2 (50.0)	6 (30.0)	5 (31.3)	1 (25.0)
Current smoker	1 (20.0)	0 (0.0)	1 (33.3)	3 (14.3)	3 (17.6)	0 (0.0)	1 (5.0)	0 (0.0)	1 (25.0)
[2003-2009]	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**8 (38.1)**	**8 (47.1)**	**0 (0.0)**	**1 (5.0)**	**1 (6.3)**	**0 (0.0)**
Smoking status, n (%)									
Never smoker	0 (0.0)	0 (0.0)	0 (0.0)	5 (62.5)	5 (62.5)	0 (0.0)	1 (100.0)	1 (100.0)	0 (0.0)
Former smoker	0 (0.0)	0 (0.0)	0 (0.0)	2 (25.0)	2 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Current smoker	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
[2010-2016]	**5 (100.0)**	**2 (100.0)**	**3 (100.0)**	**13 (61.9)**	**9 (52.9)**	**4 (100.0)**	**19 (95.0)**	**15 (93.8)**	**4 (100.0)**
Smoking status, n (%)									
Never smoker	3 (60.0)	2 (100.0)	1 (33.3)	8 (61.5)	6 (66.7)	2 (50.0)	12 (63.2)	10 (66.7)	2 (50.0)
Former smoker	1 (20.0)	0 (0.0)	1 (33.3)	3 (23.1)	1 (11.1)	2 (50.0)	6 (31.6)	5 (33.3)	1 (25.0)
Current smoker	1 (20.0)	0 (0.0)	1 (33.3)	2 (15.4)	2 (22.2)	0 (0.0)	1 (5.3)	0 (0.0)	1 (25.0)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB

Statistical analysis report

CORPUS_BMI_smoking

Description

V02 - 08/01/2021

Statistician :
Mr. Soudant

Méthodologist :
Prof. F. Guillemin

This document presents the data analysis of the **"PR" (RA) cohort** from **the CORPUS project** based on the **statistical analysis plan in its version N°01**.

Data used were frozen in **March 2011.**

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ABBREVIATIONS LIST

ACR	
BMI	Body Mass Index (Indice de masse corporelle)
CORPUS	Cohorte d'Observation Rhumatologique des Pratiques et des USages
CRF	Case Report Form (Cahier d'observations)
CRP	C-reactive protein
DAS28	The 28 joint Disease Activity Score
JIA (AJI)	Juvenile Idiopathic Arthritis (Arthrite Juvénile Idiopathique In French)
HAQ	Health Assessment Questionnaire
RA (PR)	Rheumatoid arthritis (Polyarthrite Rhumatoïde in french)
SA (SPA)	Ankylosing Spondylitis (SPondylarthrite Ankylosante in French)
SAP	Statistical analysis plan
VAS	Visual Analogue Scale

I. THE CORPUS STUDY

The CORPUS study is a longitudinal prospective population-based cohort study of patients with RA ("CORPUS PR"), SA ("CORPUS SPA"), or JIA ("CORPUS AJI") recruited in private practices and hospitals.

Physicians and patients
All physicians authorised to prescribe biologics in France, *i.e.* rheumatologists (members of the French Society for Rheumatology [SFR]), paediatricians (members of the French-Speaking Society for Paediatric Rheumatology and Inflammatory Diseases [SOFREMIP] and/or French Society for Paediatrics [SFP]), and internists (members of the French Society for Internal Medicine[SNFMI]) were invited to participate in this observational study between 2007 and 2009. The available data about the type of centre (primary, tertiary hospital), practice (private or public), and region of inclusion confirmed the good representativity (data not shown).
Physicians who agreed to participate to the "CORPUS PR" cohort were asked to recruit all patients with active disease fulfilling the following inclusion criteria: RA meeting 1987 ACR criteria with DAS28>3.2 despite methotrexate therapy. Exclusion criteria was a previous treatment by biologic agent.

Biological agents
In 2007–2009, the only biologics available in France for treating RA were TNF-α antagonists (infliximab, etanercept, and adalimumab). Patients who received at least one TNF-α antagonist dose during the 1-year study period were classified as treated with TNF-α antagonists.

Follow-up and questionnaires
Participating physicians were asked to complete a form for each patient, both at inclusion and every 1 year of prospective follow-up. The form had items on physician and practice characteristics, including the number of patients managed by the physician and receiving methotrexate and/or biologics, as well as the physician's practice patterns for these drugs. Other items collected data on the patient, including patient characteristics, co-morbidities, history of inflammatory rheumatic disease, variables needed to compute the 28-joint Disease Activity Score (DAS28) (*i.e.* tender and swollen joint counts, erythrocyte sedimentation rate [ESR], and disease activity as assessed by the patient on a visual analogue scale [VAS] from 0 to 100), plasma C-reactive protein (CRP) level, extra-articular manifestations (rheumatoid nodules, Sjögren's syndrome, pulmonary disorder, tendinitis, atlanto-axial dislocation, and others), radiographic findings, current and past treatments, treatment changes decided during the visit, and whether biological therapy was considered.
At study inclusion and 1 year later, each patient was asked to complete a 0–100 VAS, a health assessment questionnaire (HAQ) and the validated French version of the quality-of-life questionnaire SF-36.

II. FLOWCHART

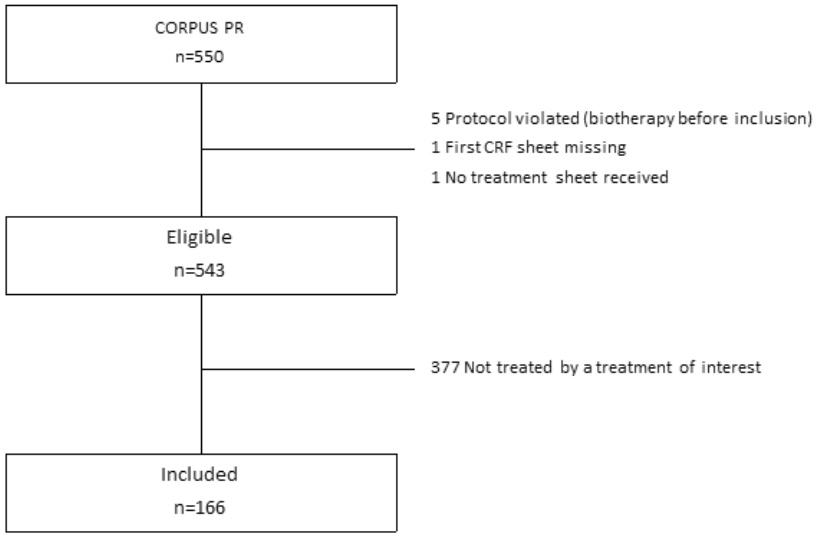

Figure 1 *Analysis flow chart*

To built up this Flow Chart, we had to use the classification mentioned in the SAP. However, some treatments do not appear among the prescriptions of CORPUS PR.
Here is the classification of interest treatments found in the CORPUS PR data :

Table 0 *Treatment in "CORPUS PR" and classification for this study*

DCI	Classification considered		n (patients)
	All drugs of interest	TNFi	
ABATACEPT	X		10
ACETATE DE METHYLPREDNISOLONE			7
ACIDE FOLIQUE			2
ADALIMUMAB	X	X	64
ANAKINRA			1
ANETHOLTRITHIONE			1
AZATHIOPRINE			6
BETAMETHASONE			1
CELECOXIB			1
CHOLECALCIFEROL			1
CICLOSPORINE			1
COLECALCIFEROL			1
CORTICOIDES			1
CORTISONE			1
CYCLOPHOSPHAMIDE			2
ETANERCEPT	X	X	92
HYDROCORTISONE			6
HYDROXYCHLOROQUINE			141
INDOMETACINE			1
INFLIXIMAB	X	X	25
KETOPROFENE			1
LEFLUNOMIDE			205
METFORMINE			1
METHOTREXATE			504
METHYLPREDNISOLONE			5
MYCOPHENOLATE MOFETIL			2
NAPROXENE			1
OMEPRAZOLE			2
PARACETAMOL			2
PENICILLAMINE			25
PREDNISOLONE			59
PREDNISONE			374
PYRITINOL CHLORHYDRATE			3
RIFAMPICINE, ISONIAZIDE			1
RISEDRONATE MONOSODIQUE			1
RITUXIMAB	X		10
ROFECOXIB			1
SELS D OR IM			90
SELS D OR ORAL			18
SULFASALAZINE			136
TIOPRONINE			26
TOCILIZUMAB	X		1
TRAMADOL			3

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There are therefore none of the 2 " JAK inhibitor " treatments (BARICITINIB, TOFACITINIB).

III. DESCRIPTIVE TABLES

III.1. By 1st line of treatment

The considered unit is the **patient** but only the first prescription in **the considered treatment group** (column of the following tables) is taken into account. It should be noticed first however that a patient recorded in the column " TNFi " is also in the "Column All drugs of interest.".

Age is calculated according to **this first initiation date**. **Weight, height and smoking status** were collected from the **CRF** closest to that date. Same strategy was carried out for the HAQ self-questionnaire completed by the patient.

Table 1 *Description of Body Mass Index (BMI) among patient with Rheumatoid Arthritis aged ≥ 18 years for overall population and according to age at the date of initiation of the first treatment line among the drugs of interest[1] and by group of patients treated*

Age in (years)	Patients with RA ≥ 18 years treated with					
	All drugs of interest[1]			TNFi[2]		
	All N=166	Women N=127	Men N=39	All N=156	Women N=120	Men N=36
Total						
BMI (kg/m²)						
Size (missing)	160 (6)	122 (5)	38 (1)	151 (5)	116 (4)	35 (1)
Mean (± SD)	25.7 (± 5.70)	25.8 (± 6.22)	25.7 (± 3.59)	25.7 (± 5.72)	25.7 (± 6.21)	25.7 (± 3.74)
median	24.9	24.7	25.3	24.9	24.7	25.1
[p25%-p75%]	[21.6-28.2]	[20.8-28.6]	[23.3-27.8]	[21.6-28.1]	[20.9-28.6]	[23.2-27.9]
[min-max]	[17.8-50.1]	[17.8-50.1]	[19.8-33.9]	[17.8-50.1]	[17.8-50.1]	[19.8-33.9]
[18-30[	8 (4.8%)	8 (6.3%)	0 (0.0%)	7 (4.5%)	7 (5.8%)	0 (0.0%)
BMI (kg/m²)						
Size (missing)	6 (2)	6 (2)	0 (0)	5 (2)	5 (2)	0 (0)
Mean (± SD)	22.3 (± 4.54)	22.3 (± 4.54)	. (± .)	22.8 (± 4.86)	22.8 (± 4.86)	. (± .)
median	19.9	19.9	.	20.3	20.3	.
[p25%-p75%]	[19.5-25.0]	[19.5-25.0]	[.-.]	[19.5-25.0]	[19.5-25.0]	[.-.]
[min-max]	[18.9-30.4]	[18.9-30.4]	[.-.]	[18.9-30.4]	[18.9-30.4]	[.-.]
[30-40[	12 (7.2%)	6 (4.7%)	6 (15.4%)	12 (7.7%)	6 (5.0%)	6 (16.7%)
BMI (kg/m²)						
Size (missing)	11 (1)	6 (0)	5 (1)	11 (1)	6 (0)	5 (1)
Mean (± SD)	24.4 (± 4.75)	24.2 (± 6.32)	24.6 (± 2.50)	24.4 (± 4.75)	24.2 (± 6.32)	24.6 (± 2.50)
median	23.2	22.5	23.7	23.2	22.5	23.7
[p25%-p75%]	[21.8-26.4]	[19.5-25.9]	[23.2-26.4]	[21.8-26.4]	[19.5-25.9]	[23.2-26.4]
[min-max]	[18.8-36.0]	[18.8-36.0]	[21.8-27.9]	[18.8-36.0]	[18.8-36.0]	[21.8-27.9]
[40-50[	41 (24.7%)	28 (22.0%)	13 (33.3%)	41 (26.3%)	28 (23.3%)	13 (36.1%)
BMI (kg/m²)						
Size (missing)	40 (1)	27 (1)	13 (0)	40 (1)	27 (1)	13 (0)
Mean (± SD)	26.4 (± 5.58)	26.5 (± 6.18)	26.1 (± 4.30)	26.4 (± 5.58)	26.5 (± 6.18)	26.1 (± 4.30)
median	25.0	24.9	25.1	25.0	24.9	25.1
[p25%-p75%]	[21.9-29.3]	[21.3-32.3]	[22.2-27.9]	[21.9-29.3]	[21.3-32.3]	[22.2-27.9]
[min-max]	[17.8-37.1]	[17.8-37.1]	[21.6-33.9]	[17.8-37.1]	[17.8-37.1]	[21.6-33.9]
[50-60[	51 (30.7%)	42 (33.1%)	9 (23.1%)	47 (30.1%)	39 (32.5%)	8 (22.2%)
BMI (kg/m²)						
Size (missing)	50 (1)	41 (1)	9 (0)	46 (1)	38 (1)	8 (0)
Mean (± SD)	25.7 (± 5.92)	25.6 (± 6.27)	25.9 (± 4.25)	25.2 (± 5.87)	25.1 (± 6.15)	26.0 (± 4.55)
median	25.0	23.1	25.7	23.2	22.9	25.5
[p25%-p75%]	[20.5-29.0]	[20.3-29.0]	[23.3-26.9]	[20.3-29.0]	[20.1-29.0]	[22.7-28.8]
[min-max]	[18.0-45.8]	[18.0-45.8]	[19.8-33.7]	[18.0-45.8]	[18.0-45.8]	[19.8-33.7]
[60-65[	19 (11.4%)	16 (12.6%)	3 (7.7%)	18 (11.5%)	15 (12.5%)	3 (8.3%)
BMI (kg/m²)						
Size (missing)	18 (1)	15 (1)	3 (0)	18 (0)	15 (0)	3 (0)
Mean (± SD)	28.3 (± 7.36)	28.4 (± 7.97)	27.5 (± 3.90)	28.3 (± 7.36)	28.4 (± 7.97)	27.5 (± 3.90)
median	26.5	26.2	28.1	26.5	26.2	28.1
[p25%-p75%]	[23.3-31.1]	[22.9-34.5]	[23.4-31.1]	[23.3-31.1]	[22.9-34.5]	[23.4-31.1]
[min-max]	[20.3-50.1]	[20.3-50.1]	[23.4-31.1]	[20.3-50.1]	[20.3-50.1]	[23.4-31.1]
≥65	35 (21.1%)	27 (21.3%)	8 (20.5%)	31 (19.9%)	25 (20.8%)	6 (16.7%)
BMI (kg/m²)						
Size (missing)	35 (0)	27 (0)	8 (0)	31 (0)	25 (0)	6 (0)
Mean (± SD)	24.9 (± 4.63)	24.9 (± 5.19)	24.8 (± 1.99)	25.1 (± 4.76)	25.3 (± 5.21)	24.4 (± 2.19)
median	25.0	24.7	25.2	25.2	25.2	25.2
[p25%-p75%]	[21.5-26.5]	[21.5-27.4]	[24.3-26.1]	[21.5-26.8]	[21.5-27.4]	[23.6-26.1]
[min-max]	[18.3-37.4]	[18.3-37.4]	[20.4-26.5]	[18.3-37.4]	[18.3-37.4]	[20.4-26.2]

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB, TOFACITINIB
2. TNFi: ADALIMUMAB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB
3. JAK inhibitors: BARICITINIB, TOFACITINIB
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Table 2 *Description of Body Mass Index (BMI) in categories among patient with Rheumatoid Arthritis aged ≥ 18 years for overall population and according to age at the date of initiation of the first treatment line among the drugs of interest[1] and by group of patients treated by therapeutic class (TNFi and JAK inhibitors) and according to age at the date of initiation of the first treatment line of the considered class.*

Age in (years)	Patients with RA ≥ 18 years treated with											
	All drugs of interest[1]						TNFi[2]					
	All N=166		Women N=127		Men N=39		All N=156		Women N=120		Men N=36	
Total												
BMI (kg/m2) (in categories)												
<18.5	5	(3.0%)	5	(3.9%)	0	(0.0%)	5	(3.2%)	5	(4.2%)	0	(0.0%)
[18.5-25[	78	(47.0%)	60	(47.2%)	18	(46.2%)	74	(47.4%)	57	(47.5%)	17	(47.2%)
[25-30[	45	(27.1%)	31	(24.4%)	14	(35.9%)	42	(26.9%)	30	(25.0%)	12	(33.3%)
≥30	32	(19.3%)	26	(20.5%)	6	(15.4%)	30	(19.2%)	24	(20.0%)	6	(16.7%)
[18-30[	8	(4.8%)	8	(6.3%)	0	(0.0%)	7	(4.5%)	7	(5.8%)	0	(0.0%)
BMI (kg/m2) (in categories)												
<18.5	0	(0.0%)	0	(0.0%)	0	-	0	(0.0%)	0	(0.0%)	0	-
[18.5-25[	5	(62.5%)	5	(62.5%)	0	-	4	(57.1%)	4	(57.1%)	0	-
[25-30[	0	(0.0%)	0	(0.0%)	0	-	0	(0.0%)	0	(0.0%)	0	-
≥30	1	(12.5%)	1	(12.5%)	0	-	1	(14.3%)	1	(14.3%)	0	-
[30-40[	12	(7.2%)	6	(4.7%)	6	(15.4%)	12	(7.7%)	6	(5.0%)	6	(16.7%)
BMI (kg/m2) (in categories)												
<18.5	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
[18.5-25[	7	(58.3%)	4	(66.7%)	3	(50.0%)	7	(58.3%)	4	(66.7%)	3	(50.0%)
[25-30[	3	(25.0%)	1	(16.7%)	2	(33.3%)	3	(25.0%)	1	(16.7%)	2	(33.3%)
≥30	1	(8.3%)	1	(16.7%)	0	(0.0%)	1	(8.3%)	1	(16.7%)	0	(0.0%)
[40-50[	41	(24.7%)	28	(22.0%)	13	(33.3%)	41	(26.3%)	28	(23.3%)	13	(36.1%)
BMI (kg/m2) (in categories)												
<18.5	2	(4.9%)	2	(7.1%)	0	(0.0%)	2	(4.9%)	2	(7.1%)	0	(0.0%)
[18.5-25[	18	(43.9%)	12	(42.9%)	6	(46.2%)	18	(43.9%)	12	(42.9%)	6	(46.2%)
[25-30[	10	(24.4%)	6	(21.4%)	4	(30.8%)	10	(24.4%)	6	(21.4%)	4	(30.8%)
≥30	10	(24.4%)	7	(25.0%)	3	(23.1%)	10	(24.4%)	7	(25.0%)	3	(23.1%)
[50-60[	51	(30.7%)	42	(33.1%)	9	(23.1%)	47	(30.1%)	39	(32.5%)	8	(22.2%)
BMI (kg/m2) (in categories)												
<18.5	1	(2.0%)	1	(2.4%)	0	(0.0%)	1	(2.1%)	1	(2.6%)	0	(0.0%)
[18.5-25[	24	(47.1%)	20	(47.6%)	4	(44.4%)	24	(51.1%)	20	(51.3%)	4	(50.0%)
[25-30[	14	(27.5%)	11	(26.2%)	3	(33.3%)	12	(25.5%)	10	(25.6%)	2	(25.0%)
≥30	11	(21.6%)	9	(21.4%)	2	(22.2%)	9	(19.1%)	7	(17.9%)	2	(25.0%)
[60-65[	19	(11.4%)	16	(12.6%)	3	(7.7%)	18	(11.5%)	15	(12.5%)	3	(8.3%)
BMI (kg/m2) (in categories)												
<18.5	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
[18.5-25[	8	(42.1%)	7	(43.8%)	1	(33.3%)	8	(44.4%)	7	(46.7%)	1	(33.3%)
[25-30[	4	(21.1%)	3	(18.8%)	1	(33.3%)	4	(22.2%)	3	(20.0%)	1	(33.3%)
≥30	6	(31.6%)	5	(31.3%)	1	(33.3%)	6	(33.3%)	5	(33.3%)	1	(33.3%)
≥65	35	(21.1%)	27	(21.3%)	8	(20.5%)	31	(19.9%)	25	(20.8%)	6	(16.7%)
BMI (kg/m2) (in categories)												
<18.5	2	(5.7%)	2	(7.4%)	0	(0.0%)	2	(6.5%)	2	(8.0%)	0	(0.0%)
[18.5-25[	16	(45.7%)	12	(44.4%)	4	(50.0%)	13	(41.9%)	10	(40.0%)	3	(50.0%)
[25-30[	14	(40.0%)	10	(37.0%)	4	(50.0%)	13	(41.9%)	10	(40.0%)	3	(50.0%)
≥30	3	(8.6%)	3	(11.1%)	0	(0.0%)	3	(9.7%)	3	(12.0%)	0	(0.0%)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB, TOFACITINIB
2. TNFi: ADALIMUMAB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB
3. JAK inhibitors: BARICITINIB, TOFACITINIB
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Table 3 *Description of smoking status among patient with Rheumatoid Arthritis aged ≥ 18 years for overall population and according to age at the date of initiation of the first treatment line among the drugs of interest[1] and by group of patients treated by therapeutic class (TNFi and JAK inhibitors) and according to age at the date of initiation of the first treatment line of the considered class.*

Age in (years)	Patients with RA ≥ 18 years treated with											
	All drugs of interest[1]						TNFi[2]					
	All N=166		Women N=127		Men N=39		All N=156		Women N=120		Men N=36	
Total												
Smoking status												
Never smoker	97	(58.4%)	86	(67.7%)	11	(28.2%)	91	(58.3%)	81	(67.5%)	10	(27.8%)
Former smoker	32	(19.3%)	19	(15.0%)	13	(33.3%)	30	(19.2%)	18	(15.0%)	12	(33.3%)
Current smoker	36	(21.7%)	21	(16.5%)	15	(38.5%)	34	(21.8%)	20	(16.7%)	14	(38.9%)
[18-30[	8	(4.8%)	8	(6.3%)	0	(0.0%)	7	(4.5%)	7	(5.8%)	0	(0.0%)
Smoking status												
Never smoker	3	(37.5%)	3	(37.5%)	0	-	3	(42.9%)	3	(42.9%)	0	-
Former smoker	0	(0.0%)	0	(0.0%)	0	-	0	(0.0%)	0	(0.0%)	0	-
Current smoker	5	(62.5%)	5	(62.5%)	0	-	4	(57.1%)	4	(57.1%)	0	-
[30-40[	12	(7.2%)	6	(4.7%)	6	(15.4%)	12	(7.7%)	6	(5.0%)	6	(16.7%)
Smoking status												
Never smoker	6	(50.0%)	4	(66.7%)	2	(33.3%)	6	(50.0%)	4	(66.7%)	2	(33.3%)
Former smoker	2	(16.7%)	1	(16.7%)	1	(16.7%)	2	(16.7%)	1	(16.7%)	1	(16.7%)
Current smoker	4	(33.3%)	1	(16.7%)	3	(50.0%)	4	(33.3%)	1	(16.7%)	3	(50.0%)
[40-50[	41	(24.7%)	28	(22.0%)	13	(33.3%)	41	(26.3%)	28	(23.3%)	13	(36.1%)
Smoking status												
Never smoker	24	(58.5%)	20	(71.4%)	4	(30.8%)	24	(58.5%)	20	(71.4%)	4	(30.8%)
Former smoker	6	(14.6%)	4	(14.3%)	2	(15.4%)	6	(14.6%)	4	(14.3%)	2	(15.4%)
Current smoker	11	(26.8%)	4	(14.3%)	7	(53.8%)	11	(26.8%)	4	(14.3%)	7	(53.8%)
[50-60[	51	(30.7%)	42	(33.1%)	9	(23.1%)	47	(30.1%)	39	(32.5%)	8	(22.2%)
Smoking status												
Never smoker	28	(54.9%)	28	(66.7%)	0	(0.0%)	25	(53.2%)	25	(64.1%)	0	(0.0%)
Former smoker	11	(21.6%)	5	(11.9%)	6	(66.7%)	11	(23.4%)	5	(12.8%)	6	(75.0%)
Current smoker	12	(23.5%)	9	(21.4%)	3	(33.3%)	11	(23.4%)	9	(23.1%)	2	(25.0%)
[60-65[	19	(11.4%)	16	(12.6%)	3	(7.7%)	18	(11.5%)	15	(12.5%)	3	(8.3%)
Smoking status												
Never smoker	12	(63.2%)	12	(75.0%)	0	(0.0%)	11	(61.1%)	11	(73.3%)	0	(0.0%)
Former smoker	5	(26.3%)	3	(18.8%)	2	(66.7%)	5	(27.8%)	3	(20.0%)	2	(66.7%)
Current smoker	2	(10.5%)	1	(6.3%)	1	(33.3%)	2	(11.1%)	1	(6.7%)	1	(33.3%)
≥65	35	(21.1%)	27	(21.3%)	8	(20.5%)	31	(19.9%)	25	(20.8%)	6	(16.7%)
Smoking status												
Never smoker	24	(68.6%)	19	(70.4%)	5	(62.5%)	22	(71.0%)	18	(72.0%)	4	(66.7%)
Former smoker	8	(22.9%)	6	(22.2%)	2	(25.0%)	6	(19.4%)	5	(20.0%)	1	(16.7%)
Current smoker	2	(5.7%)	1	(3.7%)	1	(12.5%)	2	(6.5%)	1	(4.0%)	1	(16.7%)

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB, TOFACITINIB
2. TNFi: ADALIMUMAB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB
3. JAK inhibitors: BARICITINIB, TOFACITINIB
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NB : There is no notion of the length of the smoking status (smoker or non-smoker) in the CORPUS data (only " Former smoker " but not " Former smoker (stopped > 6 months) ").

Table 4 *Description of the Health Assessment Questionnaire functional disability index (HAQ) among patient with Rheumatoid Arthritis aged ≥ 18 years for overall population and according to age at the date of initiation of the first treatment line among the drug*

Age in (years)	Patients with RA ≥ 18 years treated with					
	All drugs of interest[1]			TNFi[2]		
	All N=166	Women N=127	Men N=39	All N=156	Women N=120	Men N=36
Total						
HAQ [0-3]						
Size (missing)	163 (3)	125 (2)	38 (1)	154 (2)	119 (1)	35 (1)
Mean (± SD)	1.2 (± 0.71)	1.3 (± 0.69)	0.9 (± 0.69)	1.2 (± 0.71)	1.3 (± 0.68)	0.9 (± 0.70)
median	1.3	1.4	0.9	1.3	1.4	0.9
[p25%-p75%]	[0.6-1.8]	[0.9-1.9]	[0.4-1.5]	[0.8-1.8]	[0.9-1.9]	[0.4-1.5]
[min-max]	[0.0-3.0]	[0.0-3.0]	[0.0-2.3]	[0.0-3.0]	[0.0-3.0]	[0.0-2.3]
[18-30[8 (4.8%)	8 (6.3%)	0 (0.0%)	7 (4.5%)	7 (5.8%)	0 (0.0%)	
HAQ [0-3]						
Size (missing)	8 (0)	8 (0)	0 (0)	7 (0)	7 (0)	0 (0)
Mean (± SD)	1.0 (± 0.62)	1.0 (± 0.62)	. (± .)	1.1 (± 0.61)	1.1 (± 0.61)	. (± .)
median	1.1	1.1	.	1.1	1.1	.
[p25%-p75%]	[0.5-1.6]	[0.5-1.6]	[.-.]	[0.6-1.6]	[0.6-1.6]	[.-.]
[min-max]	[0.1-1.9]	[0.1-1.9]	[.-.]	[0.1-1.9]	[0.1-1.9]	[.-.]
[30-40[12 (7.2%)	6 (4.7%)	6 (15.4%)	12 (7.7%)	6 (5.0%)	6 (16.7%)	
HAQ [0-3]						
Size (missing)	11 (1)	6 (0)	5 (1)	11 (1)	6 (0)	5 (1)
Mean (± SD)	0.8 (± 0.52)	0.6 (± 0.33)	1.0 (± 0.64)	0.8 (± 0.52)	0.6 (± 0.33)	1.0 (± 0.64)
median	0.8	0.6	1.1	0.8	0.6	1.1
[p25%-p75%]	[0.3-1.1]	[0.3-0.8]	[0.9-1.3]	[0.3-1.1]	[0.3-0.8]	[0.9-1.3]
[min-max]	[0.0-1.8]	[0.1-1.0]	[0.0-1.8]	[0.0-1.8]	[0.1-1.0]	[0.0-1.8]
[40-50[41 (24.7%)	28 (22.0%)	13 (33.3%)	41 (26.3%)	28 (23.3%)	13 (36.1%)	
HAQ [0-3]						
Size (missing)	40 (1)	27 (1)	13 (0)	40 (1)	27 (1)	13 (0)
Mean (± SD)	1.2 (± 0.70)	1.2 (± 0.70)	1.2 (± 0.72)	1.2 (± 0.70)	1.2 (± 0.70)	1.2 (± 0.72)
median	1.1	1.0	1.1	1.1	1.0	1.1
[p25%-p75%]	[0.7-2.1]	[0.8-2.1]	[0.6-2.0]	[0.7-2.1]	[0.8-2.1]	[0.6-2.0]
[min-max]	[0.0-2.3]	[0.0-2.3]	[0.3-2.3]	[0.0-2.3]	[0.0-2.3]	[0.3-2.3]
[50-60[51 (30.7%)	42 (33.1%)	9 (23.1%)	47 (30.1%)	39 (32.5%)	8 (22.2%)	
HAQ [0-3]						
Size (missing)	50 (1)	41 (1)	9 (0)	47 (0)	39 (0)	8 (0)
Mean (± SD)	1.2 (± 0.71)	1.3 (± 0.66)	0.6 (± 0.62)	1.2 (± 0.70)	1.3 (± 0.65)	0.6 (± 0.65)
median	1.4	1.4	0.4	1.4	1.4	0.4
[p25%-p75%]	[0.5-1.8]	[1.0-1.9]	[0.0-1.0]	[0.5-1.8]	[1.0-1.9]	[0.0-1.3]
[min-max]	[0.0-2.4]	[0.0-2.4]	[0.0-1.5]	[0.0-2.4]	[0.0-2.4]	[0.0-1.5]
[60-65[19 (11.4%)	16 (12.6%)	3 (7.7%)	18 (11.5%)	15 (12.5%)	3 (8.3%)	
HAQ [0-3]						
Size (missing)	19 (0)	16 (0)	3 (0)	18 (0)	15 (0)	3 (0)
Mean (± SD)	1.2 (± 0.66)	1.4 (± 0.60)	0.4 (± 0.36)	1.3 (± 0.64)	1.4 (± 0.54)	0.4 (± 0.36)
median	1.3	1.4	0.6	1.3	1.4	0.6
[p25%-p75%]	[0.6-1.6]	[1.1-1.7]	[0.0-0.6]	[0.9-1.6]	[1.1-1.8]	[0.0-0.6]
[min-max]	[0.0-2.4]	[0.3-2.4]	[0.0-0.6]	[0.0-2.4]	[0.3-2.4]	[0.0-0.6]
≥65 35 (21.1%)	27 (21.3%)	8 (20.5%)	31 (19.9%)	25 (20.8%)	6 (16.7%)	
HAQ [0-3]						
Size (missing)	35 (0)	27 (0)	8 (0)	31 (0)	25 (0)	6 (0)
Mean (± SD)	1.5 (± 0.75)	1.7 (± 0.69)	0.9 (± 0.67)	1.5 (± 0.78)	1.7 (± 0.70)	0.8 (± 0.75)
median	1.5	1.8	0.9	1.6	1.8	0.8
[p25%-p75%]	[0.9-2.1]	[1.3-2.1]	[0.4-1.3]	[0.9-2.1]	[1.4-2.1]	[0.1-1.1]
[min-max]	[0.1-3.0]	[0.4-3.0]	[0.1-2.1]	[0.1-3.0]	[0.4-3.0]	[0.1-2.1]

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB, TOFACITINIB
2. TNFI: ADALIMUMAB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB
3. JAK inhibitors: BARICITINIB, TOFACITINIB
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III.2. By treatment of interest

As with the previous tables, **the unit** is always the **patient**. Here the first prescription treatment of interest is taken into account. In the same way as before, a patient could be counted several times if he has had several treatments of interest during the follow-up.

The age is calculated according to the date of the **first initiation** of the considered treatment. **Weight, height and smoking status** were collected from the **CRF** closest to that date.

III.2.i. BMI

Table 5 *Description of Body Mass Index (BMI) among patient with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and according to age at the date of initiation of the considered drug, whatever the rank of treatment line, table for TNFi.*

Age in (years)	Patients with RA ≥ 18 years treated with								
	ADALIMUMAB			ETANERCEPT			INFLIXIMAB		
	All N=61	Women N=45	Men N=16	All N=89	Women N=67	Men N=22	All N=24	Women N=19	Men N=5
Total									
BMI (kg/m²)									
Size (missing)	57 (4)	42 (3)	15 (1)	88 (1)	66 (1)	22 (0)	23 (1)	18 (1)	5 (0)
Mean (± SD)	26.0 (± 5.82)	26.1 (± 6.53)	25.5 (± 3.18)	25.4 (± 5.23)	25.1 (± 5.71)	26.1 (± 3.42)	26.6 (± 6.27)	27.2 (± 6.63)	24.5 (± 4.76)
median	25.4	25.9	25.1	24.7	24.4	26.0	25.3	25.5	22.1
[p25%-p75%]	[21.9-28.6]	[21.3-29.0]	[23.6-26.4]	[21.2-27.9]	[20.3-27.9]	[23.4-27.8]	[22.1-30.5]	[22.5-30.5]	[21.6-27.9]
[min-max]	[18.0-50.1]	[18.0-50.1]	[21.6-33.9]	[17.8-37.4]	[17.8-37.4]	[20.4-33.7]	[18.9-45.8]	[18.9-45.8]	[19.8-31.1]
[18-30[	2 (3.3%)	2 (4.4%)	0 (0.0%)	4 (4.5%)	4 (6.0%)	0 (0.0%)	1 (4.2%)	1 (5.3%)	0 (0.0%)
BMI (kg/m²)									
Size (missing)	1 (1)	1 (1)	0 (0)	3 (1)	3 (1)	0 (0)	1 (0)	1 (0)	0 (0)
Mean (± SD)	30.4 (± .)	30.4 (± .)	. (± .)	21.6 (± 2.96)	21.6 (± 2.96)	. (± .)	18.9 (± .)	18.9 (± .)	. (± .)
median	30.4	30.4	.	20.3	20.3	.	18.9	18.9	.
[p25%-p75%]	[30.4-30.4]	[30.4-30.4]	[.-.]	[19.5-25.0]	[19.5-25.0]	[.-.]	[18.9-18.9]	[18.9-18.9]	[.-.]
[min-max]	[30.4-30.4]	[30.4-30.4]	[.-.]	[19.5-25.0]	[19.5-25.0]	[.-.]	[18.9-18.9]	[18.9-18.9]	[.-.]
[30-40[	9 (14.8%)	4 (8.9%)	5 (31.3%)	5 (5.6%)	3 (4.5%)	2 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
BMI (kg/m²)									
Size (missing)	8 (1)	4 (0)	4 (1)	5 (0)	3 (0)	2 (0)	0 (0)	0 (0)	0 (0)
Mean (± SD)	23.2 (± 2.22)	22.6 (± 2.63)	23.8 (± 1.92)	25.6 (± 7.02)	24.8 (± 9.74)	27.0 (± 1.33)	. (± .)	. (± .)	. (± .)
median	23.1	22.5	23.4	26.0	19.5	27.0	.	.	.
[p25%-p75%]	[21.9-24.8]	[20.7-24.4]	[22.5-25.0]	[19.5-27.9]	[18.8-36.0]	[26.0-27.9]	[.-.]	[.-.]	[.-.]
[min-max]	[19.5-26.4]	[19.5-25.9]	[21.8-26.4]	[18.8-36.0]	[18.8-36.0]	[26.0-27.9]	[.-.]	[.-.]	[.-.]
[40-50[	17 (27.9%)	12 (26.7%)	5 (31.3%)	21 (23.6%)	13 (19.4%)	8 (36.4%)	5 (20.8%)	3 (15.8%)	2 (40.0%)
BMI (kg/m²)									
Size (missing)	16 (1)	11 (1)	5 (0)	21 (0)	13 (0)	8 (0)	5 (0)	3 (0)	2 (0)
Mean (± SD)	24.4 (± 4.65)	23.3 (± 4.24)	26.9 (± 5.02)	27.6 (± 5.99)	28.7 (± 6.91)	25.9 (± 3.87)	27.2 (± 4.62)	28.8 (± 4.80)	24.7 (± 4.41)
median	23.6	21.8	25.1	27.8	28.1	25.2	27.3	27.3	24.7
[p25%-p75%]	[21.0-27.3]	[20.2-26.0]	[23.7-30.1]	[23.1-33.6]	[23.1-35.2]	[22.8-27.8]	[24.9-27.9]	[24.9-34.2]	[21.6-27.9]
[min-max]	[18.5-33.9]	[18.5-32.3]	[21.6-33.9]	[17.8-37.1]	[17.8-37.1]	[22.0-33.6]	[21.6-34.2]	[24.9-34.2]	[21.6-27.9]
[50-60[	16 (26.2%)	14 (31.1%)	2 (12.5%)	29 (32.6%)	22 (32.8%)	7 (31.8%)	10 (41.7%)	8 (42.1%)	2 (40.0%)
BMI (kg/m²)									
Size (missing)	16 (0)	14 (0)	2 (0)	29 (0)	22 (0)	7 (0)	9 (1)	7 (1)	2 (0)
Mean (± SD)	25.7 (± 5.00)	25.6 (± 5.35)	26.8 (± 0.57)	24.3 (± 4.74)	23.5 (± 4.74)	27.1 (± 3.78)	27.5 (± 8.76)	29.4 (± 9.15)	21.0 (± 1.63)
median	26.8	26.7	26.8	23.3	21.5	25.9	22.9	30.5	21.0
[p25%-p75%]	[21.0-28.8]	[20.1-29.0]	[26.4-27.2]	[20.3-26.9]	[19.5-26.4]	[24.5-30.7]	[21.8-32.3]	[21.8-33.4]	[19.8-22.1]
[min-max]	[18.0-35.6]	[18.0-35.6]	[26.4-27.2]	[19.0-36.3]	[19.0-36.3]	[23.3-33.7]	[19.0-45.8]	[19.0-45.8]	[19.8-22.1]
[60-65[	5 (8.2%)	5 (11.1%)	0 (0.0%)	11 (12.4%)	9 (13.4%)	2 (9.1%)	3 (12.5%)	2 (10.5%)	1 (20.0%)
BMI (kg/m²)									
Size (missing)	5 (0)	5 (0)	0 (0)	11 (0)	9 (0)	2 (0)	3 (0)	2 (0)	1 (0)
Mean (± SD)	34.1 (± 10.32)	34.1 (± 10.32)	. (± .)	26.2 (± 5.27)	26.3 (± 5.76)	25.7 (± 3.32)	28.1 (± 4.56)	26.7 (± 5.33)	31.1 (± .)
median	34.5	34.5	.	24.9	24.9	25.7	30.4	26.7	31.1
[p25%-p75%]	[27.0-35.5]	[27.0-35.5]	[.-.]	[22.0-28.1]	[22.0-26.8]	[23.4-28.1]	[22.9-31.1]	[22.9-30.4]	[31.1-31.1]
[min-max]	[23.3-50.1]	[23.3-50.1]	[.-.]	[20.3-36.7]	[20.3-36.7]	[23.4-28.1]	[22.9-31.1]	[22.9-30.4]	[31.1-31.1]
≥65	12 (19.7%)	8 (17.8%)	4 (25.0%)	19 (21.3%)	16 (23.9%)	3 (13.6%)	5 (20.8%)	5 (26.3%)	0 (0.0%)
BMI (kg/m²)									
Size (missing)	11 (1)	7 (1)	4 (0)	19 (0)	16 (0)	3 (0)	5 (0)	5 (0)	0 (0)
Mean (± SD)	26.5 (± 5.28)	27.3 (± 6.62)	25.0 (± 1.10)	24.4 (± 4.33)	24.5 (± 4.60)	23.9 (± 3.07)	25.0 (± 2.94)	25.0 (± 2.94)	. (± .)
median	26.0	26.1	25.2	24.7	24.6	25.3	25.3	25.3	.
[p25%-p75%]	[23.6-26.4]	[22.4-34.5]	[24.3-25.8]	[21.3-26.8]	[21.4-27.1]	[20.4-26.1]	[22.5-25.7]	[22.5-25.7]	[.-.]
[min-max]	[18.3-37.3]	[18.3-37.3]	[23.6-26.2]	[18.5-37.4]	[18.5-37.4]	[20.4-26.1]	[22.1-29.4]	[22.1-29.4]	[.-.]

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB, TOFACITINIB

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Table 6 *Description of Body Mass Index (BMI) in categories among patient with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and according to age at the date of initiation of the considered drug, whatever the rank of treatment line, table for TNFi.*

Age in (years)	Patients with RA ≥ 18 years treated with																	
	ADALIMUMAB						ETANERCEPT						INFLIXIMAB					
	All N=61		Women N=45		Men N=16		All N=89		Women N=67		Men N=22		All N=24		Women N=19		Men N=5	
Total																		
BMI (kg/m2) (in categories)																		
<18.5	3	(4.9%)	3	(6.7%)	0	(0.0%)	2	(2.2%)	2	(3.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
[18.5-25[	24	(39.3%)	17	(37.8%)	7	(43.8%)	46	(51.7%)	37	(55.2%)	9	(40.9%)	11	(45.8%)	8	(42.1%)	3	(60.0%)
[25-30[	19	(31.1%)	13	(28.9%)	6	(37.5%)	26	(29.2%)	16	(23.9%)	10	(45.5%)	5	(20.8%)	4	(21.1%)	1	(20.0%)
≥30	11	(18.0%)	9	(20.0%)	2	(12.5%)	14	(15.7%)	11	(16.4%)	3	(13.6%)	7	(29.2%)	6	(31.6%)	1	(20.0%)
[18-30[	2	(3.3%)	2	(4.4%)	0	(0.0%)	4	(4.5%)	4	(6.0%)	0	(0.0%)	1	(4.2%)	1	(5.3%)	0	(0.0%)
BMI (kg/m2) (in categories)																		
<18.5	0	(0.0%)	0	(0.0%)	0	-	0	(0.0%)	0	(0.0%)	0	-	0	(0.0%)	0	(0.0%)	0	-
[18.5-25[	0	(0.0%)	0	(0.0%)	0	-	3	(75.0%)	3	(75.0%)	0	-	1	(100.0%)	1	(100.0%)	0	-
[25-30[	0	(0.0%)	0	(0.0%)	0	-	0	(0.0%)	0	(0.0%)	0	-	0	(0.0%)	0	(0.0%)	0	-
≥30	1	(50.0%)	1	(50.0%)	0	-	0	(0.0%)	0	(0.0%)	0	-	0	(0.0%)	0	(0.0%)	0	-
[30-40[	9	(14.8%)	4	(8.9%)	5	(31.3%)	5	(5.6%)	3	(4.5%)	2	(9.1%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
BMI (kg/m2) (in categories)																		
<18.5	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-
[18.5-25[	6	(66.7%)	3	(75.0%)	3	(60.0%)	2	(40.0%)	2	(66.7%)	0	(0.0%)	0	-	0	-	0	-
[25-30[	2	(22.2%)	1	(25.0%)	1	(20.0%)	2	(40.0%)	0	(0.0%)	2	(100.0%)	0	-	0	-	0	-
≥30	0	(0.0%)	0	(0.0%)	0	(0.0%)	1	(20.0%)	1	(33.3%)	0	(0.0%)	0	-	0	-	0	-
[40-50[	17	(27.9%)	12	(26.7%)	5	(31.3%)	21	(23.6%)	13	(19.4%)	8	(36.4%)	5	(20.8%)	3	(15.8%)	2	(40.0%)
BMI (kg/m2) (in categories)																		
<18.5	1	(5.9%)	1	(8.3%)	0	(0.0%)	1	(4.8%)	1	(7.7%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
[18.5-25[	9	(52.9%)	7	(58.3%)	2	(40.0%)	8	(38.1%)	4	(30.8%)	4	(50.0%)	2	(40.0%)	1	(33.3%)	1	(50.0%)
[25-30[	3	(17.6%)	2	(16.7%)	1	(20.0%)	6	(28.6%)	3	(23.1%)	3	(37.5%)	2	(40.0%)	1	(33.3%)	1	(50.0%)
≥30	3	(17.6%)	1	(8.3%)	2	(40.0%)	6	(28.6%)	5	(38.5%)	1	(12.5%)	1	(20.0%)	1	(33.3%)	0	(0.0%)
[50-60[	16	(26.2%)	14	(31.1%)	2	(12.5%)	29	(32.6%)	22	(32.8%)	7	(31.8%)	10	(41.7%)	8	(42.1%)	2	(40.0%)
BMI (kg/m2) (in categories)																		
<18.5	1	(6.3%)	1	(7.1%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
[18.5-25[	5	(31.3%)	5	(35.7%)	0	(0.0%)	17	(58.6%)	14	(63.6%)	3	(42.9%)	5	(50.0%)	3	(37.5%)	2	(100.0%)
[25-30[	8	(50.0%)	6	(42.9%)	2	(100.0%)	8	(27.6%)	6	(27.3%)	2	(28.6%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
≥30	2	(12.5%)	2	(14.3%)	0	(0.0%)	4	(13.8%)	2	(9.1%)	2	(28.6%)	4	(40.0%)	4	(50.0%)	0	(0.0%)
[60-65[	5	(8.2%)	5	(11.1%)	0	(0.0%)	11	(12.4%)	9	(13.4%)	2	(9.1%)	3	(12.5%)	2	(10.5%)	1	(20.0%)
BMI (kg/m2) (in categories)																		
<18.5	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%)
[18.5-25[	1	(20.0%)	1	(20.0%)	0	-	6	(54.5%)	5	(55.6%)	1	(50.0%)	1	(33.3%)	1	(50.0%)	0	(0.0%)
[25-30[	1	(20.0%)	1	(20.0%)	0	-	3	(27.3%)	2	(22.2%)	1	(50.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
≥30	3	(60.0%)	3	(60.0%)	0	-	2	(18.2%)	2	(22.2%)	0	(0.0%)	2	(66.7%)	1	(50.0%)	1	(100.0%)
≥65	12	(19.7%)	8	(17.8%)	4	(25.0%)	19	(21.3%)	16	(23.9%)	3	(13.6%)	5	(20.8%)	5	(26.3%)	0	(0.0%)
BMI (kg/m2) (in categories)																		
<18.5	1	(8.3%)	1	(12.5%)	0	(0.0%)	1	(5.3%)	1	(6.3%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	-
[18.5-25[	3	(25.0%)	1	(12.5%)	2	(50.0%)	10	(52.6%)	9	(56.3%)	1	(33.3%)	2	(40.0%)	2	(40.0%)	0	-
[25-30[	5	(41.7%)	3	(37.5%)	2	(50.0%)	7	(36.8%)	5	(31.3%)	2	(66.7%)	3	(60.0%)	3	(60.0%)	0	-
≥30	2	(16.7%)	2	(25.0%)	0	(0.0%)	1	(5.3%)	1	(6.3%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	-

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB, TOFACITINIB
«CORPUS BMI smoking» Project
Analysis «Description» v02
CORPUS data frozen in March 2011
Data preparation v02
CIC-EC 1433 INSERM CHRU de Nancy le 07/01/202

Table 7 *Description of Body Mass Index (BMI) among patient with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and according to age at the date of initiation of the considered drug, whatever the rank of treatment line, table for non-TNFi*

Age in (years)	Patients with RA ≥ 18 years treated with								
	RITUXIMAB			TOCILIZUMAB			ABATACEPT		
	All N=10	Women N=8	Men N=2	All N=1	Women N=1	Men N=0	All N=10	Women N=8	Men N=2
Total									
BMI (kg/m²)									
Size (missing)	9 (1)	7 (1)	2 (0)	1 (0)	1 (0)	0 (0)	10 (0)	8 (0)	2 (0)
Mean (± SD)	27.2 (± 4.92)	27.6 (± 5.58)	25.8 (± 1.12)	21.6 (± .)	21.6 (± .)	. (± .)	28.2 (± 10.96)	29.3 (± 12.16)	24.2 (± 2.16)
median	27.0	27.7	25.8	21.6	21.6	.	26.3	27.6	24.2
[p25%-p75%]	[25.0-29.7]	[21.6-32.3]	[25.0-26.5]	[21.6-21.6]	[21.6-21.6]	[.-.]	[21.1-30.8]	[20.0-32.0]	[22.7-25.7]
[min-max]	[19.6-35.4]	[19.6-35.4]	[25.0-26.5]	[21.6-21.6]	[21.6-21.6]	[.-.]	[18.5-56.2]	[18.5-56.2]	[22.7-25.7]
[18-30[	1 (10.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 -	0 (0.0%)	0 (0.0%)	0 (0.0%)
BMI (kg/m²)									
Size (missing)	1 (0)	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Mean (± SD)	19.6 (± .)	19.6 (± .)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)
median	19.6	19.6	.	.	.	.	.	.	.
[p25%-p75%]	[19.6-19.6]	[19.6-19.6]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]
[min-max]	[19.6-19.6]	[19.6-19.6]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]
[30-40[	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%)
BMI (kg/m²)									
Size (missing)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Mean (± SD)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)
median	.	.	.	.	.	.	.	.	.
[p25%-p75%]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]
[min-max]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]
[40-50[	1 (10.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 -	1 (10.0%)	0 (0.0%)	1 (50.0%)
BMI (kg/m²)									
Size (missing)	1 (0)	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0)	0 (0)	1 (0)
Mean (± SD)	27.7 (± .)	27.7 (± .)	. (± .)	. (± .)	. (± .)	. (± .)	22.7 (± .)	. (± .)	22.7 (± .)
median	27.7	27.7	.	.	.	.	22.7	.	22.7
[p25%-p75%]	[27.7-27.7]	[27.7-27.7]	[.-.]	[.-.]	[.-.]	[.-.]	[22.7-22.7]	[.-.]	[22.7-22.7]
[min-max]	[27.7-27.7]	[27.7-27.7]	[.-.]	[.-.]	[.-.]	[.-.]	[22.7-22.7]	[.-.]	[22.7-22.7]
[50-60[	3 (30.0%)	3 (37.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 -	5 (50.0%)	4 (50.0%)	1 (50.0%)
BMI (kg/m²)									
Size (missing)	3 (0)	3 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (0)	4 (0)	1 (0)
Mean (± SD)	32.5 (± 2.83)	32.5 (± 2.83)	. (± .)	. (± .)	. (± .)	. (± .)	27.3 (± 5.66)	27.7 (± 6.45)	25.7 (± .)
median	32.3	32.3	.	.	.	.	28.3	29.6	25.7
[p25%-p75%]	[29.7-35.4]	[29.7-35.4]	[.-.]	[.-.]	[.-.]	[.-.]	[25.7-30.8]	[23.4-32.0]	[25.7-25.7]
[min-max]	[29.7-35.4]	[29.7-35.4]	[.-.]	[.-.]	[.-.]	[.-.]	[18.5-33.2]	[18.5-33.2]	[25.7-25.7]
[60-65[	2 (20.0%)	2 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 -	2 (20.0%)	2 (25.0%)	0 (0.0%)
BMI (kg/m²)									
Size (missing)	1 (1)	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0)	2 (0)	0 (0)
Mean (± SD)	27.0 (± .)	27.0 (± .)	. (± .)	. (± .)	. (± .)	. (± .)	41.5 (± 20.74)	41.5 (± 20.74)	. (± .)
median	27.0	27.0	.	.	.	.	41.5	41.5	.
[p25%-p75%]	[27.0-27.0]	[27.0-27.0]	[.-.]	[.-.]	[.-.]	[.-.]	[26.8-56.2]	[26.8-56.2]	[.-.]
[min-max]	[27.0-27.0]	[27.0-27.0]	[.-.]	[.-.]	[.-.]	[.-.]	[26.8-56.2]	[26.8-56.2]	[.-.]
≥65	3 (30.0%)	1 (12.5%)	2 (100.0%)	1 (100.0%)	1 (100.0%)	0 -	2 (20.0%)	2 (25.0%)	0 (0.0%)
BMI (kg/m²)									
Size (missing)	3 (0)	1 (0)	2 (0)	1 (0)	1 (0)	0 (0)	2 (0)	2 (0)	0 (0)
Mean (± SD)	24.4 (± 2.50)	21.6 (± .)	25.8 (± 1.12)	21.6 (± .)	21.6 (± .)	. (± .)	20.0 (± 1.49)	20.0 (± 1.49)	. (± .)
median	25.0	21.6	25.8	21.6	21.6	.	20.0	20.0	.
[p25%-p75%]	[21.6-26.5]	[21.6-21.6]	[25.0-26.5]	[21.6-21.6]	[21.6-21.6]	[.-.]	[19.0-21.1]	[19.0-21.1]	[.-.]
[min-max]	[21.6-26.5]	[21.6-21.6]	[25.0-26.5]	[21.6-21.6]	[21.6-21.6]	[.-.]	[19.0-21.1]	[19.0-21.1]	[.-.]

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB, TOFACITINIB
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Table 8 *Description of Body Mass Index (BMI) in categories among patient with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and according to age at the date of initiation of the considered drug, whatever the rank of treatment line, table for non-TNFi.*

Age in (years)	Patients with RA ≥ 18 years treated with																	
	RITUXIMAB						TOCILIZUMAB						ABATACEPT					
	All N=10		Women N=8		Men N=2		All N=1		Women N=1		Men N=0		All N=10		Women N=8		Men N=2	
Total																		
BMI (kg/m2) (in categories)																		
<18.5	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%)
[18.5-25[	3	(30.0%)	2	(25.0%)	1	(50.0%)	1	(100.0%)	1	(100.0%)	0	-	4	(40.0%)	3	(37.5%)	1	(50.0%)
[25-30[	4	(40.0%)	3	(37.5%)	1	(50.0%)	0	(0.0%)	0	(0.0%)	0	-	3	(30.0%)	2	(25.0%)	1	(50.0%)
≥30	2	(20.0%)	2	(25.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	-	3	(30.0%)	3	(37.5%)	0	(0.0%)
[18-30[	1	(10.0%)	1	(12.5%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	-	0	(0.0%)	0	(0.0%)	0	(0.0%)
BMI (kg/m2) (in categories)																		
<18.5	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-	0	-	0	-	0	-	0	-
[18.5-25[	1	(100.0%)	1	(100.0%)	0	-	0	-	0	-	0	-	0	-	0	-	0	-
[25-30[	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-	0	-	0	-	0	-	0	-
≥30	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-	0	-	0	-	0	-	0	-
[30-40[	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%)
BMI (kg/m2) (in categories)																		
<18.5	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-
[18.5-25[	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-
[25-30[	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-
≥30	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-
[40-50[	1	(10.0%)	1	(12.5%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	-	1	(10.0%)	0	(0.0%)	1	(50.0%)
BMI (kg/m2) (in categories)																		
<18.5	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-	0	-	0	(0.0%)	0	-	0	(0.0%)
[18.5-25[	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-	0	-	1	(100.0%)	0	-	1	(100.0%)
[25-30[	1	(100.0%)	1	(100.0%)	0	-	0	-	0	-	0	-	0	(0.0%)	0	-	0	(0.0%)
≥30	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-	0	-	0	(0.0%)	0	-	0	(0.0%)
[50-60[	3	(30.0%)	3	(37.5%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	-	5	(50.0%)	4	(50.0%)	1	(50.0%)
BMI (kg/m2) (in categories)																		
<18.5	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-	0	-	0	(0.0%)	0	(0.0%)	0	(0.0%)
[18.5-25[	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-	0	-	1	(20.0%)	1	(25.0%)	0	(0.0%)
[25-30[	1	(33.3%)	1	(33.3%)	0	-	0	-	0	-	0	-	2	(40.0%)	1	(25.0%)	1	(100.0%)
≥30	2	(66.7%)	2	(66.7%)	0	-	0	-	0	-	0	-	2	(40.0%)	2	(50.0%)	0	(0.0%)
[60-65[	2	(20.0%)	2	(25.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	-	2	(20.0%)	2	(25.0%)	0	(0.0%)
BMI (kg/m2) (in categories)																		
<18.5	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-	0	-	0	(0.0%)	0	(0.0%)	0	-
[18.5-25[	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-	0	-	0	(0.0%)	0	(0.0%)	0	-
[25-30[	1	(50.0%)	1	(50.0%)	0	-	0	-	0	-	0	-	1	(50.0%)	1	(50.0%)	0	-
≥30	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-	0	-	1	(50.0%)	1	(50.0%)	0	-
≥65	3	(30.0%)	1	(12.5%)	2	(100.0%)	1	(100.0%)	1	(100.0%)	0	-	2	(20.0%)	2	(25.0%)	0	(0.0%)
BMI (kg/m2) (in categories)																		
<18.5	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	-	0	(0.0%)	0	(0.0%)	0	-
[18.5-25[	2	(66.7%)	1	(100.0%)	1	(50.0%)	1	(100.0%)	1	(100.0%)	0	-	2	(100.0%)	2	(100.0%)	0	-
[25-30[	1	(33.3%)	0	(0.0%)	1	(50.0%)	0	(0.0%)	0	(0.0%)	0	-	0	(0.0%)	0	(0.0%)	0	-
≥30	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	-	0	(0.0%)	0	(0.0%)	0	-

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB, TOFACITINIB
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III.2.ii. Smoking status

Table 9 *Description of smoking status among patient with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest[1] and according to age at the date of initiation of the considered drug, whatever the rank of treatment line, table for TNFi.*

Age in (years)	Patients with RA ≥ 18 years treated with																	
	ADALIMUMAB						ETANERCEPT						INFLIXIMAB					
	All N=61		Women N=45		Men N=16		All N=89		Women N=67		Men N=22		All N=24		Women N=19		Men N=5	
Total																		
Smoking status																		
Never smoker	37	(60.7%)	29	(64.4%)	8	(50.0%)	52	(58.4%)	49	(73.1%)	3	(13.6%)	10	(41.7%)	10	(52.6%)	0	(0.0%)
Former smoker	13	(21.3%)	10	(22.2%)	3	(18.8%)	18	(20.2%)	7	(10.4%)	11	(50.0%)	5	(20.8%)	3	(15.8%)	2	(40.0%)
Current smoker	10	(16.4%)	5	(11.1%)	5	(31.3%)	18	(20.2%)	10	(14.9%)	8	(36.4%)	9	(37.5%)	6	(31.6%)	3	(60.0%)
[18-30[	2	(3.3%)	2	(4.4%)	0	(0.0%)	4	(4.5%)	4	(6.0%)	0	(0.0%)	1	(4.2%)	1	(5.3%)	0	(0.0%)
Smoking status																		
Never smoker	1	(50.0%)	1	(50.0%)	0	-	2	(50.0%)	2	(50.0%)	0	-	0	(0.0%)	0	(0.0%)	0	-
Former smoker	0	(0.0%)	0	(0.0%)	0	-	0	(0.0%)	0	(0.0%)	0	-	0	(0.0%)	0	(0.0%)	0	-
Current smoker	1	(50.0%)	1	(50.0%)	0	-	2	(50.0%)	2	(50.0%)	0	-	1	(100.0%)	1	(100.0%)	0	-
[30-40[	9	(14.8%)	4	(8.9%)	5	(31.3%)	5	(5.6%)	3	(4.5%)	2	(9.1%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
Smoking status																		
Never smoker	4	(44.4%)	2	(50.0%)	2	(40.0%)	2	(40.0%)	2	(66.7%)	0	(0.0%)	0	-	0	-	0	-
Former smoker	3	(33.3%)	2	(50.0%)	1	(20.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-
Current smoker	2	(22.2%)	0	(0.0%)	2	(40.0%)	3	(60.0%)	1	(33.3%)	2	(100.0%)	0	-	0	-	0	-
[40-50[	17	(27.9%)	12	(26.7%)	5	(31.3%)	21	(23.6%)	13	(19.4%)	8	(36.4%)	5	(20.8%)	3	(15.8%)	2	(40.0%)
Smoking status																		
Never smoker	12	(70.6%)	9	(75.0%)	3	(60.0%)	10	(47.6%)	9	(69.2%)	1	(12.5%)	2	(40.0%)	2	(66.7%)	0	(0.0%)
Former smoker	2	(11.8%)	2	(16.7%)	0	(0.0%)	4	(19.0%)	2	(15.4%)	2	(25.0%)	1	(20.0%)	0	(0.0%)	1	(50.0%)
Current smoker	3	(17.6%)	1	(8.3%)	2	(40.0%)	7	(33.3%)	2	(15.4%)	5	(62.5%)	2	(40.0%)	1	(33.3%)	1	(50.0%)
[50-60[	16	(26.2%)	14	(31.1%)	2	(12.5%)	29	(32.6%)	22	(32.8%)	7	(31.8%)	10	(41.7%)	8	(42.1%)	2	(40.0%)
Smoking status																		
Never smoker	9	(56.3%)	9	(64.3%)	0	(0.0%)	15	(51.7%)	15	(68.2%)	0	(0.0%)	4	(40.0%)	4	(50.0%)	0	(0.0%)
Former smoker	4	(25.0%)	2	(14.3%)	2	(100.0%)	10	(34.5%)	3	(13.6%)	7	(100.0%)	1	(10.0%)	1	(12.5%)	0	(0.0%)
Current smoker	3	(18.8%)	3	(21.4%)	0	(0.0%)	4	(13.8%)	4	(18.2%)	0	(0.0%)	5	(50.0%)	3	(37.5%)	2	(100.0%)
[60-65[	5	(8.2%)	5	(11.1%)	0	(0.0%)	11	(12.4%)	9	(13.4%)	2	(9.1%)	3	(12.5%)	2	(10.5%)	1	(20.0%)
Smoking status																		
Never smoker	3	(60.0%)	3	(60.0%)	0	-	9	(81.8%)	9	(100.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
Former smoker	2	(40.0%)	2	(40.0%)	0	-	1	(9.1%)	0	(0.0%)	1	(50.0%)	2	(66.7%)	1	(50.0%)	1	(100.0%)
Current smoker	0	(0.0%)	0	(0.0%)	0	-	1	(9.1%)	0	(0.0%)	1	(50.0%)	1	(33.3%)	1	(50.0%)	0	(0.0%)
≥65	12	(19.7%)	8	(17.8%)	4	(25.0%)	19	(21.3%)	16	(23.9%)	3	(13.6%)	5	(20.8%)	5	(26.3%)	0	(0.0%)
Smoking status																		
Never smoker	8	(66.7%)	5	(62.5%)	3	(75.0%)	14	(73.7%)	12	(75.0%)	2	(66.7%)	4	(80.0%)	4	(80.0%)	0	-
Former smoker	2	(16.7%)	2	(25.0%)	0	(0.0%)	3	(15.8%)	2	(12.5%)	1	(33.3%)	1	(20.0%)	1	(20.0%)	0	-
Current smoker	1	(8.3%)	0	(0.0%)	1	(25.0%)	1	(5.3%)	1	(6.3%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	-

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB, TOFACITINIB
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NB : same remark concerning the length of the smoking status and therefore the " Former smoker " and " Current smoker " classes.

Table 10 *Description of smoking status among patient with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest1 and according to age at the date of initiation of the considered drug, whatever the rank of treatment line, table for non-TNFi.*

Age in (years)	Patients with RA ≥ 18 years treated with																	
	RITUXIMAB						TOCILIZUMAB						ABATACEPT					
	All			Women			Men			All			Women			Men		
	N=10			N=8			N=2			N=1			N=1			N=0		
Total																		
Smoking status																		
Never smoker	6	(60.0%)	5	(62.5%)	1	(50.0%)	0	(0.0%)	0	(0.0%)	0	-	5	(50.0%)	5	(62.5%)	0	(0.0%)
Former smoker	2	(20.0%)	1	(12.5%)	1	(50.0%)	1	(100.0%)	1	(100.0%)	0	-	2	(20.0%)	2	(25.0%)	0	(0.0%)
Current smoker	2	(20.0%)	2	(25.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	-	3	(30.0%)	1	(12.5%)	2	(100.0%)
[18-30[	1	(10.0%)	1	(12.5%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	-	0	(0.0%)	0	(0.0%)	0	(0.0%)
Smoking status																		
Never smoker	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-	0	-	0	-	0	-	0	-
Former smoker	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-	0	-	0	-	0	-	0	-
Current smoker	1	(100.0%)	1	(100.0%)	0	-	0	-	0	-	0	-	0	-	0	-	0	-
[30-40[	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%)
Smoking status																		
Never smoker	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-
Former smoker	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-
Current smoker	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-
[40-50[	1	(10.0%)	1	(12.5%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	-	1	(10.0%)	0	(0.0%)	1	(50.0%)
Smoking status																		
Never smoker	1	(100.0%)	1	(100.0%)	0	-	0	-	0	-	0	-	0	(0.0%)	0	-	0	(0.0%)
Former smoker	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-	0	-	0	(0.0%)	0	-	0	(0.0%)
Current smoker	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-	0	-	1	(100.0%)	0	-	1	(100.0%)
[50-60[	3	(30.0%)	3	(37.5%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	-	5	(50.0%)	4	(50.0%)	1	(50.0%)
Smoking status																		
Never smoker	2	(66.7%)	2	(66.7%)	0	-	0	-	0	-	0	-	2	(40.0%)	2	(50.0%)	0	(0.0%)
Former smoker	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-	0	-	1	(20.0%)	1	(25.0%)	0	(0.0%)
Current smoker	1	(33.3%)	1	(33.3%)	0	-	0	-	0	-	0	-	2	(40.0%)	1	(25.0%)	1	(100.0%)
[60-65[	2	(20.0%)	2	(25.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	-	2	(20.0%)	2	(25.0%)	0	(0.0%)
Smoking status																		
Never smoker	1	(50.0%)	1	(50.0%)	0	-	0	-	0	-	0	-	1	(50.0%)	1	(50.0%)	0	-
Former smoker	1	(50.0%)	1	(50.0%)	0	-	0	-	0	-	0	-	1	(50.0%)	1	(50.0%)	0	-
Current smoker	0	(0.0%)	0	(0.0%)	0	-	0	-	0	-	0	-	0	(0.0%)	0	(0.0%)	0	-
≥65	3	(30.0%)	1	(12.5%)	2	(100.0%)	1	(100.0%)	1	(100.0%)	0	-	2	(20.0%)	2	(25.0%)	0	(0.0%)
Smoking status																		
Never smoker	2	(66.7%)	1	(100.0%)	1	(50.0%)	0	(0.0%)	0	(0.0%)	0	-	2	(100.0%)	2	(100.0%)	0	-
Former smoker	1	(33.3%)	0	(0.0%)	1	(50.0%)	1	(100.0%)	1	(100.0%)	0	-	0	(0.0%)	0	(0.0%)	0	-
Current smoker	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	-	0	(0.0%)	0	(0.0%)	0	-

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB, TOFACITINIB
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III.2.iii. HAQ

Table 11 *Description of the Health Assessment Questionnaire functional disability index (HAQ) among patient with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest1 and according to age at the date of initiation of the considered drug, whatever the rank of treatment line, table for TNFi.*

Age in (years)	Patients with RA ≥ 18 years treated with								
	ADALIMUMAB			ETANERCEPT			INFLIXIMAB		
	All N=61	Women N=45	Men N=16	All N=89	Women N=67	Men N=22	All N=24	Women N=19	Men N=5
Total									
HAQ [0-3]									
Size (missing)	59 (2)	44 (1)	15 (1)	88 (1)	66 (1)	22 (0)	24 (0)	19 (0)	5 (0)
Mean (± SD)	1.1 (± 0.67)	1.2 (± 0.68)	1.0 (± 0.62)	1.2 (± 0.72)	1.3 (± 0.66)	0.7 (± 0.74)	1.5 (± 0.70)	1.6 (± 0.68)	1.0 (± 0.62)
median	1.1	1.3	1.1	1.1	1.4	0.6	1.6	1.6	1.0
[p25%-p75%]	[0.6-1.6]	[0.6-1.6]	[0.5-1.5]	[0.6-1.8]	[0.9-1.9]	[0.0-1.1]	[1.0-2.1]	[1.0-2.1]	[0.6-1.0]
[min-max]	[0.0-2.5]	[0.0-2.5]	[0.0-2.1]	[0.0-3.0]	[0.0-3.0]	[0.0-2.3]	[0.1-2.8]	[0.1-2.8]	[0.4-2.0]
[18-30[	2 (3.3%)	2 (4.4%)	0 (0.0%)	4 (4.5%)	4 (6.0%)	0 (0.0%)	1 (4.2%)	1 (5.3%)	0 (0.0%)
HAQ [0-3]									
Size (missing)	2 (0)	2 (0)	0 (0)	4 (0)	4 (0)	0 (0)	1 (0)	1 (0)	0 (0)
Mean (± SD)	1.7 (± 0.27)	1.7 (± 0.27)	. (± .)	1.1 (± 0.41)	1.1 (± 0.41)	. (± .)	0.1 (± .)	0.1 (± .)	. (± .)
median	1.7	1.7	.	1.1	1.1	.	0.1	0.1	.
[p25%-p75%]	[1.5-1.9]	[1.5-1.9]	[.-.]	[0.8-1.4]	[0.8-1.4]	[.-.]	[0.1-0.1]	[0.1-0.1]	[.-.]
[min-max]	[1.5-1.9]	[1.5-1.9]	[.-.]	[0.6-1.6]	[0.6-1.6]	[.-.]	[0.1-0.1]	[0.1-0.1]	[.-.]
[30-40[	9 (14.8%)	4 (8.9%)	5 (31.3%)	5 (5.6%)	3 (4.5%)	2 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HAQ [0-3]									
Size (missing)	8 (1)	4 (0)	4 (1)	5 (0)	3 (0)	2 (0)	0 (0)	0 (0)	0 (0)
Mean (± SD)	0.8 (± 0.59)	0.6 (± 0.33)	1.0 (± 0.74)	0.6 (± 0.43)	0.7 (± 0.38)	0.4 (± 0.62)	. (± .)	. (± .)	. (± .)
median	0.8	0.6	1.2	0.8	0.8	0.4	.	.	.
[p25%-p75%]	[0.3-1.2]	[0.3-0.8]	[0.6-1.5]	[0.3-0.9]	[0.3-1.0]	[0.0-0.9]	[.-.]	[.-.]	[.-.]
[min-max]	[0.0-1.8]	[0.1-0.9]	[0.0-1.8]	[0.0-1.0]	[0.3-1.0]	[0.0-0.9]	[.-.]	[.-.]	[.-.]
[40-50[	17 (27.9%)	12 (26.7%)	5 (31.3%)	21 (23.6%)	13 (19.4%)	8 (36.4%)	5 (20.8%)	3 (15.8%)	2 (40.0%)
HAQ [0-3]									
Size (missing)	17 (0)	12 (0)	5 (0)	20 (1)	12 (1)	8 (0)	5 (0)	3 (0)	2 (0)
Mean (± SD)	0.9 (± 0.72)	0.9 (± 0.80)	0.9 (± 0.57)	1.4 (± 0.66)	1.4 (± 0.60)	1.3 (± 0.76)	1.4 (± 0.43)	1.3 (± 0.31)	1.5 (± 0.71)
median	0.6	0.7	0.6	1.1	1.1	1.1	1.4	1.4	1.5
[p25%-p75%]	[0.5-1.3]	[0.4-1.6]	[0.5-1.3]	[0.9-2.1]	[0.9-2.1]	[0.7-2.1]	[1.0-1.6]	[1.0-1.6]	[1.0-2.0]
[min-max]	[0.0-2.1]	[0.0-2.1]	[0.3-1.6]	[0.4-2.3]	[0.9-2.3]	[0.4-2.3]	[1.0-2.0]	[1.0-1.6]	[1.0-2.0]
[50-60[	16 (26.2%)	14 (31.1%)	2 (12.5%)	29 (32.6%)	22 (32.8%)	7 (31.8%)	10 (41.7%)	8 (42.1%)	2 (40.0%)
HAQ [0-3]									
Size (missing)	16 (0)	14 (0)	2 (0)	29 (0)	22 (0)	7 (0)	10 (0)	8 (0)	2 (0)
Mean (± SD)	1.3 (± 0.62)	1.4 (± 0.65)	1.2 (± 0.44)	1.0 (± 0.67)	1.1 (± 0.60)	0.5 (± 0.65)	1.4 (± 0.75)	1.6 (± 0.72)	0.7 (± 0.44)
median	1.4	1.4	1.2	1.1	1.3	0.0	1.3	1.8	0.7
[p25%-p75%]	[1.0-1.7]	[1.0-1.8]	[0.9-1.5]	[0.4-1.5]	[0.5-1.6]	[0.0-1.3]	[1.0-2.1]	[1.0-2.2]	[0.4-1.0]
[min-max]	[0.0-2.3]	[0.0-2.3]	[0.9-1.5]	[0.0-2.0]	[0.0-2.0]	[0.0-1.5]	[0.4-2.4]	[0.4-2.4]	[0.4-1.0]
[60-65[	5 (8.2%)	5 (11.1%)	0 (0.0%)	11 (12.4%)	9 (13.4%)	2 (9.1%)	3 (12.5%)	2 (10.5%)	1 (20.0%)
HAQ [0-3]									
Size (missing)	5 (0)	5 (0)	0 (0)	11 (0)	9 (0)	2 (0)	3 (0)	2 (0)	1 (0)
Mean (± SD)	1.5 (± 0.23)	1.5 (± 0.23)	. (± .)	1.2 (± 0.76)	1.4 (± 0.68)	0.3 (± 0.44)	1.2 (± 0.56)	1.5 (± 0.35)	0.6 (± .)
median	1.6	1.6	.	1.3	1.4	0.3	1.3	1.5	0.6
[p25%-p75%]	[1.5-1.6]	[1.5-1.6]	[.-.]	[0.6-1.5]	[1.0-1.5]	[0.0-0.6]	[0.6-1.8]	[1.3-1.8]	[0.6-0.6]
[min-max]	[1.1-1.8]	[1.1-1.8]	[.-.]	[0.0-2.4]	[0.3-2.4]	[0.0-0.6]	[0.6-1.8]	[1.3-1.8]	[0.6-0.6]
≥65	12 (19.7%)	8 (17.8%)	4 (25.0%)	19 (21.3%)	16 (23.9%)	3 (13.6%)	5 (20.8%)	5 (26.3%)	0 (0.0%)
HAQ [0-3]									
Size (missing)	11 (1)	7 (1)	4 (0)	19 (0)	16 (0)	3 (0)	5 (0)	5 (0)	0 (0)
Mean (± SD)	1.2 (± 0.71)	1.3 (± 0.69)	1.1 (± 0.83)	1.5 (± 0.82)	1.7 (± 0.68)	0.3 (± 0.29)	2.1 (± 0.46)	2.1 (± 0.46)	. (± .)
median	1.1	1.3	1.0	1.8	1.8	0.1	2.1	2.1	.
[p25%-p75%]	[0.6-1.6]	[0.6-1.6]	[0.5-1.6]	[0.6-2.1]	[1.4-2.1]	[0.1-0.6]	[1.9-2.3]	[1.9-2.3]	[.-.]
[min-max]	[0.1-2.5]	[0.5-2.5]	[0.1-2.1]	[0.1-3.0]	[0.4-3.0]	[0.1-0.6]	[1.5-2.8]	[1.5-2.8]	[.-.]

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB, TOFACITINIB
«CORPUS BMI smoking» Project
Analysis «Description» v02
CORPUS data frozen in March 2011
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Table 12 *Description of the Health Assessment Questionnaire functional disability index (HAQ) among patient with Rheumatoid Arthritis aged ≥ 18 years by group of patients treated by same drug of interest1 and according to age at the date of initiation of the considered drug, whatever the rank of treatment line, table for non-TNFi.*

Age in (years)	Patients with RA ≥ 18 years treated with								
	RITUXIMAB			TOCILIZUMAB			ABATACEPT		
	All N=10	Women N=8	Men N=2	All N=1	Women N=1	Men N=0	All N=10	Women N=8	Men N=2
Total									
HAQ [0-3]									
Size (missing)	10 (0)	8 (0)	2 (0)	1 (0)	1 (0)	0 (0)	8 (2)	7 (1)	1 (1)
Mean (± SD)	0.9 (± 0.64)	0.8 (± 0.69)	1.2 (± 0.44)	1.5 (± .)	1.5 (± .)	. (± .)	1.3 (± 0.84)	1.5 (± 0.77)	0.3 (± .)
median	0.8	0.6	1.2	1.5	1.5	.	1.4	1.8	0.3
[p25%-p75%]	[0.3-1.5]	[0.3-1.4]	[0.9-1.5]	[1.5-1.5]	[1.5-1.5]	[.-.]	[0.6-2.1]	[0.9-2.4]	[0.3-0.3]
[min-max]	[0.3-2.0]	[0.3-2.0]	[0.9-1.5]	[1.5-1.5]	[1.5-1.5]	[.-.]	[0.3-2.4]	[0.4-2.4]	[0.3-0.3]
[18-30[	1 (10.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 - 0	0 (0.0%)	0 (0.0%)	0 (0.0%)
HAQ [0-3]									
Size (missing)	1 (0)	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Mean (± SD)	0.4 (± .)	0.4 (± .)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)
median	0.4	0.4	.	.	.	.	.	.	.
[p25%-p75%]	[0.4-0.4]	[0.4-0.4]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]
[min-max]	[0.4-0.4]	[0.4-0.4]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]
[30-40[	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%)
HAQ [0-3]									
Size (missing)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Mean (± SD)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)
median	.	.	.	.	.	.	.	.	.
[p25%-p75%]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]
[min-max]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]
[40-50[	1 (10.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 - 1	(10.0%)	0 (0.0%)	1 (50.0%)
HAQ [0-3]									
Size (missing)	1 (0)	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (1)	0 (0)	0 (1)
Mean (± SD)	2.0 (± .)	2.0 (± .)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)	. (± .)
median	2.0	2.0	.	.	.	.	.	.	.
[p25%-p75%]	[2.0-2.0]	[2.0-2.0]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]
[min-max]	[2.0-2.0]	[2.0-2.0]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]	[.-.]
[50-60[	3 (30.0%)	3 (37.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 - 5	(50.0%)	4 (50.0%)	1 (50.0%)
HAQ [0-3]									
Size (missing)	3 (0)	3 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (1)	3 (1)	1 (0)
Mean (± SD)	0.9 (± 0.70)	0.9 (± 0.70)	. (± .)	. (± .)	. (± .)	. (± .)	1.3 (± 0.92)	1.7 (± 0.69)	0.3 (± .)
median	0.8	0.8	.	.	.	.	1.4	1.8	0.3
[p25%-p75%]	[0.3-1.6]	[0.3-1.6]	[.-.]	[.-.]	[.-.]	[.-.]	[0.6-2.1]	[1.0-2.4]	[0.3-0.3]
[min-max]	[0.3-1.6]	[0.3-1.6]	[.-.]	[.-.]	[.-.]	[.-.]	[0.3-2.4]	[1.0-2.4]	[0.3-0.3]
[60-65[	2 (20.0%)	2 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 - 2	(20.0%)	2 (25.0%)	0 (0.0%)
HAQ [0-3]									
Size (missing)	2 (0)	2 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0)	2 (0)	0 (0)
Mean (± SD)	0.7 (± 0.63)	0.7 (± 0.63)	. (± .)	. (± .)	. (± .)	. (± .)	1.4 (± 1.41)	1.4 (± 1.41)	. (± .)
median	0.7	0.7	.	.	.	.	1.4	1.4	.
[p25%-p75%]	[0.3-1.1]	[0.3-1.1]	[.-.]	[.-.]	[.-.]	[.-.]	[0.4-2.4]	[0.4-2.4]	[.-.]
[min-max]	[0.3-1.1]	[0.3-1.1]	[.-.]	[.-.]	[.-.]	[.-.]	[0.4-2.4]	[0.4-2.4]	[.-.]
≥65	3 (30.0%)	1 (12.5%)	2 (100.0%)	1 (100.0%)	1 (100.0%)	0 - 2	(20.0%)	2 (25.0%)	0 (0.0%)
HAQ [0-3]									
Size (missing)	3 (0)	1 (0)	2 (0)	1 (0)	1 (0)	0 (0)	2 (0)	2 (0)	0 (0)
Mean (± SD)	0.9 (± 0.63)	0.3 (± .)	1.2 (± 0.44)	1.5 (± .)	1.5 (± .)	. (± .)	1.3 (± 0.62)	1.3 (± 0.62)	. (± .)
median	0.9	0.3	1.2	1.5	1.5	.	1.3	1.3	.
[p25%-p75%]	[0.3-1.5]	[0.3-0.3]	[0.9-1.5]	[1.5-1.5]	[1.5-1.5]	[.-.]	[0.9-1.8]	[0.9-1.8]	[.-.]
[min-max]	[0.3-1.5]	[0.3-0.3]	[0.9-1.5]	[1.5-1.5]	[1.5-1.5]	[.-.]	[0.9-1.8]	[0.9-1.8]	[.-.]

1. Drugs of interest: ABATACEPT, ADALIMUMAB, BARICITINIB, CERTOLIZUMAB PEGOL, ETANERCEPT, GOLIMUMAB, INFLIXIMAB, RITUXIMAB, SARILUMAB, TOCILIZUMAB, TOFACITINIB
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Annex 19. Study B023 Protocol(f)

Post-authorization Safety Study (PASS) Information

Title	Comparative Assessment of VTE and Other Risks among Patients with Rheumatoid Arthritis treated with Baricitinib versus Tumor Necrosis Factor Inhibitors: A Multi-database Observational Cohort Study
Version identifier	6.0
Date of last version	03 May 2021
EU PAS Register No:	EU PAS 32271
Active substance	L04AA37 Baricitinib
Medicinal product(s):	Baricitinib: Olumiant®
Product reference:	EU/1/16/1170
Procedure number:	Not Applicable
Marketing authorization holder(s)	Eli Lilly and Company
Joint PASS	No
Research question and objectives	This study aims to evaluate the safety of patients with RA treated with baricitinib. This aim will be achieved using postmarketing data from multiple sources and through the following objectives, to be addressed by a meta-analysis of analytic results across individual data sources: **Primary Objective:** To compare the risk of VTE among patients with RA treated with baricitinib with the risk among similar patients treated with TNFi. **Secondary Objectives:** • To compare the risk of MACE among patients with RA treated with baricitinib with the risk among similar patients treated with TNFi. • To compare the risk of incident serious infection among patients with RA treated with baricitinib with the risk among similar patients treated with TNFi. • To describe the risk of tuberculosis (TB) requiring hospitalization among patients with RA treated with baricitinib.

Abbreviations: EU = European Union; MACE = major adverse cardiovascular events; RA = rheumatoid arthritis; TNFi = tumor necrosis factor inhibitor; VTE = venous thromboembolism.

Approval Date: 29-Jun-2021 GMT

Post-authorization Safety Study (PASS) Information

Country(-ies) of study	United States France Sweden Japan
Author	GPS Epidemiology Eli Lilly and Company Lilly Corporate Canter Indianapolis, IN 46285 United States

Marketing Authorization Holder

Marketing authorization holder (MAH)	Eli Lilly and Company
MAH contact person	GPS Epidemiology Eli Lilly and Company Indianapolis, IN 46285

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2. List of Abbreviations

Term	Definition
ACS	acute coronary syndrome
AE	adverse event: Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.
ARTIS	Anti-Rheumatic Therapy in Sweden
ATC/DDD	Anatomical Therapeutic Chemical classification defined daily dose
bDMARD	biologic disease-modifying anti-rheumatic drug
BKK	Betriebskrankenkasse
BMI	body mass index
cDMARD	conventional disease-modifying anti-rheumatic drug
CFR	Code of Federal Regulations
CPT	Current Procedural Terminology
DMARD	disease-modifying anti-rheumatic drug
DoD	Department of Defense
DVT	deep vein thrombosis
ERB	ethical review board
GKV	Gesetzliche Krankenversicherung
GPS	Global Patient Safety
HCPCS	Health Care Common Procedure Coding System
HIPAA	Health Insurance Portability and Accountability Act
HIRD	HealthCore Integrated Research Database℠
HR	hazard ratio
ICD	International Classification of Disease
IRB	Institutional Review Board

Term	Definition
JAK	Janus kinase
MACE	major adverse cardiovascular events
MDR	Military Database Repository
MHS	Military Health System
MI	myocardial infarction
MICE	multiple imputation by chained equations
OUS	Outside of United States
PE	pulmonary embolism
PHI	protected health information
PMSI	programme de médicalisation des systèmes d'information
PPV	positive predictive value
PY	person-years
RA	rheumatoid arthritis
SAP	statistical analysis plan
SHI	statutory health insurance
SNDS	Système National des Données de Santé
SNIIRAM	Système National d'Informations Inter-Régimes de l'Assurance Maladie
TNF	tumor necrosis factor
TNFi	tumor necrosis factor inhibitor
tsDMARD	targeted synthetic disease-modifying anti-rheumatic drug
VTE	venous thromboembolism

3. Responsible Parties

Not applicable.

4. Abstract

Study I4V-MC-B023: Comparative Assessment of VTE and Other Risks among Patients with Rheumatoid Arthritis treated with Baricitinib versus Tumor Necrosis Factor Inhibitors: A Multi-database Observational Cohort Study

Main Author: GPS Pharmacoepidemiologist, Eli Lilly and Company

Rationale and Background

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease characterized by progressive joint destruction, systemic complications, reduced survival, and a profoundly reduced quality of life among those affected. Baricitinib is a Janus kinase (JAK)1/JAK2 selective inhibitor indicated for the treatment of moderate-to-severe RA. In clinical studies, baricitinib led to clinically meaningful improvement across multiple measures of efficacy, including signs and symptoms, low disease activity and remission rates, physical function, patient-reported outcomes, and inhibited progressive radiographic joint damage. Data from clinical trials in patients with RA have been evaluated and demonstrate that baricitinib is an effective therapy for RA.

The safety profile of baricitinib is based on integrated clinical data from over 10,000 person-years (PY) of exposure. In the 24-week placebo-controlled safety data, there was a numerical imbalance in reported venous thromboembolism (VTE) between baricitinib and placebo-treated patients. Given the limited placebo-controlled data and infrequent occurrence of VTE, the available information does not support a definitive assessment of the risk of VTE associated with baricitinib treatment, nor with other outcomes such as major adverse cardiovascular events (MACE). Postmarketing safety studies will provide insight into the safety of real-world populations receiving treatment and will help to better establish the safety profile of baricitinib.

The present cohort study will evaluate the risk of VTE, MACE, and serious infection relative to the standard of care (i.e., tumor necrosis factor inhibitor [TNFi]) in a large number of patients with RA, based on exposures observed in multiple data sources. This approach will replicate analyses across different populations, healthcare systems, and data sources, ranging from prospective registries to retrospective claims data. By combining results from analyses of individual sources using meta-analysis, the potential association of VTE, an uncommon event, with baricitinib treatment will be investigated. In addition, although the statistical power of analyses in individual sources will be low compared to the meta-analysis result, results of individual risk estimates will also be available.

Research Question and Objectives

This study aims to evaluate the safety of patients with RA treated with baricitinib. This aim will be achieved using postmarketing data from multiple sources and through the following objectives, to be addressed by a meta-analysis of analytic results across individual data sources:

- **Primary Objective**: To compare the risk of VTE among patients with RA treated with baricitinib with the risk among similar patients treated with TNFi.

- **Secondary Objectives**:
    - To compare the risk of MACE among patients with RA treated with baricitinib with the risk among similar patients treated with TNFi.
    - To compare the risk of incident serious infection among patients with RA treated with baricitinib with the risk among similar patients treated with TNFi.
    - To describe the risk of tuberculosis (TB) requiring hospitalization among patients with RA treated with baricitinib. Due to the small number of events expected overall, incidence rates of hospitalized TB will be estimated and no comparison will be made between treatment groups. A comparative analysis will be done if a sufficient number of events accrue to support at least 80% statistical power to detect a relative difference as small as 3.0 between treatment cohorts, if such a difference truly exists.

Due to the small number of expected events and consequently limited statistical power in individual data sources, an exploratory objective is to investigate the risk of VTE associated with baricitinib versus TNFi in these individual sources.

Study Design

This study will use a retrospective cohort design to assess the safety of baricitinib among adult patients with RA using data from multiple United States (US) and European commercial claims databases (e.g., HealthCore Integrated Research Database, French national healthcare data) as well as US and outside of US prospective registries of patients with RA (e.g., Anti-Rheumatic Therapy in Sweden [ARTIS], CorEvitas (formerly Corrona) RA registry, Japanese CorEvitas RA registry). The study will include only new users, defined as patients with no prior exposure to baricitinib or the specific TNF antagonist that corresponds to the index medication use.

The scientific rigor of this study will be increased through collection of additional information from medical charts to validate the case definition for VTE, where feasible, and by evaluating the potential for unmeasured confounding by body mass index (BMI) and by smoking status. Although information about BMI and smoking status is not typically available from administrative claims data, it will be extracted from medical records.

Population

This study will include adult patients with RA who are included in databases (e.g., prospective registries, commercial insurance claims, national healthcare claims) and are newly receiving treatment with baricitinib or a specific TNFi.

Variables

In administrative claims data, the following will be ascertained from the healthcare database: 1) exposure to baricitinib and other RA medications and occurrence of the targeted adverse events and 2) potential confounding factors such as medical history, comorbidities, and healthcare resource utilization. For prospective registries such as the CorEvitas RA registry,

information on exposures and events of interest will be based on targeted collection and clinical judgment.

Drug Exposure

Study medications will be classified into 2 groups or cohorts: TNF antagonists, which represent the standard of care for the majority of patients who receive advanced therapies, and baricitinib. An as-treated approach will be used such that person-time will accrue based simply on the treatment received. Patients with exposure to drugs in the same pharmacologic class as baricitinib (i.e., JAK inhibitors) before the index date, will be excluded from exposure cohorts in main analyses to prevent the possibility that a potential class effect might mask the existence of an increased risk associated with the use of baricitinib.

Data Sources

Data for this study will come from several sources in the US, Europe, and Japan, including patient-level administrative claims databases and prospective registries. Additional sources of clinical information obtained by linkage to external data sources will be used to validate the algorithm used for the VTE case definition. Similar clinical data from medical charts will be used to provide information on BMI and smoking status for a random sample of patients in administrative claims data for the evaluation of unmeasured confounding.

Study Size

This study is designed to allow detection of a hazard ratio, as a measure of the association between RA treatment and VTE risk, as small as 1.8 with 80% power, once it has accrued a total of 118 patients with primary events of VTE across the study cohorts. Since the secondary outcomes excluding TB are more common than VTE, this study will have >80% power to evaluate a difference in risk of MACE and serious infection between patients treated with baricitinib and those treated with TNFi. The statistical power is based on a 1:3 matching of baricitinib-treated to TNFi-treated patients. Based on a background incidence rate of 0.5 to 0.9 per 100 PY for VTE, it is anticipated that at least the required number of patients with events will be observed in 6000 PY of exposure to baricitinib.

Control for Confounding

Propensity score estimation and nearest neighbor matching will be used to control for confounding, based on information included in data sources. The propensity score model will be finalized before initiating any comparative safety outcome analyses. Use of concomitant methotrexate or other conventional disease-modifying anti-rheumatic drugs (cDMARDs) may be included as a covariate in statistical models. Other immune disorders that are risk factors for MACE, VTE, and serious infections requiring hospitalization will be included as covariates in the propensity score.

The potential for unmeasured confounding by BMI will be assessed. In a subset of data sources where patient records may be linked, information on BMI will be abstracted from medical charts for a random sample of patients and compared across treatment groups. Several methods exist to

address unmeasured confounding, such as propensity score calibration and prior event rate ratio adjustment. The method selected will be based on the data linkage available but will prioritize methods that allow for an adjusted estimate of the relative risk to be computed.

Data Analysis

For all analyses, baricitinib will be the treatment of interest. The primary analysis will focus on risk of VTE, and secondary analyses on risk of MACE and serious infection, as estimated through calculation of an appropriately adjusted hazard ratio. Descriptive analyses will be provided for TB requiring hospitalization. Sensitivity analyses are planned to examine the effect of varying the case definition for VTE and to evaluate unmeasured confounding.

Cox proportional hazards regression models will be used to compare the risk of an outcome among patients treated with baricitinib versus with TNFi. Any variables that remain unbalanced after propensity score matching, based on review of standardized differences, may also be included in the regression model. Follow-up time will begin at treatment initiation and continue until censoring. Patients under follow-up, will be censored at the earliest of: occurrence of an incident event, discontinuation of the study medication plus 30 days or switching to a medication in another exposure cohort, initiation of a concomitant biologic disease-modifying anti-rheumatic drug (bDMARD) or targeted synthetic disease-modifying anti-rheumatic drug (tsDMARD), disenrollment from the database or registry, or, where available, death, or the end of the study period. Descriptive analyses will be conducted to estimate the incidence rates of events over time and an additional sensitivity analysis will be conducted to evaluate the existence of a class effect of JAK inhibitors.

5. Amendments and Updates

Amendment	Date	Section of study protocol	Amendment or update	Reason
2.0	15 Nov 2019	4	Updated Version Identifier to 2.0	The original version number was erroneously numbered 0.1 rather than 1.0. The current amendment will make this version 2.0.
2.0	15 Nov 2019	4	Add immune disorders as a covariate in the propensity score.	Added upon the request of FDA.
2.0	15 Nov 2019	4	Updated matching ratio under "Study Size"	Study groups will be matched 1:3 for baricitinib-treated to TNFi-treated patients.
2.0	15 Nov 2019	4	Updated number of primary events needed for 80% power	Updated for clarity
2.0	15 Nov 2019	8.5	Clarified matching ratio	Clarified that study groups will be matched 1:3 baricitinib-treated to TNFi-treated patients.
2.0	15 Nov 2019	8.5	Updated number of primary events needed for 80% power	Updated for clarity.
2.0	15 Nov 2019	8.2.2	Updated Figure 1	Revised to correct the exclusion assessment window for intermittent medical and drug coverage upon the request of FDA
2.0	15 Nov 2019	8.3.1.1	Updated the description of the exposure definition.	Clarified the exposure extension period upon the request of FDA
2.0	15 Nov 2019	8.3.1.1	Added figure to describe example exposure	Clarified the exposure extension period upon the request of FDA
2.0	15 Nov 2019	8.3.1.1	Added table listing gap thresholds for defining exposure for each medication	Document exposure definition for each medication upon the request of FDA
2.0	15 Nov 2019	8.3.2.2	Revised description of patients included in chart validation of VTE case definition	Updated for clarity
2.0	15 Nov 2019	8.3.2.3	Revised the case definition for myocardial infarction to align with definition from RCT-DUPLICATE	Updated in response to FDA concern about sensitivity, by removing length restriction for patients with MI with less than 3 days hospitalization
2.0	15 Nov 2019	8.3.3	Added immune disorders as a covariate in the propensity score	Added upon the request of FDA

Amendment	Date	Section of study protocol	Amendment or update	Reason
2.0	15 Nov 2019	8.3.3	Details added about the specific RA severity algorithm to be used for claims data analyses	Updated upon the request of FDA
2.0	15 Nov 2019	8.7.10	Citations added for Bayesian twin regression	Updated for clarity
2.0	15 Nov 2019	8.7.3	Citations added for propensity score matching method	Updated for clarity
2.0	15 Nov 2019	8.7.4	Clarified one-to-many matching with specific information	Specifies that matching of study groups will be a 1:3 match of baricitinib-treated to TNFi-treated patients.
2.0	15 Nov 2019	8.7.6	Additional periods included for assessment of VTE risk prior to initiating study drug	Updated upon the request of FDA (3 months) and to maximize events available for assessment (12 months)
2.0	15 Nov 2019	8.7.6	Updated matching ratio	Clarifies that study population will be matched 1:3 baricitinib-treated to TNFi-treated patients.
2.0	15 Nov 2019	8.7.7.1	Added initiation of concomitant bDMARD and tsDMARD to censoring criteria	Clarified upon the request of FDA
2.0	15 Nov 2019	8.7.7.2	Added initiation of concomitant bDMARD and tsDMARD to censoring criteria	Clarified upon the request of FDA
2.0	15 Nov 2019	8.7.7.3	Added initiation of concomitant bDMARD and tsDMARD to censoring criteria	Clarified upon the request of FDA
2.0	15 Nov 2019	8.7.7.4	Added initiation of concomitant bDMARD and tsDMARD to censoring criteria	Clarified upon the request of FDA
2.0	15 Nov 2019	8.7.8	Additional information added on the approach to the random-effects meta-analysis	Updated to match the SAP. Removed reference to Cox proportional hazards regression, which will not be used to generate an overall result
2.0	15 Nov 2019	8.7.9.4	New section	Updated to describe approach to random-effects meta-analysis when zero events are observed.
3.0	21 May 2020	4	Modify text describing statistical power of analyses	Updated for clarity

Amendment	Date	Section of study protocol	Amendment or update	Reason
3.0	21 May 2020	4	Deleted text about 6-month washout period	Updated to match protocol
3.0	21 May 2020	4	Modified text for Drug Exposure and index date	Updated for clarity
3.0	21 May 2020	4	Modified text describing censoring rules	Updated to match protocol
3.0	21 May 2020	4	Modified text for descriptive analyses	Updated for clarity
3.0	21 May 2020	6	Modified text for statistical power of analyses	Updated for clarity
3.0	21 May 2020	8.2.1	Deleted text about 6-month washout period	Corrected description of new users
3.0	21 May 2020	8.2.1	Added text for naive patients prior to JAK inhibitor	Updated for clarity
3.0	21 May 2020	8.2.1	Added reference to exclusion criteria	Updated for clarity
3.0	21 May 2020	8.2.2	Corrected start of follow-up to day after cohort entry	Correction
3.0	21 May 2020	8.2.2	Modified text for censoring rules	Updated for clarity
3.0	21 May 2020	8.2.2	Figure 1 Use of anticoagulant added to exclusions, hospitalized TB added to washout	Correction
3.0	21 May 2020	8.2.2	Figure 1 footnote 2	Added TNFi treatment group
3.0	21 May 2020	8.2.2	Figure 1 footnote 3	Updated Table number
3.0	21 May 2020	8.2.2	Figure 1 footnote 4	Updated to match protocol
3.0	21 May 2020	8.2.2	Added information about treatment episodes	Clarification
3.0	21 May 2020	8.2.2	Changed claims data source to IBM Watson Marketscan	Correction (not noted again)

Amendment	Date	Section of study protocol	Amendment or update	Reason
3.0	21 May 2020	8.3	Symbol corrected for baseline period months	Correction
3.0	21 May 2020	8.3.1.1	Added meeting eligibility criteria	Updated to clarify
3.0	21 May 2020	8.3.1.1	Added 2 paragraphs	Updated to clarify cohort definitions and censoring
3.0	21 May 2020	8.3.1.1	Defined concomitant cDMARD use	Updated for clarity
3.0	21 May 2020	8.3.1.1	Modified description of cDMARD censoring	Updated for clarity
3.0	21 May 2020	8.3.1.1	Added description of exposure extension period	Updated for clarity
3.0	21 May 2020	8.3.1.1	Added description of exposure period for registries	Additional information
3.0	21 May 2020	8.3.2	Added “incident”	Updated for clarity
3.0	21 May 2020	8.3.2	Added reference to primary outcome in 8.3.2.1	Addition of new information
3.0	21 May 2020	8.3.2.1	Modified VTE occurrence wording	Updated for clarity
3.0	21 May 2020	8.3.2.1	Added “or other venous thrombosis”	Added detailed case definition for VTE
3.0	21 May 2020	8.3.2.1	Corrected days after diagnosis to 31	Correction
3.0	21 May 2020	8.3.2.1	Added extensive description of VTE case definition throughout	Added detailed case definition for VTE
3.0	21 May 2020	8.3.2.1	Added Table 3	Added detailed case definition for VTE
3.0	21 May 2020	8.3.2.2	Modified text for RA patients selected for validation	Updated for clarity
3.0	21 May 2020	8.3.2.3	Added “incident” to MACE definition	Updated for clarity
3.0	21 May 2020	8.3.2.3	Added “primary” to hospital codes for stroke and deleted redundant text	Updated for clarity

Amendment	Date	Section of study protocol	Amendment or update	Reason
3.0	21 May 2020	8.3.2.4	Added case definition details for serious infection	Added new information
3.0	21 May 2020	8.3.2.5	Added “incident”	Updated for clarity
3.0	21 May 2020	8.3.3	Table 3 now Table 4	Renumbering
3.0	21 May 2020	8.3.3	Added text describing random sample of patients	Updated for clarity
3.0	21 May 2020	8.4	Table 4 now Table 5	Renumbering
3.0	21 May 2020	8.6.1.1	Added evaluation of the pattern of missingness	Added new information
3.0	21 May 2020	8.7.3	Reference to Table 3 updated to Table 4	Renumbering
3.0	21 May 2020	8.7.4	Deleted first sentence	Correction
3.0	21 May 2020	8.7.7	Added “separate” to time to event analyses	Updated for clarity
3.0	21 May 2020	8.7.7	Added exclusion criteria	Added new information
3.0	21 May 2020	8.7.7.1	Added “incident” to VTE	Updated for clarity
3.0	21 May 2020	8.7.7.1	Replaced “observation” with “follow-up”	Updated for consistent language
3.0	21 May 2020	8.7.7.1	Added estimate or hazard ratio text	Updated for clarity
3.0	21 May 2020	8.7.7.1	Deleted sentence on patient censoring	Defined in 8.2.2
3.0	21 May 2020	8.7.7.2	Deleted sentence on patient censoring	Defined in 8.2.2
3.0	21 May 2020	8.7.7.3	Deleted sentence on patient censoring	Defined in 8.2.2
3.0	21 May 2020	8.7.7.4	Added option for comparative analysis	Updated upon request of FDA

Amendment	Date	Section of study protocol	Amendment or update	Reason
3.0	21 May 2020	8.7.8	Deleted sentence on separate SAP	Deleted for accuracy
3.0	21 May 2020	8.7.8	Modified wording around individual database	Updated for clarity
3.0	21 May 2020	8.7.9	Added exclusion criteria	Added new information
3.0	21 May 2020	8.7.9.1	Removed definition and added reference to VTE case definition	Added new information
3.0	21 May 2020	8.7.9.1	Renumbered sections after Section 8.7.9.1	Updated for clarity
3.0	21 May 2020	8.7.9.3	Added ≥1 event	Clarify number of events
3.0	21 May 2020	8.7.9.6	Added “VTE”	Updated for clarity
3.0	21 May 2020	8.7.10	Modified sentence structure for abstracting patient information	Updated for clarity
3.0	21 May 2020	8.9.1	Deleted “in France”	Effect is not restricted to France
3.0	21 May 2020	12	Added references	Added new information
3.0	21 May 2020	Annex 1	Added new Annex: VTE Case Definitions	Added VTE-related case definitions for analyses
3.0	21 May 2020	Annex 1	Added ICD-10 codes for VTE	Added new information
3.0	21 May 2020	Annex 1	Added Anticoagulant codes	Anticoagulant codes for claims
3.0	21 May 2020	Annex 1	Added NDC codes	NDC codes for claims
3.0	21 May 2020	Annex 1	Deletion of original Annex 1. ENCePP Checklist for Study Protocols	Checklist no longer needed
3.0	21 May 2020	Through out	Minor editorial and formatting changes	Minor, therefore not detailed
4.0	21 July 2020	8.2.1	Added inclusion criteria for US data	To improve comparability of treatment groups based on USPI

Amendment	Date	Section of study protocol	Amendment or update	Reason
4.0	21 July 2020	Throughout	Updated Olumiant USPI reference	To reflect current version
4.0	21 July 2020	8.7.4	Updated section title to include “other sources of”	Added new information
4.0	21 July 2020	8.7.4	Added new information for non-US data	To improve comparability of treatment groups based on OUS labels
4.0	21 July 2020	8.7.8	Clarified the alternative as Poisson regression when zero events observed	There is no need for pooling when using Poisson regression
4.0	21 July 2020	8.7.8	Removed details of supplemental analysis for meta-analysis	After substantial review, the original counterfactual imputation is not feasible and will not provide the intended information
4.0	21 July 2020	8.7.9	Added exclusion criteria 5 for US data	To improve comparability of treatment groups based on USPI
5.0	09 Oct 2020	8.2.2	Updated Figure 1	Defined study baseline as 180 days, corrected washout window for outcome
5.0	09 Oct 2020	8.4	Updated data sources in Table 5	Added new information
5.0	09 Oct 2020	8.7.4	Added “variable ratio matching” as an option	To provide alternatives in the event of limited PS matches using fixed ratio matching
5.0	09 Oct 2020	8.7.8	Updated details of supplemental meta-analyses	Updated to clarify possible approaches to heterogeneity and zero events in a cohort
6.0	03 May 2021	8.3.2.1	Updated primary case definition for ‘Other venous thrombosis’	Correction
6.0	03 May 2021	8.3.2.2	Updated administrative claims database from Anthem’s HIRD to Optum	To increase the number of cases available for validation
6.0	03 May 2021	8.3.2.2	Updated case validation to include events identified in non-TNFi bDMARDs patients	To increase the number of cases available for validation
6.0	03 May 2021	8.3.3	Table 4 updated to specify ‘count of’ previous bDMARDs use during baseline as a baseline covariate	Updated upon the request of FDA
6.0	03 May 2021	8.3.3	Table 4 updated to specify that MACE should not be included in the history of cardiovascular disease and removed prescription aspirin.	Clarification and correction due to incomplete claims information about aspirin

Amendment	Date	Section of study protocol	Amendment or update	Reason
6.0	03 May 2021	8.4	Table 5 added data source Private Source 20 (HealthVerity)	Added information
6.0	03 May 2021	8.7.9.5	Added sensitivity analysis OUS data stratified by bDMARD naive/experienced status	Updated upon the request of FDA
7.0	See cover page	throughout the document where applicable	Updated name of Corrona to CorEvitas	Registry changed name
7.0	See cover page	8.3.2.2	Clarified that up to 100 to 200 charts would be reviewed	To increase clarity
7.0	See cover page	8.3.3	Table 4: (a) removed previous VTE and previous infection; (b) added prescription aspirin; (c) added “fibrillation” to atrial (d) added “smoking (as available)” and “obesity (as available)” (e) removed current hypertension	(a) Patients with prior events are excluded from analyses of incident (first) events; (b) will be considered after all; (c) clarity; (d) adding to PS variables for consideration; (e) captured in history of hypertension

Abbreviations: bDMARD = biologic disease-modifying anti-rheumatic drug; FDA = the US Food and Drug Administration; GVP = good pharmacovigilance practices; OUS = outside of the United States; PS = propensity score; RA= rheumatoid arthritis; TNFi = tumor necrosis factor inhibitor; tsDMARD = targeted synthetic disease-modifying anti-rheumatic drug; US = United States; USPI = United States package insert; VTE = venous thromboembolism.

6. Rationale and Background

Rheumatoid arthritis is a common, systemic autoimmune inflammatory disease characterized by synovial inflammation leading to pain, swelling, stiffness, and progressive destruction and deformity of small and large joints. Patients with RA experience impaired physical function, social participation, and health-related quality of life (Smolen et al. 2016). Patients with RA also have increased risk of significant nonmusculoskeletal comorbidities, including the following:

- malignancy (Simon et al. 2015)
- infection (Doran et al. 2002)
- VTE (Kim et al. 2013; Lee and Pope 2014; Ogdie et al. 2018)
    - deep vein thrombosis (DVT) and pulmonary embolism (PE) (Choi et al. 2013)
- cardiovascular (CV) disease (Picerno et al. 2015)
    - MACE of myocardial infarction, stroke, and CV death (Aviña-Zubieta et al. 2008, 2012)
- overall early mortality (Mutru et al. 1985; Sihvonen et al. 2004).

Cardiovascular risk in RA features the "lipid paradox," whereby active RA increases CV risk, but with decreased low-density lipoprotein (LDL), and effective treatment of RA disease activity appears to reduce CV risk while increasing LDL (Myasoedova et al. 2011). Among disease-modifying anti-rheumatic drugs (DMARDs), treatment-associated increases in LDL (predominantly larger particles) appear most pronounced for targeted interleukin (IL) 6 and JAK inhibitors (Robertson et al. 2013; Souto et al. 2015; Gabay et al. 2016; Olumiant package insert, 2020; Taylor et al. 2018; Xeljanz package insert, 2018; Actemra package insert, 2019). A recent randomized CV outcomes trial was successful in demonstrating that the risk of MACE for the IL-6 inhibitor tocilizumab was well within a prespecified noninferiority margin compared with the TNFi etanercept (Giles et al. 2016).

Current treatment of RA prioritizes timely initiation and modification of DMARD therapy to bring patients to a target of sustained low disease activity or remission (Singh et al. 2016; Smolen et al. 2017). Achievement of these targets improves short- and long-term patient health outcomes, including prevention of progressive, irreversible structural joint damage (Maini et al. 2004; Smolen et al. 2017). Patients typically begin treatment with oral cDMARDs, such as methotrexate, and modify treatment as needed and tolerated to achieve these targets.

Treatment modification often involves use of a targeted DMARD therapy. With enhanced focus on tight disease control and increased availability of novel targeted therapies, the prognosis has greatly improved in patients with RA in recent years. Targeted DMARD options currently include injectable biologic DMARDs (bDMARDs), such as TNF inhibitors, and oral targeted synthetic DMARDs (tsDMARDs), including JAK inhibitors.

Members of the JAK family of protein tyrosine kinases (JAK1, JAK2, JAK3, and tyrosine kinase-2 [TYK2]) play an important role in intracellular signal transduction following extracellular cytokines and growth factors binding to their respective cell membrane receptors. Aberrant production of cytokines and growth factors has been associated with a number of

chronic inflammatory conditions, including RA. Many of the proinflammatory cytokines implicated in the pathogenesis of RA, including IL-6, granulocyte-macrophage colony-stimulating factor, and interferon-gamma, use cell signaling that involves the JAK/signal transducers and activators of transcription (STAT) pathways. Inhibition of JAK-STAT signaling can target multiple RA-associated cytokine pathways and thereby reduce inflammation, cellular activation, and proliferation of key immune cells (Kremer et al. 2009).

The safety profile of baricitinib is based on integrated clinical data from over 10,000 PY of exposure but includes limited information in relation to placebo. The duration of the placebo-controlled period was restricted to 24 weeks based on ethical considerations. This limits the ability to compare risk across treatment groups and to assess the potential association of baricitinib with safety outcomes. This is especially true for rare events. In the 24-week placebo-controlled safety data, there was a numerical imbalance in reports of VTE between baricitinib- and placebo-treated patients. The available information does not support a definitive assessment of the risk of VTE associated with baricitinib treatment. The limited amount of placebo-controlled data also affects the ability to assess the risk of other safety outcomes, such as MACE and TB. These outcomes were observed among baricitinib treated patients and are also observed more frequently in the general RA population relative to age-matched controls (Gabriel 2008; van den Hoek et al. 2017). Patients in clinical trials may also not be representative of the population of patients who may be treated with a medication in the real-world. Therefore, postmarketing safety studies conducted within real-world populations are needed to better characterize establish the safety profile of baricitinib.

This cohort study will evaluate the safety of baricitinib relative to the standard of care therapy (i.e., treatment with TNF inhibitors) in a large number of patients with RA, across multiple data sources. This approach will allow for replication across different populations, healthcare systems, and data sources, ranging from prospective registries of RA therapies (e.g., CorEvitas, Anti-Rheumatic Therapy in Sweden [ARTIS]), to retrospective claims data (e.g., Anthem's HealthCore Integrated Research Database (HIRD®), French national healthcare data), providing important additional characterization of the safety profile of baricitinib. Since some outcomes such as VTE and TB are uncommon, data from multiple sources must be considered to investigate any potential association with baricitinib treatment. Although the statistical power of analyses in individual sources may be low compared to the meta-analysis result, results of individual risk estimates will also be available. Such replication represents standard, if infrequently applied, practice within epidemiological research when results may inform substantial decisions (Peng et al. 2006).

7. Research Question and Objectives

This study aims to evaluate the safety of patients with RA treated with baricitinib. This aim will be achieved using postmarketing data from multiple sources and through the following objectives, to be addressed by a meta-analysis of analytic results across individual data sources:

- **Primary objective**: To compare the risk of VTE among patients with RA treated with baricitinib with the risk among similar patients treated with TNFi.
- **Secondary objectives**:
    - To compare the risk of MACE among patients with RA treated with baricitinib with the risk among similar patients treated with TNFi.
    - To compare the risk of incident serious infection among patients with RA treated with baricitinib with the risk among similar patients treated with TNFi.
    - To describe the risk of TB requiring hospitalization among patients with RA treated with baricitinib. Due to the small number of events expected overall, incidence rates of hospitalized TB will be estimated and no comparison will be made between treatment groups. A comparative analysis will be done if a sufficient number of events accrue to support at least 80% statistical power to detect a relative difference as small as 3.0 between treatment cohorts, if such a difference truly exists.

Due to the small number of expected events, and consequently limited statistical power in individual data sources, investigating the potential association of each outcome with baricitinib in individual data sources will be an exploratory objective.

8. Research Methods

8.1. Study Design

This study will rely on cohorts from multiple data sources, ranging from prospective cohorts in independent biologic disease-modifying anti-rheumatic drug (DMARD) and disease registries to retrospective cohorts from administrative claims databases and national healthcare systems. A partial list of data sources from which study cohorts will be drawn is provided in Section 8.4, with other data sources to be added pending assessment. The data sources selected for this study will include information on patient demographics, RA diagnosis, records of filled prescriptions or administration of RA treatment, comorbidities, hospitalizations, and medication use, among others. Some data sources, such as the CorEvitas registry, are based on primary data collection, while others, such as administrative claims data, are secondary data sources that have been developed for other purposes. All data sources are independent and have not been established or modified for the purposes of this study. The diversity of the data sources and populations represented provides a good foundation for ensuring the generalizability of any findings, since this study will analyze data from a large proportion of the total available baricitinib exposure. The algorithms for identifying the primary study outcome, VTE, will be validated based on clinical information (i.e., chart review), as feasible.

Time-to-event analyses will be conducted in each data source. Although analyses from individual data sources may have limited statistical power to estimate the association between treatment and the study outcomes, point estimates will nonetheless be available for comparison with regard to trend and direction. Meta-analysis will be used to obtain a single combined estimate of the potential association between treatment and primary or secondary study outcomes from analytic results of individual data sources.

8.2. Setting

8.2.1. Study Population

The study population will consist of adult patients diagnosed with RA who, during the study period, were incident users of baricitinib or a specific TNFi. In healthcare claims data, RA will be defined based on a combination of diagnostic codes and treatment with DMARDs. A previous study showed that RA patients can be accurately identified using a combination of diagnosis codes for RA and any DMARD prescriptions in claims data, with a positive predictive value (PPV) of 86% (Kim et al. 2011). Alternate, but equivalent, criteria will be implemented in data sources where clinical judgment has been used to classify patient information. In claims data, detailed algorithms using diagnostic codes, procedures, and/or pharmacy codes to identify the study population will be outlined in the separate statistical analysis plan (SAP). Among all patients exposed to baricitinib, those who meet the eligibility criteria will be identified and included in the analytic dataset. Only new users of baricitinib or a specific TNFi (see Section 8.3.1) will be included in the study, defined as patients without prior evidence of use of baricitinib or the specific TNFi or the equivalent based on medical records or data collection forms. All patients in the main analyses must also be new users of JAK inhibitors. Additional or

alternate exclusions may be employed for specific analyses, which will be clearly identified in the analysis sections of the SAP.

Eligibility Criteria

All patients meeting the criteria below will be included in the main analyses and an attrition table generated.

Inclusion Criteria: RA Registry or other source relying on primary data collection

1. Adult patients diagnosed with RA who have newly initiated treatment with baricitinib or a TNFi; the date of treatment initiation is the cohort entry date (also known as the index date).

Inclusion Criteria: Administrative claims data

1. Patients have an RA diagnosis code from a physician encounter and initiated baricitinib or a TNFi*; the date of treatment initiation is the cohort entry date (also known as the index date);
2. Patients are aged ≥18 years on the cohort entry date;
3. Patients have continuous medical and prescription drug coverage for at least 6 months before cohort entry.

   *Initiation of a TNFi is defined as dispensing of one of the following TNFi without prior dispensing of that same TNFi during the baseline period: adalimumab, certolizumab pegol, etanercept, golimumab, or infliximab.

Inclusion Criteria: US Data

Patients with RA who newly initiate treatment with a specific TNFi require prior treatment with at least 1 TNFi. This aligns the comparison groups in US data with the indicated population for baricitinib, which is patients with moderate to severe RA who have had an inadequate response to 1 or more TNF antagonist therapies (i.e., Olumiant package insert, 2020). If more than 5% of patients treated with baricitinib appear to be TNF-naïve, an additional sensitivity analysis will be executed in US data.

Exclusion criteria are specific for specific analyses and are therefore included in Sections 8.7.7 and 8.7.9, as appropriate.

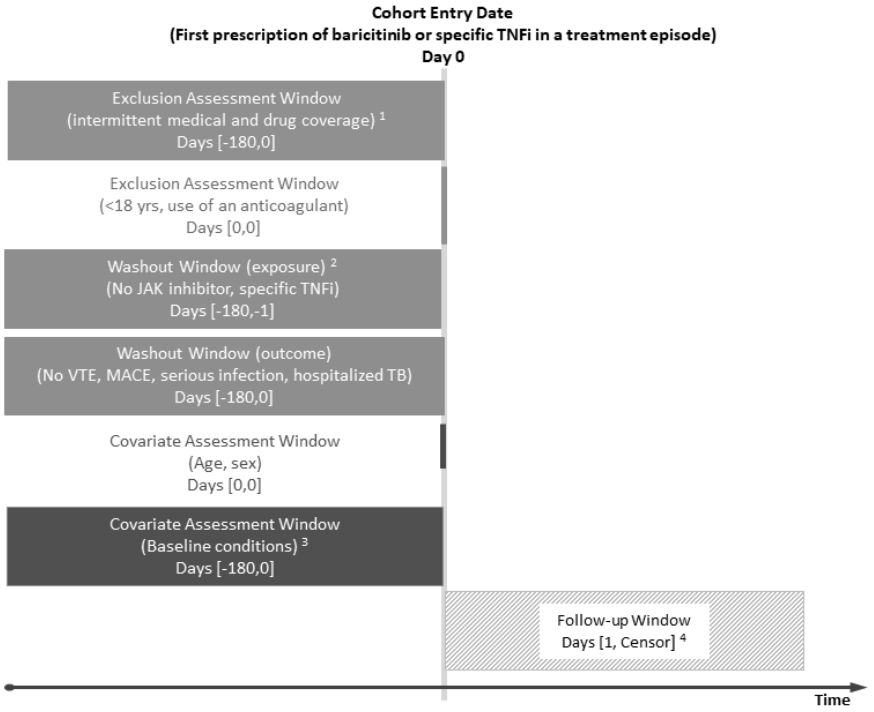
Sensitivity analyses will be performed in which the inclusion/exclusion criteria, exposure ascertainment, and outcome identification will vary from those in the primary analyses (e.g., patients exposed to both baricitinib and tofacitinib, which are both JAK inhibitors, will be evaluated to assess potential class effects). Sensitivity analyses are summarized in Section 8.7.9.

8.2.2. Study Period and Study Follow-up

The study will include eligible patients who are enrolled in the data source and receive treatment with baricitinib or TNFi during the study period. The study period will commence at the time of market launch, which will differ by region, and will continue until the most recent data available

at the time of data extraction. The specific dates will vary by geography and individual data source.

The study will use the 'new user' design, in which patients who initiate baricitinib or a TNFi will be identified (Lund et al. 2015). The cohort entry date (or index date) is defined as the date of the first prescription fill or dispensing (claims data) or the first recorded prescribing or order entry of either baricitinib or a specific TNFi (primary data). Follow-up starts on the day after cohort entry. The covariate assessment window for claims data analysis will rely on the 6-month enrollment period prior to the index dispensing, including the day of dispensing, while for data sources with primary data collection, medical history and physician diagnosis of RA on the day of prescribing will suffice. In claims data, during follow-up all patients will be required to maintain continuous enrollment, defined as continuous medical and prescription drug coverage with a gap no longer than 45 days. Lack of enrollment leads to censoring at the point of discontinuation as defined above. Patients under follow-up will be censored at the earliest of: occurrence of an incident event , discontinuation of the study medication plus 30 days or switch to a medication in another exposure cohort, initiation of a concomitant bDMARD, including TNFi, or tsDMARD, disenrollment from the database or registry, or, where available, death, or the end of the study period. The study design for an administrative claims data source is illustrated in Figure 1.



Abbreviations: RA = rheumatoid arthritis; TNFi = tumor necrosis factor inhibitor.
[1] Up to 45-day gaps in medical or pharmacy enrollment will be allowed.
[2] After cohort entry, patients in the TNFi treatment group may not be exposed to a specific TNFi used during the washout window.
[3] Baseline conditions vary by outcome and are described in Table 4.
[4] Earliest occurrence of the outcome of interest (i.e., incident VTE, MACE, serious infection, or hospitalized TB, depending on the analysis), discontinuation of study medication + 30 days or switch to a medication in another exposure cohort, initiation of a concomitant bDMARD or tsDMARD, disenrollment from the database or registry, or, where available, death, or the end of the study period.

Figure 1. Schematic of study design for an administrative claims data source.

Patients receiving treatment with one of the study medications will contribute varying amounts of person-time to analyses depending on the duration of their therapy. Patients will contribute only a single treatment episode within a given analysis. For TNFi, the median time to discontinuation for first-line therapy is estimated to be 15.6 months and for second and subsequent-line therapies, 12.3 months (Ogale et al. 2011). In claims data the duration of observation is also based on the length of time an individual is insured by a specific provider. In the US, the average plan enrollment is typically approximately 2 years, although patients with chronic diseases such as RA tend to be enrolled for longer periods (e.g., approximately 3 years in IBM Watson Marketscan). In other geographies with national health coverage, enrollment is much longer.

8.3. Variables

Data on patient demographics (age, sex, geographic region), history of prior RA treatment, prior medical history, (e.g., comorbidities including prior VTE, hospitalizations, concomitant medication use, and healthcare resource utilization) will be assessed. The following sections detail the variables that will be available for this study. Information will be based on primary data collection (e.g., CorEvitas registry) or on administrative claims data (e.g., the HIRD data). Confirmation of the primary outcome, VTE, when not already included as part of data collection, will be based on additional clinical information, as appropriate per Section 8.7.10. Details of the clinical review and adjudication process will be described in a forthcoming medical record plan.

Baseline variables will be ascertained from claims occurring in the baseline period, up to 6 months prior to cohort entry when patients begin contributing person-time and events to analyses. Baseline covariates that are not routinely available in claims data, but which are important potential confounding factors, (i.e., body mass index [BMI], smoking status), will be assessed by sampling a random selection of patients, typically 200, for medical chart review, as possible (Wahl et al. 2010). Unlike validation of the case definition for the primary outcome, data abstraction for this purpose will include patients who have not experienced VTE during the study. Further information on the approach to evaluating unmeasured confounding is described in Section 8.7.10.

8.3.1. Drug Exposure

In claims data sources, exposure to baricitinib or other medications indicated for the treatment of RA will be ascertained based on a recognized classification scheme such as the Anatomical Therapeutic Chemical classification defined daily dose (ATC/DDD) system (WHO 2018), or the National Drug Code or Generic Product Identifier for outpatient pharmacy dispensing and based on Health Care Common Procedure Coding System (HCPCS) for injections or infusions that occur in a healthcare setting. Specific applicable codes will be detailed in a separate SAP. Exposure will be defined as a dispensing or administration of a study drug to a patient diagnosed with RA within the period of the study. Table 1 displays medications available at the time this protocol was developed that are eligible for inclusion in the study.

Table 1. Eligible Treatments for RA Patients

Conventional DMARD (as concomitant medications)		TNFi Treatment Group		Targeted Synthetic DMARD
Cyclosporine	Methotrexate	Adalimumab	Infliximab	Baricitinib
Gold sodium thiomalate	Mycophenolate mofetil	Certolizumab pegol		Tofacitinib - for sensitivity analysis only
Hydroxychloroquine	Penicillamine	Etanercept		
Leflunomide	Sulfasalazine	Golimumab		

Abbreviations: DMARD = disease-modifying anti-rheumatic drug; RA = rheumatoid arthritis; TNFi = tumor necrosis factor inhibitor.

A patient treated with a biosimilar will be defined as initiating a TNFi only if the patient has not had prior exposure to the originator drug or another applicable biosimilar. Tofacitinib, a JAK

inhibitor used to treat patients with moderate-to-severe RA, will be excluded from all analyses, except for sensitivity analyses where it will be included to allow for identification of potential class effects (Section 8.7.9.4).

8.3.1.1. Drug Exposure and Cohort Identification

All available patients meeting the eligibility criteria and with exposure to baricitinib during the period of the study will be included in the baricitinib cohort. For the TNFi cohort, exposure status will be classified based on use of any specific, eligible TNFi medication. Two treatment groups will be created for these analyses:

- **TNFi cohort:** Patients newly initiating a specific TNFi.
- **Baricitinib cohort:** Patients newly initiating baricitinib.

Since the United States Prescribing Information for baricitinib requires prior treatment with a TNFi, and many insurance formularies, including European national formularies, require prior use of at least one TNFi, many patients eligible for inclusion in the baricitinib cohort may also qualify for inclusion in the TNFi cohort. Nonetheless, patients will be permitted to contribute person-time and events to only a single treatment group in an analysis, *either* the TNFi cohort or the baricitinib cohort. Study results will therefore apply to 'persons' rather than to "treatment episodes." Because patients treated with baricitinib are expected to represent a smaller proportion of patients with RA than patients treated with TNFi, inclusion in the baricitinib cohort will be prioritized, when possible, to maximize the size. Given the relatively larger size of the TNFi population, this should not impact the availability of patients for the TNFi cohort.

Since patients will contribute only a single treatment episode to an analysis, no switching will be permitted between treatment groups. Patients in the TNFi cohort will be censored if they switch to a new TNFi treatment. This will establish similar censoring criteria for both treatment groups: patients will be censored when they stop baricitinib or TNFi. Although some patients may receive treatment with more than one TNFi during follow-up, the first eligible TNFi treatment episode will be selected as the index exposure. This accommodates a limitation of the selected analysis platform for the majority of the US data and ensures that analyses are executed consistently across data sources. This approach may tend to increase differences between the baricitinib and TNFi cohorts with respect to duration or severity of RA, with patients treated with baricitinib potentially tending to experience longer periods and more severe RA than patients treated with TNFi. If disease duration or severity are risk factors for any of the study outcomes, this could lead to bias in the results, such that patients treated with baricitinib may appear to be at higher risk of the outcome than they truly are compared to patients treated with TNFi. After assignment of patients to the appropriate exposure group and identification of the relevant TNFi treatment episode are completed, propensity scores will be calculated for patients in both cohorts and matching will occur as described in Section 8.7.

Patients treated with baricitinib or TNFi may receive concomitant treatment with cDMARDs. Concomitant use of cDMARDs will be described by treatment group. Patients will not be censored based on starting or stopping concomitant cDMARDs. The impact on the results of including a covariate for cDMARD use in the statistical model will be assessed. Concomitant use

of cDMARDs will be defined as at least 2 dispensings of the cDMARD. Concomitant use of other biologic DMARDs (bDMARDs), including TNFi, or tsDMARDs will not be permitted and patients initiating such concomitant DMARD use will be censored at the time of such dispensing.

Each patient will be assigned an index date when the patient will begin contributing person-time for a time-to-event analysis. At the time of discontinuation, the exposure period will be defined based on the recommended dosing interval from each medication's label plus a 30-day exposure extension. During this period, patients continue to accrue time "at risk." The addition of this "exposure extension period," after the last prescription dispensing and recommended dosing interval (when relevant, e.g., infliximab) in the exposure period, accounts for the possibility that discontinuation is related to the probability of experiencing the outcome (e.g., if a patient discontinues due to symptoms that are subsequently diagnosed as an event of interest). A gap in exposure that is longer than the recommended dosing interval plus 30 days will be defined as a discontinuation of study medication. A gap that is less than or equal to the recommended dosing interval plus 30 days will be bridged and the exposure defined as continuous. See Figure 2 for an example of an exposure period and Table 2 for the list of gap durations used for each medication to determine whether to bridge or discontinue an exposure.

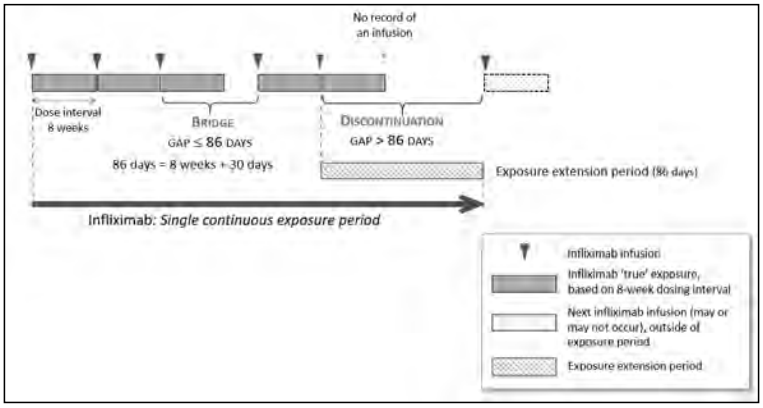


Figure 2. Infliximab exposure period.

Table 2. Dose Intervals and Gap Duration Used to Determine Whether to Bridge or Discontinue Exposure, by Study Medication

DMARD	Recommended Dose Interval (in days, from USPI)	Gap Threshold* (in days)
Baricitinib	1	31
Adalimumab	14	44
Certolizumab pegol	28	58
Etanercept	7	37
Golimumab	Simponi (subcutaneous) 30	60
	Simponi Aria (infusion) 56	86
Infliximab	56	86

Abbreviations: DMARD = disease-modifying anti-rheumatic drug; USPI = United States Package Insert.

* Gaps that are less than or equal to this threshold will be bridged for a continuous exposure. Gaps that are longer than this threshold will be defined as discontinuation of the study medication. This gap threshold is calculated as the dose interval recommended for maintenance plus 30 days.

Source: Enbrel USPI 2012; Humira USPI 2018; Olumiant USPI 2020; Remicade USPI 2018; Simponi Aria USPI 2018; Simponi USPI 2018; Cimzia USPI 2019.

Data from registries such as CorEvitas and ARTIS, will define exposure differently than in claims data, as rheumatologists will collect information about medications used to treat RA directly from patients. Exposure to specific medications will be based on the start and stop dates for therapies for RA, which are collected from patients by their rheumatologists. Lilly's intent for this analysis is to define exposure for registry data, similar to how it is defined in claims data, with the addition of an exposure extension period.

Information on relevant potential confounding factors, such as history of VTE, will be collected at baseline (claims data) or based on recorded information (primary or registry data). This information will be used to assess potential channeling in a sensitivity analysis described in Section 8.7.6, to help ensure that confounding factors are evenly distributed across the groups being compared.

8.3.2. Outcomes

The primary outcome measure is VTE and the secondary outcome measures consist of the following: MACE, a composite CV endpoint; incident serious infection; and TB requiring hospitalization. In claims data, VTE will be defined based on diagnosis, clinical setting of the diagnosis, and evidence of dispensing of anticoagulant therapy. Major adverse cardiovascular events will be defined as hospitalization for myocardial infarction or stroke, and serious infection will be defined as an infection requiring hospitalization. In the CorEvitas RA registry and any electronic medical record data, these outcomes will be defined based on clinical information such as physician diagnosis and adjudication of endpoints. The primary outcome will be validated based on medical chart review as described in Section 8.3.2.2.

In registry data or other sources where outcomes have been recorded based on clinical evaluation (e.g., claims data), relevant variables will be used to identify the specified outcomes. The specific information used to ascertain each incident outcome in each data source will be described in the SAP except for the primary outcome, which is described below. Where adjudication of outcomes has occurred in the process of primary data collection (e.g., CorEvitas RA registry), a description of the validation process will be provided in the final report, but no further confirmation or validation will be conducted. In administrative claims data, incident cases of each targeted outcome will be identified based on International Classification of Disease, 10th Revision (ICD-10) diagnosis and procedure, Current Procedural Terminology (CPT-4®), HCPCS codes, and/or National Drug Codes (NDC). Validated, well-established, claims-based algorithms will be used to identify the study outcomes where available (e.g., acute MI [Kiyota et al. 2004]). The specific codes and algorithms that will be used to ascertain the outcomes in claims data will be detailed in a separate SAP.

The following sections describe each outcome, as it will be identified in administrative claims data.

8.3.2.1. Venous Thromboembolism

Venous thromboembolism is the primary outcome measure. For claims data, the occurrence of incident venous thromboembolic events will be defined based on ICD-10 diagnostic and procedure codes available in administrative claims data and includes both pulmonary embolism (PE) and deep vein thrombosis (DVT). The primary means of ascertaining VTE in administrative claims data will rely on an emergency care (ED) or hospital discharge code of PE, DVT, or other venous thrombosis or an outpatient diagnosis code of PE, DVT, or other venous thrombosis with evidence of low molecular-weight heparin or oral anticoagulant dispensing within 31 days after diagnosis. The requirement for evidence of dispensing of an anticoagulant will be based on the diagnostic setting and, for inpatient diagnoses, the position of the code (primary/secondary). This additional detail optimizes the operating definition based on a large validation study of VTE in 4 US integrated health care delivery systems that participated in the Cardiovascular Research Network VTE study (Fang et al. 2017). The event date is the date of the first recorded diagnosis of VTE during follow-up.

Additional analyses, based on more and less stringent case definitions of VTE, e.g., requiring anticoagulant dispensing in all diagnostic settings, will be implemented to delimit the possible range of results for a broad range of sensitivity, specificity, and PPV. The primary algorithm used to identify VTE in claims data will be validated as described in Section 8.3.2.2 through review of medical charts and in other data sources as feasible, based on the availability of linkage to clinical data. Specific ICD-10 codes and medications used in the VTE algorithm are described below.

The Fang et al. (2017) study based on ICD-9-CM coding, confirmed the importance of the diagnosis setting and evidence of anticoagulation to the PPV of the case definition and additionally demonstrated the importance of the position of codes used in inpatient settings (primary versus secondary). The algorithms used in the present study to define the individual components of VTE (PE, DVT, and other venous thrombosis) are based, in part, on achieving optimal PPV. For example, primary inpatient PE diagnoses had a PPV of 89.1% and secondary inpatient PE diagnoses with evidence of anticoagulation had a PPV of 84.8%. The PPV for outpatient VTE diagnoses, even with evidence of anticoagulation, was 54.5%. For this reason, the present study will not include outpatient PEs in the primary case definition.

Although restricting the definition of VTE to events accompanied by anticoagulant prescriptions after discharge raises the PPV, in the CVRN cohorts it also excluded 30.9% of patients with chart-validated VTE who did not have evidence of an anticoagulant prescription. For this reason, this most stringent case definition was not selected as the primary case definition for the present multi-database study. Instead, it is included as Alternative case definition I in a sensitivity analysis. Specific ICD-10 codes and medications used to define the primary VTE case definition are described below and in Table 3.

Primary case definition: (see Annex 1 for ICD-10 codes)

- **VTE** = PE or DVT or other venous thromboses
    a. **Pulmonary embolism**: ICD-10 diagnosis codes in the primary position for inpatient or ED setting. Inpatient PE diagnoses in the secondary position further require anticoagulation within 31 days of the event. No outpatient codes for PE will be included.
    b. **Deep vein thrombosis:**
        i. **of the lower extremity**: ICD-10 diagnosis codes in the primary position for inpatient or ED setting. Inpatient diagnoses in the secondary position and outpatient diagnoses require anticoagulation within 31 days of the event.
        ii. **of the upper extremity**: ICD-10 diagnosis codes in the primary position for inpatient or ED settings and outpatient diagnoses require anticoagulation within 31 days of the event. No inpatient diagnoses in the secondary position will be included.

c. **Other venous thrombosis:** ICD-10 diagnosis codes in the primary or secondary position for inpatient or ED settings and outpatient diagnoses require anticoagulation with 31 days of the event.

Table 3. Primary (Main) Case Definition for VTE and Alternate (Alt I and Alt II) Case Definitions for Sensitivity Analyses

VTE Type	Hospital/Emergency Department				Outpatient	
	Code in Primary Position		Code in Secondary Position			
	No A/C	A/C	No A/C	A/C	No A/C	A/C
PE	Main, Alt I, Alt II	-	Alt II	Main, Alt I	-	Alt II
Lower extremity DVT	Main, Alt II	Alt I	Alt II	Main, Alt I	Alt II	Main, Alt I
Upper extremity DVT	Alt II	Main, Alt I	-	Alt II	-	Main, Alt I, Alt II
Other venous thromboses	Alt II	Main, Alt I	-	Main, Alt I, Alt II	-	Main, Alt I, Alt II

Abbreviations: A/C = anticoagulation; Alt I = alternative case definition 1 for sensitivity analysis; Alt II = alternative case definition 2 for sensitivity analysis; DVT = deep vein thrombosis; Main = main case definition for primary analysis; PE = pulmonary embolism; VTE = venous thromboembolism.

Case definitions for sensitivity analyses: Alternate definitions will assess more (Definition number 1) and less (Definition number 2) restrictive criteria that should encompass the reasonable range of the true incidence rate of VTE. Regardless of whether these alternate case definitions under- or over-ascertain VTE, any comparative analyses that rely on them should retain their internal validity, provided no difference exists between treatments with respect to the proportion of misclassification.

I. **Sensitivity analysis case definition 1**: VTE diagnosis codes (see Annex 1 from any setting (inpatient, ED, or outpatient) are required to have evidence of anticoagulation within 31 days, except for inpatient PE codes in primary position. This more stringent case definition is expected to result in lower incidence rates of VTE, but to have a higher PPV than the primary case definition.

II. **Sensitivity analysis case definition 2:** Inpatient VTE diagnosis codes in the primary position will not require evidence of anticoagulation. VTE codes in the secondary position from inpatient or ED settings require evidence of anticoagulation within 31 days of the event, with the exception of PE and lower extremity DVT which do not require evidence of anticoagulation. Except for lower extremity DVT, VTE codes in an

outpatient setting always require evidence of anticoagulation within 31 days. This case definition relaxes the primary case definition and should have greater sensitivity, leading to a higher incidence rate of VTE than the primary case definition, at the cost of a lower PPV.

8.3.2.2. Validation of Outcome Definition: Venous Thromboembolism

To ensure that the VTE events identified in claims data provide an accurate estimate of true VTE, this study will validate the case definition used to identify the occurrence of VTE using clinical information from medical chart review. This evaluation will assess the PPV of the VTE algorithm in claims data. A PPV of at least 80% will be considered acceptable, consistent with sufficiently robust evidence to support the assessment of baricitinib safety. This validation will be conducted in at least one US claims data source as well as in one European claims database, based on the feasibility of linkage to medical charts. It is reasonable that validation in a large US administrative claims database (e.g., Optum) will generalize to other US claims databases. Validation in EU data sources (e.g., French claims data) will also be conducted, but specific sources remain under investigation. Validation will be performed based on a simple random sample of patients who have experienced VTE based on the case definition, with up to 100 to 200 charts reviewed from the above data sources. Ascertainment of patient claims records in Europe may differ from the approach used for US records as a result of the General Data Protection Regulation compliance guidelines (GDPR EU [WWW]), but as far as possible, the EU validation will aim to provide similar information on the performance of the VTE case definition as the US validation. Details will be provided in a separate medical record plan. Registers and other data sources that rely on primary collection of clinical information may include clinical validation of outcomes (e.g., CorEvitas RA registry) and will not undergo further validation.

As VTE is not a common event, the number of available events may be low, so patients with events will be selected from the eligible population of RA patients or those treated with other b/tsDMARDs (e.g. non-TNFi bDMARDs and tofacitinib). Thus, validation will include patients who will not be included in the main analyses to provide sufficient VTE events. It is unlikely that the way VTEs are documented in claims data is related to treatment with TNFi or non-TNFi bDMARDs. Given the similarities of US administrative claims databases, it is reasonable to consider that the algorithm and findings of the validation from one US claims data source may apply across the majority, if not all, US claims data. Frequencies of individual ICD codes in the study population will be assessed in each claims data source to provide some information on the comparability of data beyond the information provided by the details of each source (e.g., geography). Additional details of this validation will be provided in a separate medical record plan. This work will be conducted concurrently with the present study.

8.3.2.3. Major Adverse Cardiovascular Events

One of the secondary outcomes is a composite MACE of incident myocardial infarction (MI) and incident stroke. Within US claims data, incident MI will be identified with a primary discharge code of acute MI for an inpatient visit. This is based on the case definition used by the RCT DUPLICATE project (RCT DUPLICATE [WWW]) which had a PPV of 93% or higher (Fralick

et al. 2018). Information about the death of a patient is not routinely available in health insurance claims data and only a portion of the data sources included in this project may have access to death data. Therefore, deaths due to acute MI will only be available in those data sources. Incident stroke will be defined with a primary hospital discharge diagnosis code of ischemic or hemorrhagic stroke. This measure has a PPV of >92% (Kumamaru et al. 2014).

As feasible based on the total number of events identified, acute MI and stroke may also be evaluated separately.

8.3.2.4. Serious Infections

Incident serious infection is another secondary outcome. In claims data, this outcome will be captured based on ICD diagnostic and procedure codes and will be defined as a composite endpoint of any serious infection, including bacterial, opportunistic, or viral infection requiring hospitalization. Serious bacterial infection will be identified based on inpatient codes in the primary position, following a previously validated algorithm with high PPV (>80%) (Schneeweiss et al. 2007). Serious opportunistic infections, for example, TB, systemic candidiasis, cryptococcosis, or aspergillosis, will also be defined using primary inpatient diagnosis codes. Serious viral infections will be similarly defined using inpatient diagnosis codes. In primary data sources, serious infection will be based on clinical judgment and, in the case of CorEvitas data, based on adjudicated events.

8.3.2.5. Tuberculosis

Incident hospitalized TB, another secondary outcome, will be defined based on evidence of hospitalization and ICD diagnostic and procedure codes in claims data and based on clinical data collected from physicians in registries. As the incidence of TB is expected to be limited, this outcome will be included as a descriptive objective. There are limitations to the use of administrative claims data for identifying patients with TB, with a recent review noting wide variations in diagnostic accuracy (i.e., PPV ranging from 1.3% to 100% and sensitivity ranging from 20% to 100%) (Ronald et al. 2017). These limitations are particularly relevant for case definitions relying solely on diagnostic codes, although a recent validation of confirmed TB in Medicaid patients with RA noted both sensitivity and PPV ≤25% when the case definition combined prescription data and diagnostic codes (Fiske et al. 2012). In the present descriptive analysis, the addition of a requirement for hospitalization should improve the accuracy of TB case identification. Regardless, particularly in light of the small number of cases expected, results will need to be interpreted cautiously.

8.3.3. Covariates

In addition to information on safety outcomes of interest for this study, depending on the data source, information on several other characteristics may be evaluated, including demographics, medical history and comorbidities, and RA disease treatment. Geographic region or urban/rural location may be considered, depending on the availability of information, to address potential confounding by socioeconomic status. The covariates listed in Table 4 will be considered in the analyses for their potential to confound the association between exposure to a medication indicated for RA and the outcomes under investigation. Geographic region, as described above,

may be evaluated as a potential confounder and may help to address confounding by BMI. Further explanation is provided in Section 8.7.

Table 4. Baseline Covariates for Consideration in Outcome-Specific Analysis

Outcome	Baseline Covariates for Consideration in the Propensity-Score Model
VTE	Age, sex, history of cancer, cardiovascular disease (hospitalized congestive heart failure, ventricular arrhythmia, atrial arrhythmia/fibrillation), immune disorders[a], diabetes mellitus, obesity (as available), recent pregnancy; recent hospitalization, surgery or trauma; smoking (as available), use of prescription aspirin, anticoagulants, glucocorticoids, methotrexate; oral contraceptives, hormone replacement therapy or SERMs, count of previous bDMARDs use during the baseline period, health care resource utilization
Major adverse cardiovascular event	Age, sex, history of cardiovascular disease excluding MACE (unstable angina, hospitalized congestive heart failure, ventricular arrhythmia, cardiovascular revascularization procedure, coronary artery disease, and transient ischemic attack), immune disorders[a], diabetes mellitus, obesity (as available), history of hypertension, dyslipidemia, smoking (as available), use of prescription aspirin or glucocorticoids, use of lipid-lowering agents or antiplatelet agents during the baseline period, count of previous bDMARDs use during the baseline period, health care resource utilization
Serious infections	Age, sex, immune disorders[a], diabetes mellitus, chronic lung disease, liver disorder, ischemic heart disease, smoking (as available), obesity (as available), previous antibiotic use, glucocorticoid use, count of previous bDMARDs use during the baseline period, health care resource utilization

Abbreviations: bDMARD = biologic disease-modifying anti-rheumatic drug; DMARD = disease-modifying anti-rheumatic drug; MACE = major adverse cardiovascular events; MI = myocardial infarction; SERM = selective estrogen receptor modulator; VTE = venous thromboembolism.

[a] Examples of immune disorders include human immunodeficiency virus, acquired immunodeficiency syndrome, systemic lupus erythematosus, antiphospholipid syndrome, and primary Sjogren Syndrome.

Some covariates are typically not available in claims data, including race, BMI, alcohol use, smoking, education, RA disease activity, and disease duration. This limitation is discussed in Section 8.9. When these covariates are not available, statistical models may adjust for proxies of some of these covariates as possible based on availability of suitable proxies; for example, by adjusting for concomitant cDMARD use and oral or injectable glucocorticoids, which are proxies of disease activity. RA severity will be adjusted using the Claims-Based Index for RA Severity (CIRAS) (Ting et al. 2008). In addition to disease severity, prior use of TNFi and smoking status will be included as potential confounding factors where possible. Because information on smoking is not typically available from administrative claims data, other approaches with limited sensitivity, but acceptable specificity and PPV for identifying smokers will be used (Desai et al. 2016). This will at least allow the direction of the potential impact of smoking on analytic results to be investigated.

In addition, quantitative bias analysis methods, as described in Section 8.7.9.3, will be considered to quantify the potential impact of unmeasured confounding by such factors as described in Section 8.7.10. Body mass index, in particular, is an established risk factor for VTE

(Stein et al. 2005; Allman-Farinelli 2011) and is typically not available from administrative claims data. The potential impact of unmeasured confounding by BMI on the relation between VTE and treatment with baricitinib will be assessed as described in Section 8.7.10. In particular, information on the distribution of BMI across treatment groups will be obtained from a review of medical records or charts in a random sample of patients from each treatment group and applied in the manner described, based on the availability of linkage between claims data patients and clinical information sources. Quantitative bias analysis will also be undertaken to evaluate the impact of RA severity and duration, as necessary to investigate their potential impact on results in claims data where this information is not available.

8.4. Data Sources

The study will be conducted using multiple data sources in several geographies (Table 5). In the US, data from administrative claims, RA registries, and Medicare will be included. In the EU, national healthcare data from France will be included, as will data from the Swedish registry of bDMARDs (and tsDMARDs) linked to claims data. Data from Japanese patients (e.g., the Japanese CorEvitas RA registry), will also be included. Details of these data sources are provided below, along with the relative size of each data source. The total exposures accrued over the study period will depend on the accuracy of market forecast estimates and may, in turn, affect the total number of events observed.

In each data source, information will be provided in the SAP on the ascertainment and validation of key variables including each outcome as well as TB requiring hospitalization and exposures at index date and within the prior 6 months; treatment duration for baricitinib and TNFi; BMI and smoking; and RA diagnosis, duration, and severity. In US data sources, when possible, the proportion of the baricitinib group without use of JAK inhibitors prior to cohort entry will be estimated. Tofacitinib has been available for several years in the US as a treatment for RA, and a portion of patients treated with baricitinib is expected to have received prior treatment with tofacitinib.

Table 5. Study Data Sources

Data Source	Type of Data
US Postmarketing Data	
Aetna	US administrative claims database
CorEvitas US RA Registry	US prospective registry of patients with RA; primary data collection with targeted collection of VTE, MACE, and serious infection: >40,000 patients with RA (Kremer 2016).
HealthCore Integrated Research Database (HIRD)	US administrative claims data from commercial health insurance billing; Anthem health insurance plan enrollees, approximately 15 million.
Humana Medical claims and pharmacy Data	US administrative claims database
IMS PharMetrics Plus (IQVIA real-world data adjudicated claims)	US administrative claims data from commercial health insurance billing, and other insurance types, (e.g., Medicare); Blue Cross Blue Shield health insurance plan enrollees; approximately 150 million.
Marketscan (IBM Watson)	US commercial health plan and Medicare Advantage members; approximately 50 million persons are enrolled annually.
Military Health System Data Repository (MDR)	Comprehensive medical care is recorded in the MDR, which is a continually updated longitudinal EMR database, capturing and integrating all health care events for the entire DoD network since 2000. Approximately 90,000 patients with RA were identified between 01 June 2018 and 31 July 2019.
Optum Clinformatics Data Mart	US administrative services only and fully insured healthcare plan; United Healthcare insurance plan enrollees; 10-25 million.
Private Source 20 or PS20 (HealthVerity)	US administrative claims, multiple health plans
European Postmarketing Data	
ARTIS (Anti-Rheumatic Therapy in Sweden)	Swedish Biologic Register – RA patients receiving treatment with bDMARDs, linked to other national healthcare data (Wadström et al. 2015).
Betriebskrankenkasse (BKK) [Germany]	The BKK sick fund includes healthcare claims data on more than 5 million German persons (6-8% of the government or statutory health insurance population [GKV]) who are representative, in terms of age and sex, of the larger GKV population. Over 88,000 persons had at least 1 ICD-10 code for RA (M05.xx-M06.xx) between 01 January 2016 and 31 December 2017.
Cegedim THIN (France)	The Health Improvement Network (THIN) is a large European database of fully anonymized and non-extrapolated electronic health records collected by physicians.
Clinical Practice Research Database (CPRD) [United Kingdom]	A UK-based primary care EMR database of anonymized patient medical records (Herrett et al. 2015).

Data Source	Type of Data
French national healthcare or Système National des Données de Santé (SNDS) data	Administrative claims data for over 66 million French people; data available from 2011; approximately 67 million (Bezin et al. 2017).
Japan Postmarketing Data	
CorEvitas Japan (Yamanaka et al. 2018)	Japanese prospective registry of RA patients; primary data collection with targeted collection of VTE, MACE, and serious infections; over 1500 patients with RA.
JMDC [Japan]	Administrative claims database (Nagai et al. 2020).

Abbreviations: CMS = Centers for Medicare and Medicaid Services; DoD = Department of Defense; EMR = electronic medical records; MACE = major adverse cardiovascular events; PY = person-years; RA = rheumatoid arthritis; TBD = to be determined; VTE = venous thromboembolism.

A partial list of the planned data sources for this study is provided below. Specific information on Aetna and Humana is not included, nor on the de-identified data provided through HealthVerity's PS20, but all are databases of US administrative claims, the first two from individual insurers, and all include typical information on medical and prescription claims. For each source included in the final analysis, deidentified patient-level data will be procured for regulatory use, as feasible, based on local laws and regulations.

Primary data sources

- **ARTIS:** The Swedish Biologics Register (Anti-Rheumatic Therapy in Sweden) is a registry of patients with rheumatologic diseases maintained by the Swedish Society for Rheumatology. Data in the register are used as a clinical decision-making tool for rheumatologists, who, together with the patient, enter the data. Despite the name including the term *biologics*, the register has confirmed that information will also be collected for patients receiving treatment with baricitinib. Data in the register are linked to various other registers through a unique personal identifier assigned to all Swedish residents. The National Patient Register provides information on diagnosis codes of outpatient visits in Swedish primary care since 2001. The Prescribed Drug Register is a nationwide public register with complete coverage of dispensing of prescribed drugs in Sweden, including quantity, dose, and date. The Total Population Register provides data on residency for all subjects who have ever resided in Sweden since 1961, and the Causes of Death Register is a national register that provides information on dates and causes of death for all deceased residents since 1961. ARTIS provides a high coverage and accuracy on bDMARD and tsDMARD exposures, including baricitinib, for patients with RA (Wadström et al. 2015).
- **Cegedim THIN (France):** The French division of The Health Improvement Network (THIN) is a large database of fully anonymized electronic health records collected by 2000 general practitioners and 1000 specialists. Patients included in this data are a subset of patients included in the French SNIIRAM (or SNDS) data. Therefore, while the data will be analyzed for this study, the French Cegedim data will not be included in the data analysis.

- **Clinical Practice Research Database:** CPRD is a UK-based primary care electronic medical records (EMR) database of anonymized patient medical records representative of the UK general population in terms of age, sex, and ethnicity (Herrett et al. 2015). Both CPRD GOLD and CPRD Aurum EMR datasets will be analyzed in this study. Together, these datasets include 596 unique UK general practices and 15.9 million unique patients (Ghosh 2018), representing approximately 23.8% of the UK population (WorldOMeters 2019). The CPRD includes information on demographics (including year of birth and sex), prescriptions and diagnoses. Dates of prescriptions and receipt of diagnoses are also available. As CPRD is a general practice EMR database, specialist hospital-generated prescription data have the potential to be missing. However, guidance from the British Medical Association (BMA) Medical Ethics Department advises all specialists to inform patients' general practitioner of the results of the investigations, the treatment provided, and other information necessary for the continuing care of the patient (BMA 2009). Therefore, a number of specialist prescriptions are expected to be entered into CPRD upon receipt of this report by the general practitioner.
- **CorEvitas RA registry:** CorEvitas is a US RA registry which collects data from patients and physicians at the time of a routine clinic visit. Clinically relevant information is collected on disease activity, including joint counts, visual analogue scales for physicians and patients, laboratory values and diagnostic tests, and radiographic outcomes. Patient demographic and lifestyle habits, including smoking, alcohol consumption, BMI, employment, insurance type and status, are routinely recorded. Medication start and stop dates and reasons for the start or switch are recorded by the treating physician. As of March 2019, CorEvitas has enrolled over 51,600 patients with RA from 769 different rheumatologists in 42 US states. Data from physician-patient encounters are confirmed by medical record review in order to confirm, validate, and adjudicate reports from physician-patient encounters (Kremer 2016).
- **CorEvitas Japan RA registry:** The CorEvitas Japan registry is patterned after the US CorEvitas RA registry but collects data from Japanese patients and physicians during routine clinic visits. Data are compatible across RA registries. Currently, CorEvitas Japan has enrolled over 1500 patients with RA from 54 sites.

Administrative claims databases

- **Betriebskrankenkasse (BKK):** Germany's multi-payer healthcare system consists of a combination of health data from Sick fund providers (statutory health insurance [SHI]), that is, "Gesetzliche Krankenversicherung (GKV)," and private health insurance. Health insurance is mandatory for all citizens and permanent residents since 2009 and approximately 90% of the German population are members of SHI, entitled to comprehensive benefits, including inpatient and outpatient care, physician services, and prescriptions drugs. All prescription drugs are included unless explicitly excluded or pending evaluation. BKK consolidates data from several sick fund providers and includes healthcare claims data on >5 million patients (6-8% of the German GKV population) who are representative, in terms of age and sex, to the larger GKV population. The data

includes information on patient demographics and inpatient and outpatient care as well as outpatient medical prescriptions. Available demographic information includes sex, age, insurance status, time insured, and region of residence. Inpatient and outpatient diagnoses are coded via International Classification of Disease, 10th Revision, German Modification (ICD-10-GM) codes and procedures are available. For outpatient diagnoses, only the quarter of the diagnosis is reported (i.e., the actual date is unavailable). Outpatient physician specialty information and inpatient medical department of care can be accessed. Medical prescriptions from retail pharmacies are coded using the ATC hierarchy, and the date of the prescription dispensing is available. Information on patient anthropometric data (e.g., height, weight, BMI) is not available nor are laboratory test results (e.g., absolute lymphocyte count, blood lipid levels) or clinical measurements (e.g., blood pressure).

- **French national healthcare data:** The SNIIRAM (Système National d'Informations Inter-Régimes de l'Assurance Maladie) or SNDS (Système National des Données de Santé) data cover 98.8% of the French population, over 66 million persons, from birth (or immigration) to death (or emigration). French healthcare provides universal coverage by one of several health care insurance plans, which contribute data to SNIIRAM. The SNIIRAM data are linked to the national hospital discharge database (programme de médicalisation des systèmes d'information [PMSI]), covering both public and private hospitals, and to the Death registry (CepiDC). At this time only date of death, and not cause of death, is linked to the other data. The anonymized database includes demographic data; healthcare encounters such as physician and paramedic visits, medicines, medical devices, and lab tests (no results); ICD-10 diagnostic codes, hospitalizations with ICD-10 codes for primary, linked and associated diagnoses, date and duration, procedures, diagnostic-related groups, and cost coding.
- **HealthCore Integrated Research Database℠ (HIRD)**: A large health care database maintained by HealthCore for use in health outcomes and pharmacoepidemiologic research. The HIRD includes longitudinal medical and pharmacy claims data from health plan members across the US. Member enrollment, medical care (professional and facility claims), outpatient prescription drug use, and health care utilization may be tracked for health plan members in the database dating back to January 2006, with diagnoses recorded in the ICD-10 since October 2015, with dispensing of self-administered medications recorded in the NDC and with medications administered at physician office, hospitals, and outpatient infusion centers recorded in CPT code/HCPCS code. The HealthCore Integrated Research Environment has the ability to link the claims data in the HIRD to complementary data sources, including inpatient and outpatient medical records.

- **IMS PharMetrics Plus:** The largest claims database of integrated medical claims in the US, comprised of adjudicated claims for more than 150 million unique enrollees across the US (Hunter et al. 2017). In 2011, enrollees with both medical and pharmacy coverage represent 40 million active lives. These administrative claims data have a diverse representation of geography with coverage of data from 90% of US hospitals and 80% of all US physicians, as well as representation from 85% of the Fortune 100 companies. In addition to inpatient and outpatient diagnoses and procedures and retail and mail-order prescription records, IMS Pharmetrics Plus also has detailed information on inpatient stays (admission type and source, discharge status) and provider details (specialty, provider identification). Data on enrollees in all 3-digit zip codes in the US are included. Records in this data source are broadly representative of the national commercially insured population in terms of age and gender for individuals 65 years and under. Data are also longitudinal, with approximately 20 million patients who have both medical and pharmacy coverage with 3 or more years of continuous enrollment (IMS Health 2013).
- **JMDC:** This database, using data collected from medical institutions in Japan, consists of claims (for hospitalization and outpatient treatment), diagnosis procedure combination (DPC) assessment forms, and clinical laboratory test values. The oldest data in this database that can be accessed relate to treatment in April 2014. At the end of October 2019, the number of medical institutions was 218, consisting of 131 DPC-eligible hospitals and 87 DPC-ineligible hospitals. This database includes not only data from DPC-eligible hospitals but also data from some DPC-ineligible hospitals (Nagai et al. 2020).
- **Military Health System Data Repository**: The Military Health System (MHS) is a comprehensive medical network within the US Department of Defense (DoD) that provides health care to all US military personnel, their dependents, and retirees. MHS operates the largest cradle-to-grave health care system in the US, with over 10 million patients actively receiving care on an annual basis. Patients enrolled in the MHS receive benefits through the TRICARE nationwide managed care program, which combines health care from DoD facilities with those from the private sector. Patients are not required to use military medical facilities, and many use their MHS coverage to obtain care in civilian facilities. Thirteen percent of the MHS population are active duty military, meaning that most enrollees are non-military. Males represent 51% of the population and the age distribution of patients in the MHS is similar to the US population. Comprehensive medical care is recorded in the Military Database Repository (MDR), which is a continually updated longitudinal EMR database, capturing and integrating all health care events for the entire DoD network since 2000. DoD's EMR system is linked to laboratory, pathology, and radiology orders and results for a subset of patients receiving care in military treatment facilities (15-20%). Currently, the MDR contains data on more than 10 million active beneficiaries receiving care at more than 65 hospitals and over 500 military clinics, as well as at private hospitals and clinics throughout the country.
- **Optum Clinformatics Data Mart:** This is an administrative health claims database with information from medical and pharmacy benefits coverage for members of a large national managed care company affiliated with Optum. The population is geographically

diverse, spanning all 50 states and including approximately 12 to 13 million annual covered lives with commercial health plan data and Medicare Advantage members. For each participant, the data contain demographic information, health plan enrollment status, inpatient and outpatient medical encounters, and drugs filled on an outpatient basis, including national drug code, quantity dispensed, and days' supply. The underlying information from the study database is geographically diverse and fairly representative of the US population.

- **IBM Watson Marketscan:** The IBM Watson Marketscan database contains healthcare claims-based information for enrollees in large employer-sponsored health insurance plans across the US. Commercial claims databases contain information on inpatient claims, outpatient claims, outpatient pharmacy claims, and plan enrollment. Information available for enrollees includes sex, age, starting and ending dates of enrollment, and diagnoses and performed procedures. During the period of this study, diagnosis information was indicated using International Classification of Diseases, Revision, Clinical Modification (ICD-10-CM) codes and, in the inpatient data, procedures performed were indicated using ICD-10-CM codes and the American Medical Association's CPT code sets.

Accrual of baricitinib users in the various data sources may be evaluated over the study period, as feasible. If the projected accrual of baricitinib-treated patients lags or uptake suggests that the data source will not support the planned analyses, the data source may be replaced and/or additional data sources added. If a data source is removed from the planned analyses, a summary will be provided. Selection of any additional data source(s) will be based on various metrics including timeliness, baricitinib uptake, and capacity for medical record retrieval.

8.5. Study Size

Naive sample size and statistical power estimates were obtained from standard formulas for time-to-event studies that are based on a minimum number of events being observed. 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 are required cumulatively, 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.

To account for heterogeneity in the true hazard ratio among data sources, a simulation study was performed to determine whether adjustment in the number of required events would be needed to maintain 80% power. In the simulation study, 10 data sources were assumed, with relative contributions to the total follow-up time as 20%, 20%, 15%, 10%, 10%, 5%, 5%, 5%, 5%, and 5%, in anticipation of the range of contributions from the data sources in Study B023. For each run of the simulation, a true hazard ratio and a true combined (across cohorts) incidence rate were assigned to each data source based on ranges of approximately 1.5 to 2.2 for the hazard ratio (from a uniform distribution on the log hazard ratio scale yielding a mean of 1.8) and 0.25 to 1.75 per 100 PY for the incidence rate. Using the same number of patients with events (90), power for a random effects meta-analysis was decreased 4% relative to a naive pooled analysis across data sources. Equalizing the power for the meta-analysis to the pooled analysis requires an

increase in the number of patients with events to approximately 107 as determined by simulation using 1:1 matching. With the planned 3:1 matching (3 TNFi users for each baricitinib user), simulations demonstrated that at least 80% power was achieved with 118 patients with events.

Based on a background incidence rate of 0.5 to 0.9 per 100 PY for VTE, it is anticipated that at least the required number of patients with events (118) will be observed in 6000 PY of exposure to baricitinib.

8.6. Data Management

Data will be managed according to the standard procedures required by Eli Lilly and Company ("Lilly") and the study partners with access to the health care data. Specifically, Lilly anticipates that this will include maintenance of analytic or study datasets and analytic programs on a secure server belonging to the data partner. Procedures for acquisition and abstraction of medical record data will be described in a separate medical record plan. Full details relating to data security and quality assurance procedures will be provided in the SAP.

8.6.1. Data Collection and Retention

There is no active enrollment or active follow-up of study subjects from any source, and data will not be collected directly from individuals for the explicit purpose of this study. Data sharing agreements will be maintained by the data owners and provided to those who analyze the data. Access, use, and disclosure of protected health information (PHI) in the US will be in compliance with the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule (45 Code of Federal Regulations [CFR] Part 160 and Subparts A and E of Part 164). No access, use, or disclosure of identifiable PHI will occur unless under a specific waiver of authorization (e.g., a HIPAA Waiver of Authorization from an Institutional Review Board [IRB]). Further, access of the data will be conducted in a manner that complies with federal and state laws and regulations, including those related to the privacy and security of individually identifiable health information. Datasets and analytic programs will be kept on a secure server and archived per record retention procedures.

Refer to Section 8.3 for information about data to be included in an analytic dataset.

8.6.1.1. Missing Data

Imputation will be considered only for variables that would be used to adjust for potential confounding ("adjusting variables") or for generating propensity scores. Imputation will not be used to account for missing information about exposure to DMARDs, including baricitinib, or about the safety outcomes of interest as this would not be appropriate for the main dependent and independent variables in the Cox regression models. If missing data for a covariate needed for the control of confounding exceed 15% of the cohort size, the pattern of missingness will be evaluated and imputation of the missing values for the adjusting variables will be considered before modelling the data. If imputation is deemed necessary, multiple imputation by chained equations (MICE) will be considered (van Buuren et al. 1999; Royston 2004). Other methods may be considered as needed.

8.7. Data Analysis

Analyses will be conducted separately for each outcome and will include descriptive analyses, comparative analyses, and any relevant sensitivity analyses. Propensity scores will be used to address imbalances in the potential confounding factors across the comparison groups that may confound the association between treatment and study outcomes. For all analyses, baricitinib will be the treatment of interest and the TNFi cohort will serve as the reference group.

8.7.1. Analysis Population

The analysis population for each outcome includes all adult patients present in the data who meet the eligibility criteria and are members of the treatment groups defined in Section 8.2.1. Patients in the main analyses will be either incident new users of JAK inhibitors with no use of baricitinib or tofacitinib during the washout window (Figure 1) or incident new users of a specific TNFi.

8.7.2. Background and Rationale for Propensity Scores

Drug exposure in pharmacoepidemiologic studies does not occur at random and is the result of patient-, physician-, and health care system-related factors. When these factors are also associated with the outcome of interest, comparisons of different drug-exposure cohorts may be confounded due to channeling bias. Propensity scores address the imbalance across drug-exposure cohorts by providing a mechanism to compare patients with concordant baseline risk, but discordant exposure (Schneeweiss 2007). For clarity, covariates included in the propensity-score models are also referred to as confounders because they confound the association between exposure and outcome.

8.7.3. Propensity Score Definition and Estimation

A propensity score is an estimate of the probability that a patient receives a particular treatment, conditional on measured characteristics at the time a treatment decision is made (Rosenbaum and Rubin 1983). For this study, a patient's propensity score will reflect the predicted probability of exposure to a medication given a patient's observed characteristics at the index date. Propensity scores will be estimated using a logistic regression model predicting the probability of baricitinib exposure compared with exposures in TNFi medication users. The models will include variables that are known risk factors for the outcomes of interest. Covariates considered for inclusion in the propensity-score models are provided in Table 4. The inclusion of interaction and nonlinear terms will be guided by clinical judgement, although an automated modeling procedure to build two-way interactions may be considered if these interactions are difficult to prespecify (Dehejia and Wahba 1999, 2002). These models may be constructed separately for each comparison (Section 7) if a common model including risk factors for each outcome of interest is insufficient to address differences across treatment groups. Evaluation of the propensity-score models is discussed in Section 8.7.5.

8.7.4. Using the Propensity Score to Address Channeling and Other Sources of Bias

Propensity score matching will be performed using an objective algorithm and will be discussed further in the SAP. The effectiveness of the match will be evaluated and the propensity-score model will be adjusted as appropriate to account for covariates that remain unbalanced after matching. More information on the evaluation of the propensity score is provided in Section 8.7.5. The propensity-score model and matching will be finalized before initiating any safety outcome analyses. If the number of matched patients is prohibitively small such that it would limit the ability to conduct a comparative analysis, other applications of the propensity score, such as changing the caliper permitted for matches, allowing matching with replacement, implementing variable ratio matching, or allowing full matching, may be considered.

Non-US Data: Patients with RA from regions outside of the US may be treated with baricitinib directly after cDMARD treatment, or they may switch to baricitinib therapy after a biologic such as a TNFi. Therefore, in European or Japanese data, the baricitinib-treated group will consist of a mixture of TNFi-naïve and TNFi-experienced patients with varying proportions. To accommodate this composition of the baricitinib-treated group, the propensity score models used for matching patients may include a covariate to indicate TNFi-naïve status. Other relevant potential confounding factors will also be included, as they are for the propensity scores models in US data. Alternatively, if propensity-score matching does not adequately balance TNFi-naïve status across treatment groups, additional measures may be taken such as including this status in the Cox model or following the approach used for US data (i.e., restriction of the TNFi group to TNFi-experienced patients and addition of a sensitivity analysis, if warranted, that restricts the entire study population to the same baseline TNFi status). Additional details for this analysis will be included in the statistical analysis plan.

8.7.5. Evaluation of the Propensity-Score Model and Stratification

Before initiating any outcome analyses, the ability of the propensity-score matching to balance the distribution of baseline confounders and reduce channeling bias will be evaluated. The appropriateness of the propensity-score modeling is judged on whether balance on pretreatment characteristics is achieved between the treatment and reference groups (D'Agostino and D'Agostino 2007; Rubin 2007; Spreeuwenberg et al. 2010). Standardized differences and variance ratios will be used to assess differences between the cohorts across all measured baseline covariates before and after propensity score matching. As a general rule, standardized differences greater than 0.10 indicate an imbalance that may require further investigation (Austin and Mamdani 2006; Austin 2011). A variance ratio of 1 in a matched sample indicates good matching, but a variance ratio below 2 is generally acceptable (Zhang et al. 2019). Higher-level terms or interactions may be considered when a variable is unbalanced across the baricitinib and reference cohorts or when informed by clinical judgement (e.g., an interaction between age and sex for MACE outcomes).

8.7.6. Evaluation of Potential Channeling Bias

After adjustment for basic covariates of age and sex, treatment groups will be compared with regard to their risk of VTE *prior to* initiating study drug. This VTE risk will be assessed at 3, 6, and 12 months prior to initiating study drug (i.e., cohort entry), as possible, based on the availability of data and VTE events. A large difference in risk at baseline may suggest the presence of channeling bias. This would warrant closer examination of the ability of the propensity score matching method to adjust for differences in the characteristics of the populations being compared. An alternative approach would be to conduct the full propensity score-matched analysis after excluding the baseline VTE variable indicating events prior to cohort entry from the propensity score model, then compare VTE results from the regression. Even if differences in covariates and risk factors for VTE suggesting channeling are observed, a comparative analysis that adjusts for this imbalance beyond 1:3 propensity score matching may nonetheless be executed. These limitations would be described in the study report but would initially lead to a more detailed evaluation of unmeasured confounders such as BMI that are typically not available in administrative claims data.

This evaluation will also be conducted for secondary outcomes, except tuberculosis.

8.7.7. Main Statistical Analyses

Separate time-to-event analyses based on Cox proportion hazards regression will be performed for both primary and secondary outcomes. These analyses will include only patients initiating treatment, that is, “new users” of medications (baricitinib or a specific TNFi) and will be based on aggregate baricitinib doses (2 mg and 4 mg).

The following exclusion criteria will apply to all patients in main analyses:

1. Use of a JAK inhibitor during the 6 months prior to cohort entry.
2. Concomitant use of more than 1 advanced therapy to treat RA, i.e., dispensing of any combination of 2 or more bDMARDs and/or tsDMARDs at the time of cohort entry.
3. Patients with evidence of the outcome of interest (VTE, MACE, or serious infection, hospitalized TB respectively) in the 6 months prior to cohort entry.

For VTE and MACE analyses, the following exclusion criterion will also apply:

4. Use of an anticoagulant at the time of cohort entry. In claims data, this will be defined as having evidence of dispensing of an anticoagulant on the date of cohort entry or exposure to an anticoagulant (i.e., day’s supply) that overlaps the date of cohort entry. This will exclude patients who are not at risk of or at substantially reduced risk of the primary outcome.

Before beginning comparative analyses, a number of descriptive statistics and crude rates will be generated to understand the registry data:

- baseline demographic and clinical characteristics and standardized differences for the TNFi cohort and baricitinib cohort (all patients, matched patients, and unmatched patients)

- prevalence of the outcomes at baseline
- distribution of follow-up time for the TNFi and baricitinib cohorts (all patients, matched patients, and unmatched patients)
- distribution of baseline demographic and clinical characteristics and standardized differences for matched patients in the TNFi and baricitinib cohorts by exposure duration
- the number of new medication starts for matched patients within the TNFi and baricitinib cohort

Investigation of TB requiring hospitalization will be limited to the above analyses, based on the limited number of events expected.

Comparative analyses will be implemented using propensity-score matching to control for confounding. Model diagnostics will be performed to identify any influential observations. Sensitivity analyses will be performed accordingly. No comparative analyses will begin until finalization of the exposure cohorts and propensity-score models is achieved. Details of outcome-specific analyses are presented below. Proportional hazards of the exposure groups will be evaluated using Kaplan–Meier survival curves. If the proportional hazards assumption is violated, other models that relax the proportional hazards assumption will be considered.

8.7.7.1. Venous Thromboembolic Events

The outcome for this analysis is incident VTE (Section 8.3.2.1). Because of the recognized risk of VTEs associated with methotrexate (Methotrexate package insert, 2016), concomitant treatment with methotrexate will be evaluated by treatment group and whether inclusion of a covariate leads to any change in the final measure of association. Patients with prior evidence of a VTE will be eligible for this study, but only the first VTE during the follow-up period will be eligible for inclusion. Overall, analyses will focus on the comparative risk of VTEs among RA patients treated with baricitinib versus those treated with TNFi.

In addition to the descriptive statistics and crude rates described in Section 8.7.7, analyses for VTEs will include the following:

- Pattern of RA medication use, including drug switching and dosing, after cohort entry for the baricitinib and TNFi cohorts (all patients, matched patients, and unmatched patients). The use of methotrexate will also be described over the study period, to investigate whether there are any major differences in usage, by treatment.
- Distribution of survival time until first VTE for the TNFi and baricitinib cohorts (all patients, matched patients, and unmatched patients)
- Crude rate of first VTE for the TNFi and baricitinib cohorts (all patients, matched patients, and unmatched patients) and within cohorts of matched patients, stratified by concomitant methotrexate use

Propensity scores will be used to match patients from different exposure cohorts as described in Section 8.7.4. Cox proportional hazards regression will be used to compare risk of VTE between the baricitinib and TNFi cohorts. All models will include the exposure cohort and any variables

that remain unbalanced after propensity-score matching. Models may also include concomitant cDMARD or glucocorticoid use separately, as needed, based on whether inclusion leads to ≥10% change in the resulting estimate or hazard ratio.

8.7.7.2. Major Adverse Cardiovascular Events

The outcome for this analysis is all incident MACE (Section 8.3.2.3). Because of the potential cardioprotective effect of methotrexate (Marks and Edwards 2012), comparative analyses for MACE may include a covariate to indicate concomitant treatment with methotrexate.

In addition to the descriptive statistics and crude rates described in Section 8.7.7, analyses for MACE will include the following:

- Pattern of medication use, including drug switching and dosing, post-index date for the baricitinib and TNFi cohorts (all patients, matched patients, and unmatched patients)
- Distribution of survival time until first MACE for the TNFi and baricitinib cohorts (all patients, matched patients, and unmatched patients)
- Crude rate of first MACE as a component outcome and by individual event for the TNFi and the baricitinib cohorts (all patients, matched patients, and unmatched patients) and within cohorts of matched patients, stratified by concomitant methotrexate use.

Propensity scores will be used to match patients from different exposure cohorts as described in Section 8.7.4. Cox proportional hazards regression will be used to compare risk of MACE between the baricitinib and TNFi cohorts. All models will include the exposure cohort, any variables that remain unbalanced after propensity-score matching, and may include concomitant cDMARD use, as needed based on impact on results.

8.7.7.3. Serious Infections

The outcome of interest in this analysis is first serious infection as defined in Section 8.3.2.4.

In addition to the descriptive statistics and crude rates described in Section 8.7.7, analyses of serious infections will include:

- Pattern of medication use, including drug switching and dosing, after cohort entry for the baricitinib and TNFi cohorts (all patients, matched patients, and unmatched patients)
- Distribution of survival time until first serious infection for the baricitinib and TNFi cohort (all patients, matched patients, and unmatched patients)
- Crude rate of first serious infection for the TNFi and baricitinib cohorts (all patients, matched patients, and unmatched patients)
- The distribution of the number of serious infections per patient
- The incidence of serious infections prior to use of baricitinib and after commencing baricitinib treatment

Any patient with an existing serious infection at baseline will be excluded from all analyses, including baseline descriptive statistics, crude rates, and comparative analyses. Propensity scores will be used to match patients across different exposure cohorts as described in Section 8.7.4. Cox proportional hazards regression will be used to compare risk of first serious infection

between the baricitinib and TNFi cohorts. All models will include the exposure cohort and any variables that remain unbalanced after propensity-score matching.

8.7.7.4. Tuberculosis

The outcome of interest in this descriptive analysis is hospitalized TB as defined in Section 8.3.2.5. Analyses of hospitalized TB will include:

- Pattern of medication use, including drug switching and dosing, post index date for the baricitinib and TNFi cohorts
- Distribution of survival time until first TB hospitalization for the baricitinib and TNFi cohorts
- Crude and standardized (to the TNFi cohort) rate of first TB event for the baricitinib and TNFi cohorts
- The distribution of the number of TB hospitalizations per patient
- The incidence of hospitalized TB prior to baricitinib use and after commencing baricitinib treatment.

If sufficient events of hospitalized TB are observed across data sources to allow detecting an effect as small as a relative risk of 3.0 with at least 80% power, a comparative analysis will be conducted. If necessary, events and person-years of follow-up may be aggregated across data sources to estimate a Cochran-Mantel-Haenszel risk ratio. Such an aggregation will only be attempted if the number of events in each data source is greater than the limit for disclosure set for that data source owner, e.g., HealthCore does not permit disclosure of counts less than 10, simply an indication '≤10'.

8.7.8. Meta-analysis

Results of comparative analyses for each safety outcome from each individual data source will be combined through a random-effects meta-analysis. Hazard ratios generated from comparative analyses for each safety outcome, from each individual data source, will be combined through a random-effects meta-analysis using the DerSimonian-Laird method. Combining via meta-analysis will permit a more precise estimate of the effect size related to baricitinib exposure than is available from analyses of individual data sources. This approach simultaneously accounts for differences that may be present in the distinct population samples from each data source, such as age, a recognized risk factor for VTE. In cases where zero events are observed in any treatment group in any of the individual data sources, Poisson regression will also be used for the meta-analysis. Additional details of this analysis will be described in the statistical analysis plan.

The random-effects approach assumes that the individual analyses do not estimate a single true effect, but rather that the true effects follow a distribution. The pooled estimate represents the average of the effects and the uncertainty surrounding its location is reflected in the confidence interval. The presence of statistical heterogeneity will be assessed using the standard Cochran χ^2 test, and the magnitude of any heterogeneity will be evaluated using the I-squared statistic (Higgins et al. 2003).

Supplemental analyses based on meta-regression (Baker et al. 2009) or meta-analysis by region (US vs OUS), data source (registry vs. non-registry), or age may be conducted as feasible, based on the number of data sources, to evaluate the heterogeneity of effects.

8.7.9. Sensitivity Analyses

Sensitivity analyses will be performed to examine the impact of assumptions on study results. These analyses will be conducted across a select few data sources, with priority given to the largest data sources where access to the full data is available (e.g., IBM Watson Marketscan). Further details are presented below by outcome.

The following exclusion criterion will apply to all patients in sensitivity analyses described in Sections 8.7.9.1 through 8.7.9.7, with the exception of 8.7.9.2:

1. Use of a JAK inhibitor during the 6 months prior to cohort entry.

The following exclusion criteria will apply to all patients in sensitivity analyses described in Sections 8.7.9.1 through 8.7.9.7:

2. Use of an anticoagulant at the time of cohort entry. In claims data, this will be defined as having evidence of dispensing of an anticoagulant on the date of cohort entry or exposure to an anticoagulant (i.e., day's supply) that overlaps the date of cohort entry. This will exclude patients who are not at risk of or at substantially reduced risk of the primary outcome.
3. Concomitant use of more than one advanced therapy to treat RA, i.e., dispensing of any combination of 2 or more bDMARDs and/or tsDMARDs at the time of cohort entry.
4. Patients with evidence of the outcome of interest (VTE, MACE, or serious infection, respectively) in the 6 months prior to cohort entry.
5. US data: If more than 5% of baricitinib-treated patients appear to be TNFi-naïve based on exposure in the baseline period, a sensitivity analysis will be conducted that will restrict analyses to those patients with prior treatment with ≥1 TNFi. This will apply equally to patients treated with either baricitinib or TNFi.

8.7.9.1. Venous Thromboembolic Events: Alternate Case Definitions

Analyses will be conducted to evaluate secondary definitions of VTE, as defined in Section 8.3.2.1. Analyses will proceed as described in Section 8.7.7.1.

Executing these analyses will provide a more thorough understanding of the risk of VTE associated with baricitinib versus TNFi treatment by providing results across varying sensitivity, specificity, and PPV of the case definition.

8.7.9.2. Venous Thromboembolic Events: Including Patients with Prior Tofacitinib Exposure

Sensitivity analyses of VTE will be conducted based on removing the exclusion criterion of prior tofacitinib use. Thus, all patients treated with baricitinib or TNFi will be included, regardless of their prior use of tofacitinib. Analyses will proceed as described in Section 8.7.7.1.

Executing these analyses will permit comparison of results with the restricted population used in the main analysis. Comparison of results between analyses that exclude and include prior use of tofacitinib will be informative about the potential 'depletion of susceptibles' prior to initiation of baricitinib therapy. If there is no difference between these analyses, this sensitivity analysis should have additional statistical power to detect a difference in risk of VTE, should one truly exist, between patients treated with baricitinib and those treated with TNFi.

8.7.9.3. Venous Thromboembolic Events: Descriptive Analysis by Dose

Where feasible, based on having sufficient events (≥1 event), a descriptive analysis will estimate the incidence rate of VTE by dose of baricitinib. Patient demographics and risk factors for VTE will also be reported for both dose groups. If sufficient numbers or exposures are available to permit analysis of each dose group, a restricted analysis with only the 4-mg dose may be considered. This analysis will only be executed in data sources from regions where both doses of baricitinib are available and may be omitted in any or all data sources if fewer than 5% of patients are represented or fewer than 50 patients total are included in one dose group.

8.7.9.4. Potential Class Effects of JAK Inhibitor Medications

An analysis will be conducted to evaluate potential class effects of JAK inhibitors by comparing patients treated with tofacitinib or baricitinib with those treated with TNFi with respect to their risk of VTE. Analyses will proceed as described in Sections 8.7.7.1 and 8.7.7.2.

8.7.9.5. Analyses in OUS data stratified by bDMARD Naïve/experienced Status

Analyses described in Section 8.7.7 specifically descriptive characteristics and comparative Cox regression analyses will be stratified by bDMARD-naïve or bDMARD-experienced status in OUS data sources. These analyses are expected to be underpowered and event counts may be too limited in some cases to support analysis by Cox regression. If that occurs, differences in incidence rates will be reported.

8.7.9.6. Quantitative Bias Analysis

This analysis will aim to estimate the direction, magnitude, and uncertainty in the study results that may arise due to systematic errors in the measurement or ascertainment of exposures (Lash et al. 2014). Specifically, the potential impact on study results of covariates such as BMI and smoking that are not available or that may be poorly captured in claims data will be assessed through this method. These analyses will focus specifically on the potential impact to evaluating risk of VTE associated with RA therapy (baricitinib vs TNFi).

8.7.9.7. Random Effects Meta-analysis

In addition to pooling the hazard ratios from each analysis, a random effects meta-analysis will be fit that combines the VTE event counts and person-years of exposure estimates from each data source. Results from a previously described simulation study showed that this method yields reasonable power and bias. In cases where zero events are observed for one or more of the analyses of the individual data sources, events and person-time from data sources with similar geographic and demographic characteristics may be pooled.

8.7.10. Addressing Unmeasured Confounding

An underlying assumption for all analyses presented in this protocol is the absence of unmeasured confounding. Unmeasured confounding can bias results from any data source but may be of particular concern for administrative claims data and other data collected for purposes other than the study under investigation. Typically, administrative claims data do not include information on potential confounding factors related to demographic and lifestyle factors, over-the-counter medication use, or measures of disease activity. In the present study, unmeasured confounding by BMI, an established risk factor for VTE (Allman-Farinelli 2011), is a concern. Some authors have also reported smoking as a risk factor for VTE (Cheng et al. 2013; Zhang et al. 2014). To address these concerns, information on BMI and smoking status will be abstracted from medical charts for a random sample of patients. Information will be abstracted from patients who meet the eligibility criteria for the study.

After propensity score-matching and abstracting BMI (or smoking status), patients will be compared across treatment cohorts with regard to BMI distribution to evaluate differences in BMI distribution. If meaningful differences between groups exist, several methods exist to address unmeasured confounding (Zhang et al. 2018; Schneeweiss et al. 2005), although only a limited selection permit an adjusted estimate of the relative risk to be computed. Methods such as propensity score calibration (Stürmer et al. 2005) or other methods such as Bayesian twin regression (Faries et.al. 2013; Zhang et.al. 2016) may be used to calculate an unbiased estimate of the true treatment effect.

8.8. Quality Control

The specific details of quality control activities and procedures will likely differ for each data source and will be described separately as an addendum to this protocol. Regardless, in general, the research team will document the progress and scientific and quality review of all study activities and deliverables (e.g., protocol, data management, data analysis, reports, manuscripts, etc.). This documentation will record the major study tasks related to a specific study activity performed by the vendor to develop and execute the requirements of the protocol. Quality assurance measures performed for each study activity during the conduct of the study will also be recorded. This is necessary to ensure that such communications are appropriately documented, that the most up-to-date versions of relevant documents are readily identifiable, and that affected documents are clearly tracked.

All programming required for study database extraction and creation of the analytic datasets will follow acceptable programming standards as agreed by Lilly and the vendor. Typically, the programming standards are a set of documents describing data extraction methods and provide a guideline for basic, frequently used terms and definitions and respective coding information to maintain operational consistency. Data validation will occur throughout the data management and analysis process. Data quality checks should typically include, but would not be limited to, programming checks by an individual who is not a main programmer for the study, internal dataset consistency, and checks to ensure that protocol criteria were met. If validation checks are not satisfied then an examination of the problem is performed on the dataset(s) until the problem

resolved. All data validation, quality checks, and resolution of issues identified and resolved would be documented.

For chart validation of the case definition, the vendor is typically trained on the study-specific process for extracted data, as would also have been agreed by the IRB. A pilot phase for the chart data extraction is desirable, where a sample of e.g., 5 to 10 charts is reviewed to ensure that data collection is being conducted appropriately. Retraining would be conducted if a problem in data acquisition was identified as a result of study personnel/abstractors. Medical chart abstraction would be conducted by individuals with clinical training, with regular quality checks of the data and potentially assessments of the clinical data by clinical consultants with expertise in rheumatology. The clinical data obtained from chart abstraction would then be integrated with the administrative claims data, with quality checks conducted to ensure all variables for analysis were correctly included.

Additional details of the quality control process for data collection, analysis, and reporting will be provided in the separate medical record plan.

8.9. Limitations of the Research Methods

The current study will rely on data from several large US and non-US sources to evaluate the comparative safety of patients with RA treated with baricitinib relative to treatment with TNFi, which represents the standard of care. Since RA registries were designed to collect data directly from patients and physicians, they offer clinically more accurate data that can be used to control for important potential differences in the baricitinib and TNFi cohorts being compared in this study (e.g., disease severity or duration, lifestyle factors, and BMI). Outcomes are sometimes adjudicated as part of data collection, often by rheumatologists, so confidence is high with regard to endpoints. In contrast, administrative claims data contain information on millions of patients, including those with RA, and reflect routine clinical practice with medications prescribed at doses and combinations reflecting actual use in diverse clinics and patient populations. These data are not subject to recall bias, include patients who might not otherwise be available or choose to participate in clinical trials, and can be readily used to investigate potential safety signals. Important limitations exist for claims data, however, related to lack of detailed clinical and other information for adjustment or matching and the uncertain diagnostic validity of outcomes identified through billing codes. Because prescription records simply record dispensing, these data do not confirm patient exposure to medications. This is addressed in part by ensuring that exposures are defined based on more than one prescription record. Limitations regarding the outcomes 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. Such linkage can also help address unmeasured confounding by providing insight into the importance of a potential confounder, absent from the main data, and then allowing adjustment of the overall analysis to correct for the unmeasured cofounder.

Although many patients included in this study will come from registries, the majority will come from administrative claims data. Some steps will be taken to address the potential limitations inherent in these data; these steps are described in Sections 8.9.1 and 8.9.2 below.

8.9.1. Assessing Loss to Follow-Up, Adverse Events, and Death

During the course of the observational period, it is expected that some patients will be lost to follow-up as a result of disenrollment from the health plan. This is more of a concern in US claims data than in Europe where national health plans ensure that people retain health insurance even if they move unless they emigrate. In US claims data, therefore, although an outcome may be missed as a result of a 'drop out,' it is expected that this would occur at random (e.g., change in employment) and would not be associated with exposure status. Linkage to the US National Death Index may also be sought for patients disenrolled from US health plans to capture disenrollment that occurs as a result of death and the cause of death for these patients, who typically represent a minority of all those who disenroll. Outside of the US, access to vital status and cause of death may also be evaluated and pursued as feasible.

8.9.2. Generalizability of the Study Results

Patients included in this study are represented in different databases with both primary and secondary data collection formats and their data was collected in different healthcare settings.

The claims databases in this study includes longitudinal medical and pharmacy claims data from a large number of health plan members across the US. Patients with RA included in the study include patients receiving RA care from rheumatologists and from other specialists (e.g., family practice). Study data also include patients located in geographic areas with limited access to specialty care. As a result, the findings will complement those from analyses of the CorEvitas Registry that consist mainly of patients under rheumatologist care. Patients included from the US may not necessarily represent all adults with RA in the US, while in some geographies the entire national representation of RA patients (France) or RA patients treated with biologic medications (Sweden) will be included. Although enrollment in commercial US health plans that contribute information to this study is employment-based, patients enrolled in Medicare will also be included. Patients in commercial US data may tend to include healthier individuals who are able to remain in the workforce, but this will represent only a fraction of the total patients evaluated. In addition, owing to the current availability of only the 2-mg dose of baricitinib in the US, results of this study may not generalize to patients with RA treated with the 4-mg dose, as in the EU. However, inclusion of European patients treated with the 4-mg tablet will provide good insight into the safety of this group.

The combined population coverage of the data sources evaluated should help ensure that any results from this study apply to a large portion, if not the majority, of patients with RA. Examination of baseline characteristics and comparison with other data sources containing patients with RA may help to clarify the extent to which results from the study have external validity. Regardless, findings from this study are expected to have internal validity and provide valuable information about the safety profile of baricitinib with regard to the primary (VTE) and secondary (MACE, incident serious infection, hospitalized TB) outcomes.

9. Protection of Human Subjects

The current study applies epidemiologic research methodologies to medical and pharmacy claims data from a large insured population in the US and other geographies and to data from RA disease and biologic medication registries, also in the US and other geographies. The study is retrospective, analyzing data from patient encounters that have already occurred.

In order to validate the occurrence of cases identified from the claims data, PHI must be accessed from medical records. Medical records will also be obtained to confirm the occurrence of select outcomes. A Health Insurance Portability and Accountability Act (HIPAA) Waiver of Authorization will be submitted prior to any PHI being identified. Approval from the IRB will be sought for this work.

As described earlier in Section 8.6.1, there is no active enrollment or active follow-up of study subjects, and no data are collected directly from individuals. Data sharing agreements and other agreements will be pursued as required, with all covered entities who provide data to the coordinating vendor or vendor analyzing this work. Access, use, and disclosure of PHI will be in compliance with the HIPAA Privacy Rule (45 CFR Part 160 and Subparts A and E of Part 164). Identifiable PHI will not be accessed, used, or disclosed unless under a specific waiver of authorization (e.g., a HIPAA Waiver of Authorization from an IRB). Data will be accessed in a manner that complies with regional and local laws and regulations, including any related to the privacy and security of individually identifiable health information.

At no time during the conduct of this study will information identifying patients or providers be provided to the Sponsor. Deidentified aggregated results will be reported to the Sponsor and the Sponsor will not attempt to reidentify any patients or provider from aggregate data provided for the study.

Observational studies will be submitted to ethical review boards (ERBs) for approval whenever required by local law. Progress reports will be submitted to ERBs and regulatory authorities as required by local laws and regulations.

This study will be conducted in accordance with applicable laws and regulations of the region, country, or countries where the study is being conducted, as appropriate.

Specific details pertaining to individual data sources will be updated in an Addendum to this protocol prior to completion of a final version.

10. Management and Reporting of Adverse Events/Adverse Reactions

10.1. Secondary Data Collection Study

This is a noninterventional study based on secondary data use, and therefore no Individual Case Safety Report (ICSR) reporting is required. The study protocol-defined AEs include those listed in Section 8.3.2. All protocol-defined AEs collected will be summarized in the final study report. No other AEs will be collected.

Management and Reporting of AEs and adverse drug reactions for the US CorEvitas registry are governed by the protocol for Study I4V-MC-B003.

11. Plans for Disseminating and Communicating Study Results

11.1. EU Post-Authorization Study Register

This study will be registered on the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) EU post-authorization study (PAS) register following finalization of the protocol. Any substantial amendments to the study protocol or to the planned progress reports, as well as the final study report will also be entered in the register.

11.2. Progress Reports and Interim Analysis Report

To monitor patient accrual, the data sources may be assessed on an ongoing basis during the study period, as feasible. No interim report is planned given the short duration of the study.

11.3. Peer-Reviewed Publications

The final report of the study results will be submitted as described in Section 6. Additionally, the study findings may be presented at a scientific congress and/or submitted to a peer-reviewed journal.

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Annex 1. VTE Codes and Medications for Main and Alternate Analyses

Note: Final lists of codes for all events will be included in the statistical analysis plan. In the event of any differences in the codes listed, the list in the statistical analysis plan will be the official listing.

ICD-10 (PE)	
I26.0	Pulmonary embolism with acute cor pulmonale
I26.02	Saddle embolus of pulmonary artery with acute cor pulmonale
I26.09	Other pulmonary embolism with acute cor pulmonale
I26.9	Pulmonary embolism without acute cor pulmonale
I26.92	Saddle embolus of pulmonary artery without acute cor pulmonale
I26.99	Other pulmonary embolism without acute cor pulmonale
ICD-10 (DVT lower extremities)	
I82.401	Acute embolism and thrombosis of unspecified deep veins of right lower extremity
I82.402	Acute embolism and thrombosis of unspecified deep veins of left lower extremity
I82.403	…… bilateral
I82.409	Acute embolism and thrombosis of unspecified deep veins of unspecified lower extremity
I82.411	Acute embolism and thrombosis of right femoral vein
I82.412	Acute embolism and thrombosis of left femoral vein
I82.413	…… bilateral
I82.419	Acute embolism and thrombosis of unspecified femoral vein
I82.421	Acute embolism and thrombosis of right iliac vein
I82.422	Acute embolism and thrombosis of left iliac vein
I82.423	…… bilateral
I82.429	Acute embolism and thrombosis of unspecified iliac vein
I82.4y1	Acute embolism and thrombosis of unspecified deep veins of right proximal lower extremity
I82.4y2	Acute embolism and thrombosis of unspecified deep veins of left proximal lower extremity
I82.4y3	…… bilateral
I82.4y9	Acute embolism and thrombosis of unspecified deep veins of unspecified proximal lower extremity
I82.491	Acute embolism and thrombosis of other specified deep vein of right lower extremity
I82.492	Acute embolism and thrombosis of other specified deep vein of left lower extremity
I82.493	…… bilateral
I82.499	Acute embolism and thrombosis of other specified deep vein of unspecified lower extremity
I82.431	Acute embolism and thrombosis of right popliteal vein
I82.432	Acute embolism and thrombosis of left popliteal vein
I82.433	…… bilateral
I82.439	Acute embolism and thrombosis of unspecified popliteal vein
I82.441	Acute embolism and thrombosis of right tibial vein

I82.442	Acute embolism and thrombosis of left tibial vein
I82.443	…… bilateral
I82.449	Acute embolism and thrombosis of unspecified tibial vein
I82.4z1	Acute embolism and thrombosis of unspecified deep veins of right distal lower extremity
I82.4z2	Acute embolism and thrombosis of unspecified deep veins of left distal lower extremity
I82.4z3	…… bilateral
I82.4z9	Acute embolism and thrombosis of unspecified deep veins of unspecified distal lower extremity
ICD-10 (DVT upper extremities)	
I82.621	Acute embolism and thrombosis of deep veins of right upper extremity
I82.622	Acute embolism and thrombosis of deep veins of left upper extremity
I82.623	…… bilateral
I82.629	Acute embolism and thrombosis of deep veins of unspecified upper extremity
I82.601	Acute embolism and thrombosis of unspecified veins of right upper extremity
I82.602	Acute embolism and thrombosis of unspecified veins of left upper extremity
I82.603	…… bilateral
I82.609	Acute embolism and thrombosis of unspecified veins of unspecified upper extremity
I82.a11	Acute embolism and thrombosis of right axillary vein
I82.a12	Acute embolism and thrombosis of left axillary vein
I82.a13	…… bilateral
I82.a19	Acute embolism and thrombosis of unspecified axillary vein
I82.c11	Acute embolism and thrombosis of right internal jugular vein
I82.c12	Acute embolism and thrombosis of left internal jugular vein
I82.c13	…… bilateral
I82.c19	Acute embolism and thrombosis of unspecified internal jugular vein
I82.210	Acute embolism and thrombosis of superior vena cava
I82.290	Acute embolism and thrombosis of other thoracic veins
ICD-10 (Phlebitis and thrombophlebitis of lower extremity)	
I80.10	Phlebitis and thrombophlebitis of unspecified femoral vein
I80.11	Phlebitis and thrombophlebitis of right femoral vein
I80.12	Phlebitis and thrombophlebitis of left femoral vein
I80.13	…… bilateral
I80.201	Phlebitis and thrombophlebitis of unspecified deep vessels of right lower extremity
I80.202	Phlebitis and thrombophlebitis of unspecified deep vessels of left lower extremity
I80.203	…… bilateral
I80.209	Phlebitis and thrombophlebitis of unspecified deep vessels of unspecified lower extremity
I80.291	Phlebitis and thrombophlebitis of other deep vessels of right lower extremity
I80.292	Phlebitis and thrombophlebitis of other deep vessels of left lower extremity
I80.293	Phlebitis and thrombophlebitis of other deep vessels of lower extremity, bilateral
I80.299	Phlebitis and thrombophlebitis of other deep vessels of unspecified lower extremity
I80.3	Phlebitis and thrombophlebitis of lower extremities, unspecified

I80.211	Phlebitis and thrombophlebitis of right iliac vein
I80.212	Phlebitis and thrombophlebitis of left iliac vein
I80.213	…… bilateral
I80.219	Phlebitis and thrombophlebitis of unspecified iliac vein
I80.221	Phlebitis and thrombophlebitis of right popliteal vein
I80.222	Phlebitis and thrombophlebitis of left popliteal vein
I80.223	…… bilateral
I80.229	Phlebitis and thrombophlebitis of unspecified popliteal vein
I80.231	Phlebitis and thrombophlebitis of right tibial vein
I80.232	Phlebitis and thrombophlebitis of left tibial vein
I80.233	…… bilateral
I80.239	Phlebitis and thrombophlebitis of unspecified tibial vein
ICD-10 (Other venous thrombosis)	
I80.8	Phlebitis and thrombophlebitis of other sites
I80.9	Phlebitis and thrombophlebitis of unspecified site
I81	Portal vein thrombosis
I82.0	Budd-Chiari syndrome
I82.1	Thrombophlebitis migrans
I82.220	Acute embolism and thrombosis of inferior vena cava
I82.3	Embolism and thrombosis of renal vein
I82.890	Acute embolism and thrombosis of other specified veins
I82.90	Acute embolism and thrombosis of unspecified vein
I82.b11	Acute embolism and thrombosis of right subclavian vein
I82.b12	Acute embolism and thrombosis of left subclavian vein
I82.b13	…… bilateral
I82.b19	Acute embolism and thrombosis of unspecified subclavian vein

Anticoagulants

Code Type	Code	Drug
ATC	B01AA03	Warfarin
ATC	B01AA04	Phenprocoumon
ATC	B01AA07	Acenocoumarol
ATC	B01AB02	Antithrombin III
ATC	B01AB04	Dalteparin
ATC	B01AB05	Enoxaparin
ATC	B01AB09	Danaparoid
ATC	B01AB10	Tinzaparin
ATC	B01AE05	Ximelagatran
ATC	B01AE07	Dabigatran etexilate
ATC	B01AF01	Rivaroxaban
ATC	B01AX05	Fondaparinux

NDC Codes

NDC	Brand Name	Generic Name
00003089321	Eliquis	APIXABAN
00003089331	Eliquis	APIXABAN
00003089421	Eliquis	APIXABAN
00003089470	Eliquis	APIXABAN
00003089431	Eliquis	APIXABAN
00597013554	Pradaxa	DABIGATRAN ETEXILATE MESYLATE
00597013560	Pradaxa	DABIGATRAN ETEXILATE MESYLATE
21695089960	Pradaxa	DABIGATRAN ETEXILATE MESYLATE
00597010860	Pradaxa	DABIGATRAN ETEXILATE MESYLATE
00597014954	Pradaxa	DABIGATRAN ETEXILATE MESYLATE
00597014960	Pradaxa	DABIGATRAN ETEXILATE MESYLATE
00597010754	Pradaxa	DABIGATRAN ETEXILATE MESYLATE
54569627600	Pradaxa	DABIGATRAN ETEXILATE MESYLATE
00597010760	Pradaxa	DABIGATRAN ETEXILATE MESYLATE
62856025101	Fragmin	DALTEPARIN SODIUM,PORCINE
62856025010	Fragmin	DALTEPARIN SODIUM,PORCINE
62856018010	Fragmin	DALTEPARIN SODIUM,PORCINE
00069022802	Fragmin	DALTEPARIN SODIUM,PORCINE
62856010201	Fragmin	DALTEPARIN SODIUM,PORCINE
00069022301	Fragmin	DALTEPARIN SODIUM,PORCINE
00069023201	Fragmin	DALTEPARIN SODIUM,PORCINE
00069019502	Fragmin	DALTEPARIN SODIUM,PORCINE
00069020601	Fragmin	DALTEPARIN SODIUM,PORCINE
62856015010	Fragmin	DALTEPARIN SODIUM,PORCINE
00069019602	Fragmin	DALTEPARIN SODIUM,PORCINE
00069021702	Fragmin	DALTEPARIN SODIUM,PORCINE
00069022801	Fragmin	DALTEPARIN SODIUM,PORCINE
62856018001	Fragmin	DALTEPARIN SODIUM,PORCINE
62856012510	Fragmin	DALTEPARIN SODIUM,PORCINE
62856010101	Fragmin	DALTEPARIN SODIUM,PORCINE
00069020602	Fragmin	DALTEPARIN SODIUM,PORCINE
62856075010	Fragmin	DALTEPARIN SODIUM,PORCINE
00069022002	Fragmin	DALTEPARIN SODIUM,PORCINE
00069019501	Fragmin	DALTEPARIN SODIUM,PORCINE
62856015001	Fragmin	DALTEPARIN SODIUM,PORCINE
62856010110	Fragmin	DALTEPARIN SODIUM,PORCINE
00069021701	Fragmin	DALTEPARIN SODIUM,PORCINE
62856050010	Fragmin	DALTEPARIN SODIUM,PORCINE
00069019601	Fragmin	DALTEPARIN SODIUM,PORCINE
62856075001	Fragmin	DALTEPARIN SODIUM,PORCINE
62856025001	Fragmin	DALTEPARIN SODIUM,PORCINE
00069022302	Fragmin	DALTEPARIN SODIUM,PORCINE
62856012501	Fragmin	DALTEPARIN SODIUM,PORCINE
62856050001	Fragmin	DALTEPARIN SODIUM,PORCINE
00069022001	Fragmin	DALTEPARIN SODIUM,PORCINE
65597020330	Savaysa	EDOXABAN TOSYLATE

65597020305	Savaysa	EDOXABAN TOSYLATE
65597020310	Savaysa	EDOXABAN TOSYLATE
65597020205	Savaysa	EDOXABAN TOSYLATE
65597020230	Savaysa	EDOXABAN TOSYLATE
65597020210	Savaysa	EDOXABAN TOSYLATE
65597020290	Savaysa	EDOXABAN TOSYLATE
65597020130	Savaysa	EDOXABAN TOSYLATE
65597020390	Savaysa	EDOXABAN TOSYLATE
00075802501	Lovenox	ENOXAPARIN SODIUM
54868511201	Lovenox	ENOXAPARIN SODIUM
63323056887	enoxaparin	ENOXAPARIN SODIUM
00548563100	enoxaparin	ENOXAPARIN SODIUM
00548563300	enoxaparin	ENOXAPARIN SODIUM
62037086220	enoxaparin	ENOXAPARIN SODIUM
00548560400	enoxaparin	ENOXAPARIN SODIUM
00075802210	Lovenox	ENOXAPARIN SODIUM
00781313363	enoxaparin	ENOXAPARIN SODIUM
00075062281	Lovenox	ENOXAPARIN SODIUM
00075062161	Lovenox	ENOXAPARIN SODIUM
00955101210	enoxaparin	ENOXAPARIN SODIUM
00075062431	Lovenox	ENOXAPARIN SODIUM
00075062160	Lovenox	ENOXAPARIN SODIUM
00075062300	Lovenox	ENOXAPARIN SODIUM
58016487201	Lovenox	ENOXAPARIN SODIUM
00703868023	enoxaparin	ENOXAPARIN SODIUM
00075062040	Lovenox	ENOXAPARIN SODIUM
63323056990	enoxaparin	ENOXAPARIN SODIUM
63323056896	enoxaparin	ENOXAPARIN SODIUM
00781312168	enoxaparin	ENOXAPARIN SODIUM
00781335603	enoxaparin	ENOXAPARIN SODIUM
00075062301	Lovenox	ENOXAPARIN SODIUM
00548563500	enoxaparin	ENOXAPARIN SODIUM
00955101510	enoxaparin	ENOXAPARIN SODIUM
00781311966	enoxaparin	ENOXAPARIN SODIUM
00075801301	Lovenox	ENOXAPARIN SODIUM
00781313301	enoxaparin	ENOXAPARIN SODIUM
00703854021	enoxaparin	ENOXAPARIN SODIUM
63323056999	enoxaparin	ENOXAPARIN SODIUM
62037086420	enoxaparin	ENOXAPARIN SODIUM
00703853023	enoxaparin	ENOXAPARIN SODIUM
00703851021	enoxaparin	ENOXAPARIN SODIUM
00075291202	Lovenox	ENOXAPARIN SODIUM
00075802201	Lovenox	ENOXAPARIN SODIUM
35356001910	Lovenox	ENOXAPARIN SODIUM
00075291502	Lovenox	ENOXAPARIN SODIUM
00548560600	enoxaparin	ENOXAPARIN SODIUM
00548563400	enoxaparin	ENOXAPARIN SODIUM
00075062430	Lovenox	ENOXAPARIN SODIUM
00548563700	enoxaparin	ENOXAPARIN SODIUM
00781365505	enoxaparin	ENOXAPARIN SODIUM

00548560700	enoxaparin	ENOXAPARIN SODIUM
00703853021	enoxaparin	ENOXAPARIN SODIUM
00703854023	enoxaparin	ENOXAPARIN SODIUM
00703861021	enoxaparin	ENOXAPARIN SODIUM
00781365569	enoxaparin	ENOXAPARIN SODIUM
55154939905	enoxaparin	ENOXAPARIN SODIUM
54868558701	Lovenox	ENOXAPARIN SODIUM
00075062041	Lovenox	ENOXAPARIN SODIUM
00075801401	Lovenox	ENOXAPARIN SODIUM
63323056984	enoxaparin	ENOXAPARIN SODIUM
00075802510	Lovenox	ENOXAPARIN SODIUM
00548560300	enoxaparin	ENOXAPARIN SODIUM
00703851023	enoxaparin	ENOXAPARIN SODIUM
00075062604	Lovenox	ENOXAPARIN SODIUM
00781311963	enoxaparin	ENOXAPARIN SODIUM
54868511200	Lovenox	ENOXAPARIN SODIUM
54868558700	Lovenox	ENOXAPARIN SODIUM
00781342804	enoxaparin	ENOXAPARIN SODIUM
00703858023	enoxaparin	ENOXAPARIN SODIUM
00781342868	enoxaparin	ENOXAPARIN SODIUM
00075801601	Lovenox	ENOXAPARIN SODIUM
63323056899	enoxaparin	ENOXAPARIN SODIUM
00703868021	enoxaparin	ENOXAPARIN SODIUM
00075801810	Lovenox	ENOXAPARIN SODIUM
00075062280	Lovenox	ENOXAPARIN SODIUM
54868583700	Lovenox	ENOXAPARIN SODIUM
00703858021	enoxaparin	ENOXAPARIN SODIUM
00075801801	Lovenox	ENOXAPARIN SODIUM
62037084920	enoxaparin	ENOXAPARIN SODIUM
00781311968	enoxaparin	ENOXAPARIN SODIUM
55154544005	enoxaparin	ENOXAPARIN SODIUM
62037086620	enoxaparin	ENOXAPARIN SODIUM
00781361204	enoxaparin	ENOXAPARIN SODIUM
00075801410	Lovenox	ENOXAPARIN SODIUM
00781322464	enoxaparin	ENOXAPARIN SODIUM
00781335666	enoxaparin	ENOXAPARIN SODIUM
00955100310	enoxaparin	ENOXAPARIN SODIUM
00703856021	enoxaparin	ENOXAPARIN SODIUM
00955101010	enoxaparin	ENOXAPARIN SODIUM
00075802010	Lovenox	ENOXAPARIN SODIUM
54868544000	Lovenox	ENOXAPARIN SODIUM
63323056995	enoxaparin	ENOXAPARIN SODIUM
00548563200	enoxaparin	ENOXAPARIN SODIUM
00075803001	Lovenox	ENOXAPARIN SODIUM
00781312293	enoxaparin	ENOXAPARIN SODIUM
54868583500	Lovenox	ENOXAPARIN SODIUM
00075801310	Lovenox	ENOXAPARIN SODIUM
63323056890	enoxaparin	ENOXAPARIN SODIUM
00781322402	enoxaparin	ENOXAPARIN SODIUM
00781312169	enoxaparin	ENOXAPARIN SODIUM

63323056883	enoxaparin	ENOXAPARIN SODIUM
00955101601	enoxaparin	ENOXAPARIN SODIUM
00075802001	Lovenox	ENOXAPARIN SODIUM
00703856023	enoxaparin	ENOXAPARIN SODIUM
63323056593	enoxaparin	ENOXAPARIN SODIUM
00781350005	enoxaparin	ENOXAPARIN SODIUM
63323056884	enoxaparin	ENOXAPARIN SODIUM
00548560500	enoxaparin	ENOXAPARIN SODIUM
00955100810	enoxaparin	ENOXAPARIN SODIUM
35356048110	Lovenox	ENOXAPARIN SODIUM
00075062603	Lovenox	ENOXAPARIN SODIUM
00548563600	enoxaparin	ENOXAPARIN SODIUM
00781350069	enoxaparin	ENOXAPARIN SODIUM
62037086320	enoxaparin	ENOXAPARIN SODIUM
63323056894	enoxaparin	ENOXAPARIN SODIUM
00075291201	Lovenox	ENOXAPARIN SODIUM
00955100410	enoxaparin	ENOXAPARIN SODIUM
00075801610	Lovenox	ENOXAPARIN SODIUM
00548560200	enoxaparin	ENOXAPARIN SODIUM
00781311969	enoxaparin	ENOXAPARIN SODIUM
63323056895	enoxaparin	ENOXAPARIN SODIUM
63323056898	enoxaparin	ENOXAPARIN SODIUM
00781361268	enoxaparin	ENOXAPARIN SODIUM
00781311964	enoxaparin	ENOXAPARIN SODIUM
62037083920	enoxaparin	ENOXAPARIN SODIUM
54868544001	Lovenox	ENOXAPARIN SODIUM
00075291501	Lovenox	ENOXAPARIN SODIUM
00548560100	enoxaparin	ENOXAPARIN SODIUM
63323056888	enoxaparin	ENOXAPARIN SODIUM
00955100610	enoxaparin	ENOXAPARIN SODIUM
55154402405	Lovenox	ENOXAPARIN SODIUM
00703861023	enoxaparin	ENOXAPARIN SODIUM
62037086120	enoxaparin	ENOXAPARIN SODIUM
63323056586	enoxaparin	ENOXAPARIN SODIUM
60505608104	fondaparinux	FONDAPARINUX SODIUM
67457059400	Arixtra	FONDAPARINUX SODIUM
67457058400	fondaparinux	FONDAPARINUX SODIUM
54868550101	Arixtra	FONDAPARINUX SODIUM
55111068111	fondaparinux	FONDAPARINUX SODIUM
67457058300	fondaparinux	FONDAPARINUX SODIUM
60505607904	fondaparinux	FONDAPARINUX SODIUM
00007323002	Arixtra	FONDAPARINUX SODIUM
00007323611	Arixtra	FONDAPARINUX SODIUM
54868565200	Arixtra	FONDAPARINUX SODIUM
67457069610	fondaparinux	FONDAPARINUX SODIUM
67457059304	Arixtra	FONDAPARINUX SODIUM
43598060910	fondaparinux	FONDAPARINUX SODIUM
55111067810	fondaparinux	FONDAPARINUX SODIUM
43598060602	fondaparinux	FONDAPARINUX SODIUM
00007323201	Arixtra	FONDAPARINUX SODIUM

67457059500	Arixtra	FONDAPARINUX SODIUM
00007323011	Arixtra	FONDAPARINUX SODIUM
00007323401	Arixtra	FONDAPARINUX SODIUM
67457058304	fondaparinux	FONDAPARINUX SODIUM
67457058210	fondaparinux	FONDAPARINUX SODIUM
00007323602	Arixtra	FONDAPARINUX SODIUM
35356007810	Arixtra	FONDAPARINUX SODIUM
67457058406	fondaparinux	FONDAPARINUX SODIUM
54868550102	Arixtra	FONDAPARINUX SODIUM
60505607800	fondaparinux	FONDAPARINUX SODIUM
43598060911	fondaparinux	FONDAPARINUX SODIUM
43598060611	fondaparinux	FONDAPARINUX SODIUM
55111068102	fondaparinux	FONDAPARINUX SODIUM
55111067910	fondaparinux	FONDAPARINUX SODIUM
43598060711	fondaparinux	FONDAPARINUX SODIUM
67457069310	fondaparinux	FONDAPARINUX SODIUM
55111067911	fondaparinux	FONDAPARINUX SODIUM
67457059210	Arixtra	FONDAPARINUX SODIUM
55111068110	fondaparinux	FONDAPARINUX SODIUM
00007323411	Arixtra	FONDAPARINUX SODIUM
60505607900	fondaparinux	FONDAPARINUX SODIUM
43598060702	fondaparinux	FONDAPARINUX SODIUM
67457069600	fondaparinux	FONDAPARINUX SODIUM
67457069400	fondaparinux	FONDAPARINUX SODIUM
67457069510	fondaparinux	FONDAPARINUX SODIUM
00007323601	Arixtra	FONDAPARINUX SODIUM
60505608004	fondaparinux	FONDAPARINUX SODIUM
67457058508	fondaparinux	FONDAPARINUX SODIUM
35356008102	Arixtra	FONDAPARINUX SODIUM
00007323402	Arixtra	FONDAPARINUX SODIUM
00007323202	Arixtra	FONDAPARINUX SODIUM
67457069410	fondaparinux	FONDAPARINUX SODIUM
67457059406	Arixtra	FONDAPARINUX SODIUM
43598060811	fondaparinux	FONDAPARINUX SODIUM
67457059200	Arixtra	FONDAPARINUX SODIUM
55111068002	fondaparinux	FONDAPARINUX SODIUM
35356008110	Arixtra	FONDAPARINUX SODIUM
55111067802	fondaparinux	FONDAPARINUX SODIUM
60505608000	fondaparinux	FONDAPARINUX SODIUM
43598060710	fondaparinux	FONDAPARINUX SODIUM
35356008010	Arixtra	FONDAPARINUX SODIUM
35356008002	Arixtra	FONDAPARINUX SODIUM
67457059300	Arixtra	FONDAPARINUX SODIUM
55111067902	fondaparinux	FONDAPARINUX SODIUM
67457069500	fondaparinux	FONDAPARINUX SODIUM
67457058200	fondaparinux	FONDAPARINUX SODIUM
60505608100	fondaparinux	FONDAPARINUX SODIUM
43598060902	fondaparinux	FONDAPARINUX SODIUM
55111068010	fondaparinux	FONDAPARINUX SODIUM
55111067811	fondaparinux	FONDAPARINUX SODIUM

43598060810	fondaparinux	FONDAPARINUX SODIUM
00007323211	Arixtra	FONDAPARINUX SODIUM
67457069300	fondaparinux	FONDAPARINUX SODIUM
54868550100	Arixtra	FONDAPARINUX SODIUM
35356007902	Arixtra	FONDAPARINUX SODIUM
00007323001	Arixtra	FONDAPARINUX SODIUM
43598060610	fondaparinux	FONDAPARINUX SODIUM
55111068011	fondaparinux	FONDAPARINUX SODIUM
67457059508	Arixtra	FONDAPARINUX SODIUM
43598060802	fondaparinux	FONDAPARINUX SODIUM
35356007910	Arixtra	FONDAPARINUX SODIUM
60505607804	fondaparinux	FONDAPARINUX SODIUM
67457058500	fondaparinux	FONDAPARINUX SODIUM
42254037601	Xarelto	RIVAROXABAN
50458057890	Xarelto	RIVAROXABAN
50458057910	Xarelto	RIVAROXABAN
50458057810	Xarelto	RIVAROXABAN
50458058451	Xarelto	RIVAROXABAN
50458058010	Xarelto	RIVAROXABAN
50458057930	Xarelto	RIVAROXABAN
50458057830	Xarelto	RIVAROXABAN
50458058030	Xarelto	RIVAROXABAN
50458057990	Xarelto	RIVAROXABAN
67211034208	Innohep	TINZAPARIN SODIUM,PORCINE
50222034208	Innohep	TINZAPARIN SODIUM,PORCINE
50222034253	Innohep	TINZAPARIN SODIUM,PORCINE
67211034253	Innohep	TINZAPARIN SODIUM,PORCINE
51138048230	Coumadin	WARFARIN SODIUM
60429078925	warfarin	WARFARIN SODIUM
00378880110	warfarin	WARFARIN SODIUM
00832121710	Jantoven	WARFARIN SODIUM
43353005053	warfarin	WARFARIN SODIUM
60429078845	warfarin	WARFARIN SODIUM
23490648001	warfarin	WARFARIN SODIUM
49999092330	warfarin	WARFARIN SODIUM
57237012201	warfarin	WARFARIN SODIUM
60429078830	warfarin	WARFARIN SODIUM
60429078930	warfarin	WARFARIN SODIUM
00832121400	Jantoven	WARFARIN SODIUM
54868525501	Coumadin	WARFARIN SODIUM
51138048330	Coumadin	WARFARIN SODIUM
00093172110	warfarin	WARFARIN SODIUM
57237012101	warfarin	WARFARIN SODIUM
55289077330	warfarin	WARFARIN SODIUM
43353004960	warfarin	WARFARIN SODIUM
68382005701	warfarin	WARFARIN SODIUM
00832121210	Jantoven	WARFARIN SODIUM
43353014235	warfarin	WARFARIN SODIUM
51138048830	Coumadin	WARFARIN SODIUM
43353002135	warfarin	WARFARIN SODIUM

67544031840	warfarin	WARFARIN SODIUM
00056017675	Coumadin	WARFARIN SODIUM
55289077390	warfarin	WARFARIN SODIUM
43063065530	warfarin	WARFARIN SODIUM
23490648402	warfarin	WARFARIN SODIUM
54569622400	warfarin	WARFARIN SODIUM
43353005038	warfarin	WARFARIN SODIUM
54868082200	Jantoven	WARFARIN SODIUM
00056016901	Coumadin	WARFARIN SODIUM
68382005301	warfarin	WARFARIN SODIUM
00832121389	Jantoven	WARFARIN SODIUM
60429079001	warfarin	WARFARIN SODIUM
58016008360	warfarin	WARFARIN SODIUM
00832121700	Jantoven	WARFARIN SODIUM
43353002378	warfarin	WARFARIN SODIUM
58016008330	warfarin	WARFARIN SODIUM
00093171310	warfarin	WARFARIN SODIUM
63629441703	warfarin	WARFARIN SODIUM
67544040115	Coumadin	WARFARIN SODIUM
00832121310	Jantoven	WARFARIN SODIUM
60429078945	warfarin	WARFARIN SODIUM
00093171901	warfarin	WARFARIN SODIUM
21695067360	warfarin	WARFARIN SODIUM
66267063400	Coumadin	WARFARIN SODIUM
51138019660	warfarin	WARFARIN SODIUM
62584098477	warfarin	WARFARIN SODIUM
43353002311	warfarin	WARFARIN SODIUM
31722033001	warfarin	WARFARIN SODIUM
31722033301	warfarin	WARFARIN SODIUM
54868125902	Coumadin	WARFARIN SODIUM
55045288108	warfarin	WARFARIN SODIUM
58864022314	Coumadin	WARFARIN SODIUM
00378880410	warfarin	WARFARIN SODIUM
00056017470	Coumadin	WARFARIN SODIUM
51138020130	warfarin	WARFARIN SODIUM
54868125907	Coumadin	WARFARIN SODIUM
00378880101	warfarin	WARFARIN SODIUM
67544005238	Coumadin	WARFARIN SODIUM
55289028650	Coumadin	WARFARIN SODIUM
60429079177	warfarin	WARFARIN SODIUM
00378882510	warfarin	WARFARIN SODIUM
51672403207	warfarin	WARFARIN SODIUM
54868212803	Coumadin	WARFARIN SODIUM
58864003030	Coumadin	WARFARIN SODIUM
49999092360	warfarin	WARFARIN SODIUM
00056018970	Coumadin	WARFARIN SODIUM
00378880510	warfarin	WARFARIN SODIUM
43353002344	warfarin	WARFARIN SODIUM
68382005616	warfarin	WARFARIN SODIUM
49999057600	warfarin	WARFARIN SODIUM

54868520700	Jantoven	WARFARIN SODIUM
00555083302	warfarin	WARFARIN SODIUM
00378887501	warfarin	WARFARIN SODIUM
00378887510	warfarin	WARFARIN SODIUM
63629401703	warfarin	WARFARIN SODIUM
68382005210	warfarin	WARFARIN SODIUM
67544005228	Coumadin	WARFARIN SODIUM
76282032901	warfarin	WARFARIN SODIUM
63187067490	warfarin	WARFARIN SODIUM
43353002359	warfarin	WARFARIN SODIUM
51138048930	Coumadin	WARFARIN SODIUM
23490648201	warfarin	WARFARIN SODIUM
49999041130	Coumadin	WARFARIN SODIUM
60429078530	warfarin	WARFARIN SODIUM
43353002130	warfarin	WARFARIN SODIUM
60429078410	warfarin	WARFARIN SODIUM
57237012001	warfarin	WARFARIN SODIUM
63187067460	warfarin	WARFARIN SODIUM
68382005510	warfarin	WARFARIN SODIUM
68382006401	warfarin	WARFARIN SODIUM
43353008960	warfarin	WARFARIN SODIUM
60429079010	warfarin	WARFARIN SODIUM
00378882501	warfarin	WARFARIN SODIUM
43353002830	warfarin	WARFARIN SODIUM
51138006230	warfarin	WARFARIN SODIUM
67544031835	warfarin	WARFARIN SODIUM
68084002777	warfarin	WARFARIN SODIUM
51138018230	warfarin	WARFARIN SODIUM
68382005601	warfarin	WARFARIN SODIUM
65162076311	warfarin	WARFARIN SODIUM
31722033201	warfarin	WARFARIN SODIUM
54868245401	Coumadin	WARFARIN SODIUM
43353002161	warfarin	WARFARIN SODIUM
54868434902	warfarin	WARFARIN SODIUM
54868428601	warfarin	WARFARIN SODIUM
68382006410	warfarin	WARFARIN SODIUM
58517036030	warfarin	WARFARIN SODIUM
63629412201	warfarin	WARFARIN SODIUM
63739036410	warfarin	WARFARIN SODIUM
43353014253	warfarin	WARFARIN SODIUM
51138005930	warfarin	WARFARIN SODIUM
67544005250	Coumadin	WARFARIN SODIUM
35356090630	warfarin	WARFARIN SODIUM
60429078935	warfarin	WARFARIN SODIUM
65162076811	warfarin	WARFARIN SODIUM
00832121410	Jantoven	WARFARIN SODIUM
23490648002	warfarin	WARFARIN SODIUM
67544005265	Coumadin	WARFARIN SODIUM
43353002315	warfarin	WARFARIN SODIUM
43353002365	warfarin	WARFARIN SODIUM

63187075030	warfarin	WARFARIN SODIUM
00056018870	Coumadin	WARFARIN SODIUM
63629412205	warfarin	WARFARIN SODIUM
51672402807	warfarin	WARFARIN SODIUM
33358036000	warfarin	WARFARIN SODIUM
57237012599	warfarin	WARFARIN SODIUM
23490647801	warfarin	WARFARIN SODIUM
54868442204	warfarin	WARFARIN SODIUM
63629401702	warfarin	WARFARIN SODIUM
43353005330	warfarin	WARFARIN SODIUM
21695094030	warfarin	WARFARIN SODIUM
57237012301	warfarin	WARFARIN SODIUM
00056017301	Coumadin	WARFARIN SODIUM
63629474802	warfarin	WARFARIN SODIUM
00832121600	Jantoven	WARFARIN SODIUM
54868212900	Coumadin	WARFARIN SODIUM
00832121801	Jantoven	WARFARIN SODIUM
43353049330	Coumadin	WARFARIN SODIUM
51672402801	warfarin	WARFARIN SODIUM
60429078615	warfarin	WARFARIN SODIUM
65162076410	warfarin	WARFARIN SODIUM
58864087930	warfarin	WARFARIN SODIUM
31722032810	warfarin	WARFARIN SODIUM
51672402903	warfarin	WARFARIN SODIUM
23490648302	warfarin	WARFARIN SODIUM
67544005235	Coumadin	WARFARIN SODIUM
49999082900	warfarin	WARFARIN SODIUM
54868487303	warfarin	WARFARIN SODIUM
51138020330	warfarin	WARFARIN SODIUM
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68258906401	Coumadin	WARFARIN SODIUM
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43353057830	warfarin	WARFARIN SODIUM
67544005260	Coumadin	WARFARIN SODIUM
60429078645	warfarin	WARFARIN SODIUM
67544005240	Coumadin	WARFARIN SODIUM
51138049030	Coumadin	WARFARIN SODIUM
00832121510	Jantoven	WARFARIN SODIUM
31722033501	warfarin	WARFARIN SODIUM
43353002145	warfarin	WARFARIN SODIUM
67544019540	Coumadin	WARFARIN SODIUM
23490648202	warfarin	WARFARIN SODIUM
00555087405	warfarin	WARFARIN SODIUM
00832121601	Jantoven	WARFARIN SODIUM
49999092390	warfarin	WARFARIN SODIUM
67544040135	Coumadin	WARFARIN SODIUM
54868487302	warfarin	WARFARIN SODIUM
54868487101	warfarin	WARFARIN SODIUM
68084002701	warfarin	WARFARIN SODIUM

54868434903	warfarin	WARFARIN SODIUM
43353049430	Coumadin	WARFARIN SODIUM
43353002155	warfarin	WARFARIN SODIUM
54868487300	warfarin	WARFARIN SODIUM
00056016970	Coumadin	WARFARIN SODIUM
00056016875	Coumadin	WARFARIN SODIUM
60429079230	warfarin	WARFARIN SODIUM
66336025230	warfarin	WARFARIN SODIUM
51138019530	warfarin	WARFARIN SODIUM
00056017601	Coumadin	WARFARIN SODIUM
67544005270	Coumadin	WARFARIN SODIUM
58016069700	warfarin	WARFARIN SODIUM
35356058230	warfarin	WARFARIN SODIUM
60429078430	warfarin	WARFARIN SODIUM
00093172001	warfarin	WARFARIN SODIUM
54868487102	warfarin	WARFARIN SODIUM
00093171801	warfarin	WARFARIN SODIUM
00378880610	warfarin	WARFARIN SODIUM
51138048510	Coumadin	WARFARIN SODIUM
43353004930	warfarin	WARFARIN SODIUM
65162076510	warfarin	WARFARIN SODIUM
00832121501	Jantoven	WARFARIN SODIUM
63629401705	warfarin	WARFARIN SODIUM
76282032910	warfarin	WARFARIN SODIUM
76282033501	warfarin	WARFARIN SODIUM
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43353003060	warfarin	WARFARIN SODIUM
51672403501	warfarin	WARFARIN SODIUM
60429078977	warfarin	WARFARIN SODIUM
63629412202	warfarin	WARFARIN SODIUM
00832121989	Jantoven	WARFARIN SODIUM
60429078777	warfarin	WARFARIN SODIUM
68382005501	warfarin	WARFARIN SODIUM
54868434905	warfarin	WARFARIN SODIUM
51138019830	warfarin	WARFARIN SODIUM
63629317702	warfarin	WARFARIN SODIUM
43353057809	warfarin	WARFARIN SODIUM
54868215400	Coumadin	WARFARIN SODIUM
54569493400	warfarin	WARFARIN SODIUM
54868440001	warfarin	WARFARIN SODIUM
76282033301	warfarin	WARFARIN SODIUM
60429078677	warfarin	WARFARIN SODIUM
58016069790	warfarin	WARFARIN SODIUM
23490648101	warfarin	WARFARIN SODIUM
54569586900	warfarin	WARFARIN SODIUM
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60429078540	warfarin	WARFARIN SODIUM
43353002153	warfarin	WARFARIN SODIUM
51138018130	warfarin	WARFARIN SODIUM
62584098401	warfarin	WARFARIN SODIUM

49999057630	warfarin	WARFARIN SODIUM
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43353002150	warfarin	WARFARIN SODIUM
76282033101	warfarin	WARFARIN SODIUM
66267063600	Coumadin	WARFARIN SODIUM
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35356039790	warfarin	WARFARIN SODIUM
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00056017370	Coumadin	WARFARIN SODIUM
67544031861	warfarin	WARFARIN SODIUM
57237012799	warfarin	WARFARIN SODIUM
54569444300	Coumadin	WARFARIN SODIUM
68382005610	warfarin	WARFARIN SODIUM
43353049260	Coumadin	WARFARIN SODIUM
31722032701	warfarin	WARFARIN SODIUM
43353002361	warfarin	WARFARIN SODIUM
51138005530	warfarin	WARFARIN SODIUM
51138020030	warfarin	WARFARIN SODIUM
68258102701	warfarin	WARFARIN SODIUM
00590032496	Coumadin	WARFARIN SODIUM
43063021830	warfarin	WARFARIN SODIUM
54868428602	warfarin	WARFARIN SODIUM
35356058260	warfarin	WARFARIN SODIUM
54868428605	warfarin	WARFARIN SODIUM
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31722033010	warfarin	WARFARIN SODIUM
63187075010	warfarin	WARFARIN SODIUM
68258910201	Coumadin	WARFARIN SODIUM
00555083205	warfarin	WARFARIN SODIUM
00832121689	Jantoven	WARFARIN SODIUM
43353014245	warfarin	WARFARIN SODIUM
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60429079045	warfarin	WARFARIN SODIUM
31722033110	warfarin	WARFARIN SODIUM
43353002940	warfarin	WARFARIN SODIUM
66267062900	Coumadin	WARFARIN SODIUM
43353049130	Coumadin	WARFARIN SODIUM
23490648103	warfarin	WARFARIN SODIUM
49999092310	warfarin	WARFARIN SODIUM
43353005015	warfarin	WARFARIN SODIUM
54868428600	warfarin	WARFARIN SODIUM
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43353005020	warfarin	WARFARIN SODIUM
55289028630	Coumadin	WARFARIN SODIUM
66267063100	Coumadin	WARFARIN SODIUM
00832121901	Jantoven	WARFARIN SODIUM
00378881010	warfarin	WARFARIN SODIUM
57237012199	warfarin	WARFARIN SODIUM
43353002345	warfarin	WARFARIN SODIUM

58016008390	warfarin	WARFARIN SODIUM
31722033101	warfarin	WARFARIN SODIUM
67544005268	Coumadin	WARFARIN SODIUM
00056017290	Coumadin	WARFARIN SODIUM
54868339900	Coumadin	WARFARIN SODIUM
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43353005047	warfarin	WARFARIN SODIUM
43353008930	warfarin	WARFARIN SODIUM
54868525500	Coumadin	WARFARIN SODIUM
49999057690	warfarin	WARFARIN SODIUM
51672403101	warfarin	WARFARIN SODIUM
43353005068	warfarin	WARFARIN SODIUM
43353058460	warfarin	WARFARIN SODIUM
54569631301	warfarin	WARFARIN SODIUM
43353002140	warfarin	WARFARIN SODIUM
55289034030	warfarin	WARFARIN SODIUM
65162076810	warfarin	WARFARIN SODIUM
55045288008	warfarin	WARFARIN SODIUM
21695067530	warfarin	WARFARIN SODIUM
67544005220	Coumadin	WARFARIN SODIUM
51672403303	warfarin	WARFARIN SODIUM
57237011999	warfarin	WARFARIN SODIUM
00555086905	warfarin	WARFARIN SODIUM
51138005430	warfarin	WARFARIN SODIUM
00056017270	Coumadin	WARFARIN SODIUM
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21695067330	warfarin	WARFARIN SODIUM
51138018430	warfarin	WARFARIN SODIUM
54868487304	warfarin	WARFARIN SODIUM
43353002930	warfarin	WARFARIN SODIUM
60429078801	warfarin	WARFARIN SODIUM
63629474801	warfarin	WARFARIN SODIUM
57237012401	warfarin	WARFARIN SODIUM
57237012601	warfarin	WARFARIN SODIUM
63187074530	warfarin	WARFARIN SODIUM
54569622500	warfarin	WARFARIN SODIUM
67544040150	Coumadin	WARFARIN SODIUM
54868440004	warfarin	WARFARIN SODIUM
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67544005261	Coumadin	WARFARIN SODIUM
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43353049230	Coumadin	WARFARIN SODIUM
51672403007	warfarin	WARFARIN SODIUM
67544005215	Coumadin	WARFARIN SODIUM

00555092502	warfarin	WARFARIN SODIUM
60429078940	warfarin	WARFARIN SODIUM
66336025130	warfarin	WARFARIN SODIUM
63629412203	warfarin	WARFARIN SODIUM
60429078545	warfarin	WARFARIN SODIUM
49999057620	warfarin	WARFARIN SODIUM
54868245402	Coumadin	WARFARIN SODIUM
60429078445	warfarin	WARFARIN SODIUM
67544019430	Coumadin	WARFARIN SODIUM
00832121289	Jantoven	WARFARIN SODIUM
51138049010	Coumadin	WARFARIN SODIUM
31722032910	warfarin	WARFARIN SODIUM
65162076210	warfarin	WARFARIN SODIUM
65162076310	warfarin	WARFARIN SODIUM
00378880210	warfarin	WARFARIN SODIUM
67544019560	Coumadin	WARFARIN SODIUM
54868442202	warfarin	WARFARIN SODIUM
54868495001	warfarin	WARFARIN SODIUM
63629254802	warfarin	WARFARIN SODIUM
00555086902	warfarin	WARFARIN SODIUM
00056016890	Coumadin	WARFARIN SODIUM
00093171301	warfarin	WARFARIN SODIUM
76282032710	warfarin	WARFARIN SODIUM
76282033001	warfarin	WARFARIN SODIUM
66267062800	Coumadin	WARFARIN SODIUM
57237012501	warfarin	WARFARIN SODIUM
54868125905	Coumadin	WARFARIN SODIUM
60429078415	warfarin	WARFARIN SODIUM
51138018530	warfarin	WARFARIN SODIUM
60429078877	warfarin	WARFARIN SODIUM
68382005401	warfarin	WARFARIN SODIUM
54868487301	warfarin	WARFARIN SODIUM
51138048775	Coumadin	WARFARIN SODIUM
63629317701	warfarin	WARFARIN SODIUM
60429079145	warfarin	WARFARIN SODIUM
68258909701	Coumadin	WARFARIN SODIUM
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00832121701	Jantoven	WARFARIN SODIUM
43353002355	warfarin	WARFARIN SODIUM
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23490647802	warfarin	WARFARIN SODIUM
43353005046	warfarin	WARFARIN SODIUM
51138048630	Coumadin	WARFARIN SODIUM
00555083105	warfarin	WARFARIN SODIUM

57237012399	warfarin	WARFARIN SODIUM
54868495003	warfarin	WARFARIN SODIUM
43353002368	warfarin	WARFARIN SODIUM
43353002340	warfarin	WARFARIN SODIUM
43353002935	warfarin	WARFARIN SODIUM
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54868440201	warfarin	WARFARIN SODIUM
51672403403	warfarin	WARFARIN SODIUM
54868125901	Coumadin	WARFARIN SODIUM
43353002325	warfarin	WARFARIN SODIUM
51138017930	warfarin	WARFARIN SODIUM
63629412204	warfarin	WARFARIN SODIUM
43063017614	warfarin	WARFARIN SODIUM
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51138048430	Coumadin	WARFARIN SODIUM
63629441701	warfarin	WARFARIN SODIUM
57237012099	warfarin	WARFARIN SODIUM
43353005025	warfarin	WARFARIN SODIUM
00832121301	Jantoven	WARFARIN SODIUM
43353005078	warfarin	WARFARIN SODIUM
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54868487103	warfarin	WARFARIN SODIUM
43353002346	warfarin	WARFARIN SODIUM
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51138005830	warfarin	WARFARIN SODIUM
60429078535	warfarin	WARFARIN SODIUM
43353002953	warfarin	WARFARIN SODIUM
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54868215403	Coumadin	WARFARIN SODIUM
43353002338	warfarin	WARFARIN SODIUM
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51672403107	warfarin	WARFARIN SODIUM
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43353002320	warfarin	WARFARIN SODIUM
43353002353	warfarin	WARFARIN SODIUM
54868542500	Jantoven	WARFARIN SODIUM
54868525800	warfarin	WARFARIN SODIUM
67544007030	Coumadin	WARFARIN SODIUM
54868434900	warfarin	WARFARIN SODIUM
00832121201	Jantoven	WARFARIN SODIUM
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65162076110	warfarin	WARFARIN SODIUM
67544040161	Coumadin	WARFARIN SODIUM
60429078515	warfarin	WARFARIN SODIUM
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54868440002	warfarin	WARFARIN SODIUM
55700000590	warfarin	WARFARIN SODIUM
51138048445	Coumadin	WARFARIN SODIUM
00832121850	Jantoven	WARFARIN SODIUM
54868212800	Coumadin	WARFARIN SODIUM
60429078990	warfarin	WARFARIN SODIUM
58864077330	warfarin	WARFARIN SODIUM
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43353005030	warfarin	WARFARIN SODIUM
60429078401	warfarin	WARFARIN SODIUM
00832121950	Jantoven	WARFARIN SODIUM
76282033310	warfarin	WARFARIN SODIUM
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54868495000	warfarin	WARFARIN SODIUM
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55045290208	warfarin	WARFARIN SODIUM
65162076111	warfarin	WARFARIN SODIUM
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65162076511	warfarin	WARFARIN SODIUM
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43353002860	warfarin	WARFARIN SODIUM
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00832121110	Jantoven	WARFARIN SODIUM
54868440203	warfarin	WARFARIN SODIUM
60429079130	warfarin	WARFARIN SODIUM
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54868339901	Coumadin	WARFARIN SODIUM
60429078975	warfarin	WARFARIN SODIUM
67544005230	Coumadin	WARFARIN SODIUM
67544019553	Coumadin	WARFARIN SODIUM
76282033210	warfarin	WARFARIN SODIUM
57237012699	warfarin	WARFARIN SODIUM
67544040145	Coumadin	WARFARIN SODIUM
43353005035	warfarin	WARFARIN SODIUM
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00378880601	warfarin	WARFARIN SODIUM
33358036130	warfarin	WARFARIN SODIUM
31722033210	warfarin	WARFARIN SODIUM
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60429079215	warfarin	WARFARIN SODIUM
35356057190	warfarin	WARFARIN SODIUM

67544040155	Coumadin	WARFARIN SODIUM
00093171210	warfarin	WARFARIN SODIUM
23490648203	warfarin	WARFARIN SODIUM
54569642700	warfarin	WARFARIN SODIUM
54868440000	warfarin	WARFARIN SODIUM
51138006030	warfarin	WARFARIN SODIUM
54868212901	Coumadin	WARFARIN SODIUM
63629401701	warfarin	WARFARIN SODIUM
60429078601	warfarin	WARFARIN SODIUM
00555083502	warfarin	WARFARIN SODIUM
54868440202	warfarin	WARFARIN SODIUM
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67544005253	Coumadin	WARFARIN SODIUM
54868440200	warfarin	WARFARIN SODIUM
67544031853	warfarin	WARFARIN SODIUM
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51138020230	warfarin	WARFARIN SODIUM
35356039730	warfarin	WARFARIN SODIUM
49999057610	warfarin	WARFARIN SODIUM
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51138048720	Coumadin	WARFARIN SODIUM
60429078630	warfarin	WARFARIN SODIUM
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54868215402	Coumadin	WARFARIN SODIUM
43353002960	warfarin	WARFARIN SODIUM
21695080130	warfarin	WARFARIN SODIUM
43353049360	Coumadin	WARFARIN SODIUM
76282032801	warfarin	WARFARIN SODIUM
68382005801	warfarin	WARFARIN SODIUM
68084014777	warfarin	WARFARIN SODIUM
35356090690	warfarin	WARFARIN SODIUM
43353002160	warfarin	WARFARIN SODIUM
43353002347	warfarin	WARFARIN SODIUM
60429078910	warfarin	WARFARIN SODIUM
00832121889	Jantoven	WARFARIN SODIUM
65162076211	warfarin	WARFARIN SODIUM
23490647803	warfarin	WARFARIN SODIUM
76282032701	warfarin	WARFARIN SODIUM
60429078920	warfarin	WARFARIN SODIUM
00832121900	Jantoven	WARFARIN SODIUM
68382005901	warfarin	WARFARIN SODIUM
00056016975	Coumadin	WARFARIN SODIUM
23490648102	warfarin	WARFARIN SODIUM
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00378881001	warfarin	WARFARIN SODIUM
43353005060	warfarin	WARFARIN SODIUM
00832121200	Jantoven	WARFARIN SODIUM
60429079015	warfarin	WARFARIN SODIUM
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00832121610	Jantoven	WARFARIN SODIUM
51672403503	warfarin	WARFARIN SODIUM
58016069760	warfarin	WARFARIN SODIUM
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31722032710	warfarin	WARFARIN SODIUM
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76282032810	warfarin	WARFARIN SODIUM
00832121789	Jantoven	WARFARIN SODIUM
67544019545	Coumadin	WARFARIN SODIUM
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67544005255	Coumadin	WARFARIN SODIUM
00832121589	Jantoven	WARFARIN SODIUM
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43353005065	warfarin	WARFARIN SODIUM
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