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

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

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

c TNF inhibitors.

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

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\jmdc_JMDC\3. Table 6.57. Pattern of RA Medication Use in Patients with Serious Infection Event [Japanese Medical Data Center Payer-Based].docx

Table 58_JMDC. Time to First Serious Infection (Days) [JMDC]

Time	Unmatched				Matched				
	Baricitinib[a]			TNFi	Baricitinib[a]			TNFi	Total
	Any (N=246)	4mg (N= 100)	2mg (N=146)	(N=1,752)	Any (N=220)	4mg (N= 130)	2mg (N= 90)	(N=220)	(N=440)
n	246	100	146	1,752	220	130	90	220	440
Mean (SD)	- (-)	- (-)	- (-)	231.00 (94.75)	- (-)	- (-)	- (-)	298.00 (0.00)	298.00 (0.00)
Median	- [-, -]	- [-, -]	- [-, -]	231.00 [164.00, 298.00]	- [-, -]	- [-, -]	- [-, -]	298.00 [298.00, 298.00]	298.00 [298.00, 298.00]
Min, Max	-,-	-,-	-,-	164.0, 298.0	-,-	-,-	-,-	298.0, 298.0	298.0, 298.0

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

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

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\jmdc_JMDC\3. [Updated 2022.03.15] Table 6.58. Time to First Seroius Infection (Days) [Japanese Medical Data Center Payer-Based].docx

Table 60_JMDC. Serious Infection Events Per Patient During All Available Follow-up [JMDC]

Number of Infections per Person	Unmatched		Matched		
	Baricitinib (N=246)	TNFi (N=1,752)	Baricitinib (N=220)	TNFi (N=220)	Total (N=440)
0	245 (99.6%)	1,736 (99.1%)	219 (99.5%)	217 (98.6%)	436 (99.1%)
1	0 (0.0%)	14 (0.8%)	0 (0.0%)	2 (0.9%)	2 (0.5%)
2	1 (0.4%)	1 (0.1%)	1 (0.5%)	1 (0.5%)	2 (0.5%)
3	0 (0.0%)	1 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
5	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
6	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
>6	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

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

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\jmdc_JMDC\3. Table 6.60. Serious Infection Events Per Patient During All Available Follow-up [Japanese Medical Data Center Payer-Based].docx

Table 61_JMDC. Comparative Risk of First Serious Infection Event [JMDC]

	TNFi	Baricitinib		p-value
		HR	95%CI	
Base Model[1,2]	Ref	-	-	-

Abbreviations: cDMARD = conventional disease-modifying antirheumatic drug; CI = confidence interval; HR = Cox proportional hazard ratio; Ref = referent group; TNFi = tumour necrosis factor inhibitor; VTE = venous thromboembolism.

1 Base model = propensity score-matched model with confounders, outcome and baricitinib exposure.

2 Zero outcome events in the Baricitinib group and TNFi group preclude the interpretation of the HR.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\jmdc_JMDC\Table 6.61. Comparative Risk of First Serious Infection Event [Japanese Medical Data Center Payer-Based].docx

Table 64_JMDC. Incidence Rate of Hospitalized TB Event [JMDC]

	Unmatched		Matched		
	Baricitinib (N=248)	**TNFi (N=1,760)**	**Baricitinib (N=223)**	**TNFi (N=223)**	**Total (N=446)**
Overall					
Person-Years	172.83	885.59	157.76	107.82	265.58
TB Events	0.0	0.0	0.0	0.0	0.0
TB Events/100 PY	0.00	0.00	0.00	0.00	0.00
95% CI	0.00, 2.13	0.00, 0.42	0.00, 2.34	0.00, 3.42	0.00, 1.39

Abbreviations: CI = confidence interval; N = number of patients in the specified category; PY = person-years; TB = tuberculosis; TNFi = tumour necrosis factor inhibitor.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\jmdc_JMDC\3. Table 6.64. Incidence Rate of Hospitalized TB Event [JMDC].docx

Table 68_JMDC. Incidence Rate of VTE (Primary Definition), by Dose and Unmatched [JMDC]

	Baricitinib 2mg (N=100)	Baricitinib 4mg (N=143)	TNFi (N=1,721)
VTE Events	0	0	3
Person-Years	59.20	111.76	865.47
IR per 100 PY	0.00	0.00	0.35
95% CI	0.00, 6.23	0.00, 3.30	0.07, 1.01

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

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\jmdc_JMDC\3. Table 6.68. Incidence Rate of VTE (Primary Definition), by Dose and Unmatched [Japanese Medical Data Center Payer-Based].docx

II. Variable Ratio Matching

All prior tables presented were based on propensity score matched baricitinib:TNFi cohorts using a 1:1 matching strategy. In this section, the tables include results that are based on a variable ratio matching (VRM) approach as described in Section 9.9.6.1 of the final study report.

The main analysis was modified to use 1:1 matching, as this allows the results in the meta-analysis to be directly proportional to the amount of baricitinib exposure in each data source. For transparency, comparative results generated using VRM prior to the adoption of the 1:1 matching are included here.

Table 45_JMDC_VRM. Incidence Rate of Event - VTE, Primary Definition [JMDC]

	Unmatched		Matched		
	Baricitinib[a] (N=243)	**TNFi (N=1,721)**	**Baricitinib[a] (N=196)**	**TNFi (N=475)**	**Total (N=671)**
Overall					
Person-Years	170.96	865.47	138.41	241.36	379.77
VTE Events	0	3	0	1	1
VTE Events/100 PY	0.00	0.35	0.00	0.41	0.26
95% CI	0.00, 2.16	0.07, 1.01	0.00, 2.67	0.01, 2.31	0.01, 1.47
Concomitant MTX Use[b]					
Total, n	155 (63.8%)	1,024 (59.5%)	128 (65.3%)	299 (62.9%)	427 (63.6%)
Person-Years	122.36	637.45	97.55	182.27	279.82
VTE Events	0	2	0	1	1
VTE Events/100 PY	0.00	0.31	0.00	0.55	0.36
95% CI	0.00, 3.02	0.04, 1.13	0.00, 3.78	0.01, 3.06	0.01, 1.99
No Concomitant MTX Use[b]					
Total, n	88 (36.2%)	697 (40.5%)	68 (34.7%)	176 (37.1%)	244 (36.4%)
Person-Years	48.60	228.03	40.85	59.09	99.95
VTE Events	0	1	0	0	0
VTE Events/100 PY	0.00	0.44	0.00	0.00	0.00
95% CI	0.00, 7.59	0.01, 2.44	0.00, 9.03	0.00, 6.24	0.00, 3.69

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

a Both 2- and 4-mg baricitinib doses are included when the 4-mg dose is available.

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

c N (%) of subgroups may not always sum precisely to total group N (%) due to rounding

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

Table 48_JMDC_VRM. Comparative Risk of Incident VTE, Primary Definition [JMDC]

	TNFi	Baricitinib		p-value
		HR	95%CI	
Base Model[1]	Ref	0.00	0, ∞	0.84
Adjusted – Model [1][2,3]	Ref	<0.001	0, ∞	1.00

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

1 Overall, rare outcome events in the exposed and/or referent groups preclude the interpretability of the HR

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

3 Zero events in the baricitinib exposure group preclude the interpretability of the HR.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\jmdc_JMDC\3. Table 6.48. Comparative Risk of Incident VTE, Primary Definition [Japanese Medical Data Center Payer-Based]_vrm.docx

Table 54_JMDC_VRM. Incidence Rate of Event - MACE [JMDC]

Model	Unmatched		Matched		
	Baricitinib[a] (N=246)	TNFi (N=1,720)	Baricitinib[a] (N=198)	TNFi (N=486)	Total (N=684)
Overall					
Person-Years	171.91	863.74	144.98	255.36	400.35
MACE	0	3	0	0	0
MACE/100 PY	0.00	0.35	0.00	0.00	0.00
95% CI	0.00, 2.15	0.07, 1.02	0.00, 2.54	0.00, 1.45	0.00, 0.92
MI					
MI	0	2	0	0	0
Person-Years	171.91	864.04	144.98	255.36	400.35
IR per100 PY	0.00	0.23	0.00	0.00	0.00
95% CI	0.00, 2.15	0.03, 0.84	0.00, 2.54	0.00, 1.45	0.00, 0.92
Stroke, any					
Stroke	0	1	0	0	0
Person-Years	171.91	863.82	144.98	255.36	400.35
IR per 100 PY	0.00	0.12	0.00	0.00	0.00
95% CI	0.00, 2.15	0.00, 0.65	0.00, 2.54	0.00, 1.45	0.00, 0.92

Model	Unmatched		Matched		
	Baricitinib[a] (N=246)	TNFi (N=1,720)	Baricitinib[a] (N=198)	TNFi (N=486)	Total (N=684)
Concomitant MTX Use[b]					
MACE	0	1	0	0	0
Person-Years	122.99	634.80	102.98	191.55	294.52
IR per 100 PY	0.00	0.16	0.00	0.00	0.00
95% CI	0.00, 3.00	0.00, 0.88	0.00, 3.58	0.00, 1.93	0.00, 1.25
No Concomitant MTX Use[b]					
MACE	0	2	0	0	0
Person-Years	48.93	228.94	42.01	63.82	105.82
IR per 100 PY	0.00	0.87	0.00	0.00	0.00
95% CI	0.00, 7.54	0.11, 3.16	0.00, 8.78	0.00, 5.78	0.00, 3.49

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

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

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

c N in subgroups may not always sum precisely to total group N due to rounding.

Source: lillyce\prd\ly3009104\i4v_mc_b023\final\output\shared\tfl\jmdc_JMDC\3. Table 6.54. Incidence Rate of Event - MACE [Japanese Medical Data Center Payer-Based]_vrm.docx

Table 59_JMDC_VRM. Incidence Rate of Event - First Serious Infection [JMDC]

	Unmatched		Matched		
	Baricitinib[a] (N=246)	TNFi (N=1,752)	Baricitinib[a] (N=199)	TNFi (N=500)	Total (N=699)
SI Events	0	2	0	0	0
Person-years	172.48	880.43	140.13	251.59	391.72
IR per 100 PY	0.00	0.23	0.00	0.00	0.00
95% CI	0.00, 2.14	0.03, 0.82	0.00, 2.63	0.00, 1.47	0.00, 0.94

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

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

Annex 16. SNDS French National Health Care – Additional Results

This annex includes information about results for the following analyses:

I. Additional analysis

The full report (584 pages) of tables generated for the main analysis, including those already included in the body of the report. These results, like those included in the report body, are based on 1:1 baricitinib:TNFi propensity score matching.

Specifically, this section of the annex includes:

- Descriptive tables for unmatched eligible patients.
- Descriptive tables for matched patient cohorts for the serious infection analyses

Table numbers are consistent with all other data sources, with the only change being the inclusion of a '6' as a prefix to the number.

II. Supplemental analysis

Results presented in this section were from post-hoc analyses designed to better understand the potential impact of the baseline duration on analysis results.

III. Variable Ratio Matching

These results were not presented in the body of this report. They are based on matching baricitinib:TNFi using Variable Ratio matching, i.e., as many matched 1:3 as possible, then the maximum number matched 1:2, then the remaining patients matched 1:1.

I. Additional analysis

Safety Outcomes in Patients Treated for RA

Comparative Assessment of VTE Risk and Other Risks among Patients with Rheumatoid Arthritis treated with Baricitinib versus Tumor Necrosis Factor Inhibitors

French part of the study program

Supplemental Analyses – Point VII

Statistical Analysis Report
1:1 propensity score matching

Version 1.0 – 28 February 2022

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LIST OF ABBREVIATIONS

Abbreviation	Description
ACR	American College of Rheumatology
ANOVA	Analysis of variance
ARR / ARR_{ed}	Apparent relative risk
ATC	Anatomical Therapeutic Chemical
APA	Anticoagulant and Antiplatelet Agents
bDMARD	Biologic Disease-Modifying Antirheumatic Drug
BMI	Body Mass Index
BPE	Bordeaux PharmacoEpi, the Pharmacoepidemiology research platform of the University of Bordeaux - INSERM CIC1401
CCAM	*Classification commune des actes médicaux* (French medical acts classification system)
cDMARD	conventional Disease-Modifying Antirheumatic Drug
CI	Confidence interval
CIRAS	Claims-Based Index for RA Severity
CNAM	*Caisse Nationale d'Assurance Maladie* (French national health insurance)
CPT-4	Current Procedural Terminology
DDD	Defined Daily Dose
DMARD	Disease-Modifying Anti-Rheumatic Drug
DOAC	Direct Oral AntiCoagulant
DVT	Deep Vein Thrombosis
ED	Emergency Department
EULAR	European League Against Rheumatism
HCPCS	Healthcare Common Procedure Coding System
HR	Hazard Ratio
ICD-10	International Classification of Disease, 10th Revision
ID	Identifier
INDS	*Institut National des Données de Santé* (French National Institut of Health Data)
JAK	Janus kinase

LMWH	Low Molecular Weight Heparin
LTD	Long-Term Disease Registration
MACE	Major Adverse Cardiovascular Events
MCO	*Médecine, Chirurgie, Obstétrique* (Medicine, Surgery, Obstetrics)
MI	Myocardial Infarction
NDC	National Drug Code
NSAID	Nonsteroidal Anti-Inflammatory Drugs
OR_{EC}	Odds Ratio as a measure of the association between the exposure (RA therapy) and the potential confounding factor
PE	Pulmonary Embolism
PMSI	*Programme de Médicalisation des Systèmes d'Information* (French national hospitalization database)
PPV	Positive Predictive Value
PS	Propensity Score
PsO	Psoriasis
PsA	Psoriatic Arthritis
PY	Person-Years
Pr(C)	Prevalence of the potential confounders
PR(E)	Prevalence of exposure
QBA	Quantitative bias analysis
RA	Rheumatoid Arthritis
RR_{CD}	Relative Risk as an estimate of the confounder-disease association
RR_{ED}	Relative Risk as an estimate of the exposure (RA therapy)-disease association
SAP	Statistical Analysis Plan
SD	Standard deviation
SERM	Selective Estrogen Receptor Modulator
SLE	Systemic lupus erythematosus
SNDS	*Système National des Données de Santé* (National healthcare data system – current name)
Std. Diff.	Standardized difference
TB	Tuberculosis

TIA	Transient ischemic attacks
TNB	*Table Nationale de Biologie* (National classification of lab tests)
TNF	Tumor Necrosis Factor
TNFi	Tumor Necrosis Factor inhibitor
tsDMARD	Targeted Synthetic Disease-Modifying Anti-Rheumatic Drug
VKA	Vitamin K Antagonist
VTE	Venous thromboembolism
USPI	United States Package Insert

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1 PATIENT CHARACTERISTICS

Note: 4 subjects who 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.

1.1 SELECTION OF PATIENTS

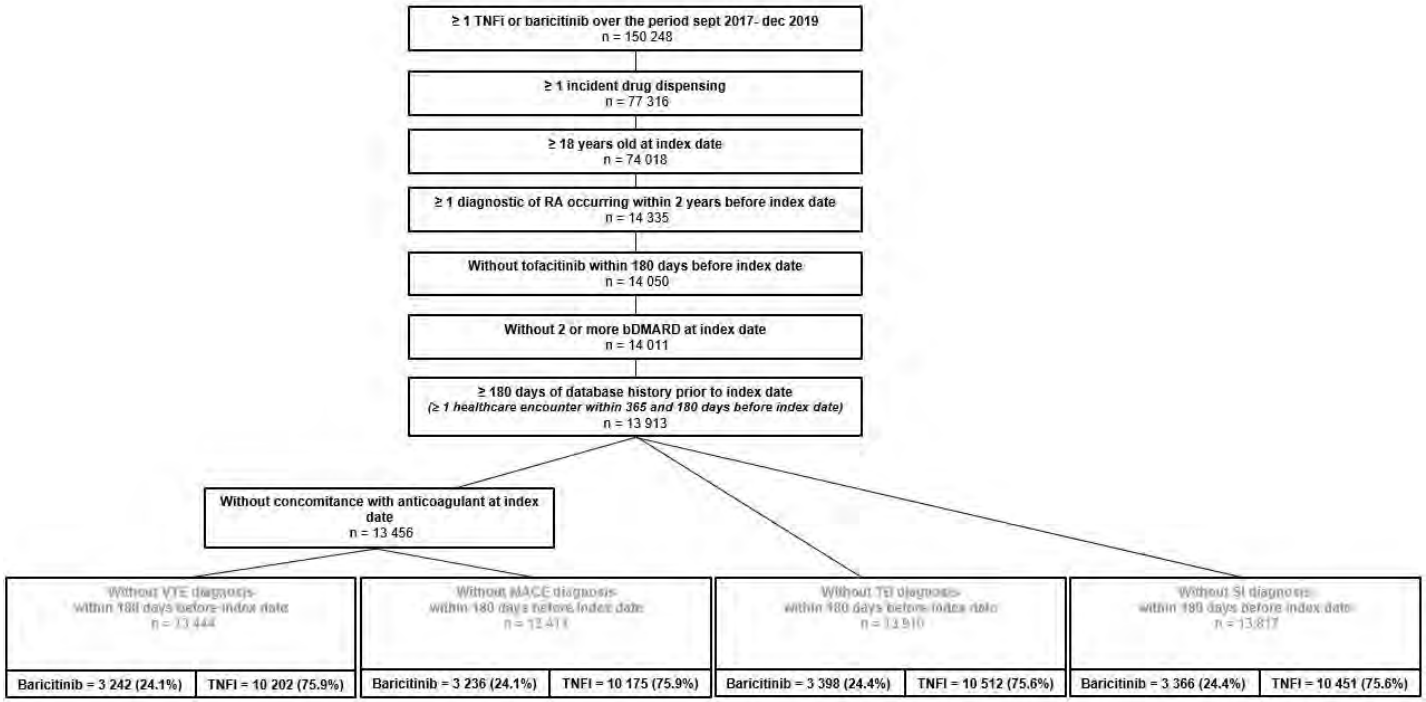

Figure 6.1. Identification and selection of populations for data analysis

1.2 BASELINE CHARACTERISTICS

Table 6.1. Baseline demographics, Unmatched cohort [SNDS]

	Baricitinib Any[a] n = 3242	Baricitinib 4 mg n = 2616	Baricitinib 2 mg n = 622	TNFi n = 10202	Std. Diff. (Any vs TNFi)
Age at index date [in years]					**0.287**
N (missing)	3242 (0)	2616 (0)	622 (0)	10202 (0)	
Mean (SD)	58.9 (13.2)	56.4 (12.0)	69.2 (12.7)	54.9 (14.2)	
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[	70 (2.2)	63 (2.4)	≤ 10	435 (4.3)	
[30-40[	208 (6.4)	195 (7.5)	13 (2.1)	1231 (12.1)	
[40-50[	462 (14.3)	424 (16.2)	38 (6.1)	1743 (17.1)	
[50-60[	899 (27.7)	835 (31.9)	62 (10.0)	2776 (27.2)	
[60-65[	461 (14.2)	403 (15.4)	57 (9.2)	1251 (12.3)	
≥65	1142 (35.2)	696 (26.6)	445 (71.5)	2766 (27.1)	
Sex, n (%)					**-0.149**
Male	645 (19.9)	536 (20.5)	109 (17.5)	2668 (26.2)	
Female	2597 (80.1)	2080 (79.5)	513 (82.5)	7534 (73.8)	

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 6.2. Baseline demographics – VTE cohort, Matched [SNDS]

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

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

[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 6.3. Baseline demographics - MACE cohort, Matched [SNDS]

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

Abbreviations: MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; N = number of patients in the specified category; Std. Diff = standardized difference; TNFi = tumor necrosis factor inhibitor; vs = versus.

[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 6.4. Baseline demographics - Incident Serious Infections cohort, Matched [SNDS]

	Baricitinib Any[b] n = 2979	Baricitinib 4 mg n = 2385	Baricitinib 2 mg n = 591	TNFi[a] n = 2979	Std. Diff. (Any vs TNFi)	Total n = 5958
Age at index date [in years]					0.009	
N (missing)	2979 (0)	2385 (0)	591 (0)	2979 (0)		5958 (0)
Mean (SD)	58.9 (13.4)	56.3 (12.2)	69.5 (12.9)	58.8 (13.4)		58.9 (13.4)
Median	59.0	57.0	72.0	60.0		59.0
Min; Max	[18.0;92.0]	[18.0;90.0]	[20.0;92.0]	[18.0;92.0]		[18.0;92.0]
Age (in years), in categories, n (%)						
[18-30[	66 (2.2)	59 (2.5)	≤ 10	73 (2.5)		139 (2.3)
[30-40[	195 (6.5)	182 (7.6)	13 (2.2)	191 (6.4)		386 (6.5)
[40-50[	424 (14.2)	391 (16.4)	33 (5.6)	415 (13.9)		839 (14.1)
[50-60[	826 (27.7)	763 (32.0)	61 (10.3)	791 (26.6)		1617 (27.1)
[60-65[	411 (13.8)	359 (15.1)	52 (8.8)	420 (14.1)		831 (13.9)
≥65	1057 (35.5)	631 (26.5)	425 (71.9)	1089 (36.6)		2146 (36.0)
Sex, n (%)					-0.001	
Male	607 (20.4)	498 (20.9)	109 (18.4)	608 (20.4)		1215 (20.4)
Female	2372 (79.6)	1887 (79.1)	482 (81.6)	2371 (79.6)		4743 (79.6)

Abbreviations: N = number of patients in the specified category; Std. Diff = standardized difference; TNFi = tumor 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

Table 6.5. Baseline demographics - Hospitalized Tuberculosis Cohort, Matched [SNDS]

	Baricitinib Any[b] n = 3005	Baricitinib 4 mg n = 2396	Baricitinib 2 mg n = 606	TNFi[a] n = 3005	Std. Diff. (Any vs TNFi)	Total n = 6010
Age at index date [in years]					-0.009	
N (missing)	3005 (0)	2396 (0)	606 (0)	3005 (0)		6010 (0)
Mean (SD)	59.0 (13.4)	56.4 (12.2)	69.6 (12.8)	59.2 (13.3)		59.1 (13.3)
Median	59.0	57.0	72.0	60.0		60.0
Min; Max	[18.0;98.0]	[18.0;90.0]	[20.0;98.0]	[18.0;94.0]		[18.0;98.0]
Age (in years), in categories, n (%)						
[18-30[	68 (2.3)	61 (2.5)	≤ 10	65 (2.2)		133 (2.2)
[30-40[	195 (6.5)	182 (7.6)	13 (2.1)	194 (6.5)		389 (6.5)
[40-50[	420 (14.0)	387 (16.2)	33 (5.4)	377 (12.5)		797 (13.3)
[50-60[	829 (27.6)	767 (32.0)	61 (10.1)	843 (28.1)		1672 (27.8)
[60-65[	416 (13.8)	362 (15.1)	53 (8.7)	416 (13.8)		832 (13.8)
≥65	1077 (35.8)	637 (26.6)	439 (72.4)	1110 (36.9)		2187 (36.4)
Sex, n (%)					0.023	
Male	621 (20.7)	506 (21.1)	115 (19.0)	593 (19.7)		1214 (20.2)
Female	2384 (79.3)	1890 (78.9)	491 (81.0)	2412 (80.3)		4796 (79.8)

Abbreviations: N = number of patients in the specified category; Std. Diff = standardized difference; TNFi = tumor 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

Table 6.6. Clinical history at baseline - Unmatched cohort [SNDS]

Characteristics[a]	Baricitinib Any[d] n = 3242	Baricitinib 4 mg n = 2616	Baricitinib 2 mg n = 622	TNFi n = 10202	Std. Diff. (Any vs TNFi)
Clinical conditions during baseline period, n (%)					
Cancer, excluding NMSC	95 (2.9)	69 (2.6)	26 (4.2)	301 (3.0)	-0.001
NMSC	≤ 10	≤ 10	≤ 10	21 (0.2)	-0.005
Chronic lung disease, excluding cystic fibrosis[c]	440 (13.6)	320 (12.2)	119 (19.1)	1049 (10.3)	**0.102**
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	34 (1.0)	18 (0.7)	16 (2.6)	53 (0.5)	0.06
Cardiovascular revascularization procedure	≤ 10	≤ 10	≤ 10	26 (0.3)	0.004
Congestive Heart Failure, hospitalized	15 (0.5)	≤ 10	12 (1.9)	30 (0.3)	0.028
Coronary artery disease	138 (4.3)	90 (3.4)	48 (7.7)	351 (3.4)	0.042
Unstable angina	≤ 10	0 (0.0)	≤ 10	16 (0.2)	-0.041
Ventricular arrhythmia	19 (0.6)	≤ 10	≤ 10	68 (0.7)	-0.01
Stroke	29 (0.9)	20 (0.8)	≤ 10	61 (0.6)	0.035
Hemorrhagic	≤ 10	≤ 10	0 (0.0)	≤ 10	0.001
Ischemic	≤ 10	≤ 10	≤ 10	16 (0.2)	0.026
Unknown	23 (0.7)	17 (0.6)	≤ 10	45 (0.4)	0.036
TIA	≤ 10	0 (0.0)	≤ 10	≤ 10	-0.009
Diabetes Mellitus[c]	321 (9.9)	234 (8.9)	86 (13.8)	884 (8.7)	0.043
Treated insulin dependent	N/A	N/A	N/A	N/A	
Treated non insulin dependent	N/A	N/A	N/A	N/A	
Dyslipidemia (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	

Characteristics[a]	Baricitinib Any[d] n = 3242	Baricitinib 4 mg n = 2616	Baricitinib 2 mg n = 622	TNFi n = 10202	Std. Diff. (Any vs TNFi)
Current hypertension	N/A	N/A	N/A	N/A	
Immune disorders	123 (3.8)	88 (3.4)	35 (5.6)	282 (2.8)	0.058
AIDS/HIV	0 (0.0)	0 (0.0)	0 (0.0)	11 (0.1)	-0.047
Antiphospholipid syndrome	N/A	N/A	N/A	N/A	
SLE	31 (1.0)	26 (1.0)	≤ 10	52 (0.5)	0.052
Primary Sjogren Syndrome	99 (3.1)	67 (2.6)	32 (5.1)	227 (2.2)	0.052
Liver or pancreatic disorder[c]	99 (3.1)	75 (2.9)	23 (3.7)	253 (2.5)	0.035
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)	144 (1.4)	**-0.129**
RA Severity (CIRAS Index)					**-0.236**
Mean (SD)	6.4 (1.4)	6.6 (1.3)	5.8 (1.4)	6.8 (1.6)	
Smoking (not available in SNDS)	N/A	N/A	N/A	N/A	
DMARDs, n (%)					
cDMARDs, during baseline period					
n, total (%)	2163 (66.7)	1782 (68.1)	378 (60.8)	7305 (71.6)	**-0.106**
Mean (SD)	0.7 (0.6)	0.8 (0.6)	0.7 (0.6)	0.8 (0.6)	-0.089
Median	1.0	1.0	1.0	1.0	
Min; Max	[0.0;4.0]	[0.0;4.0]	[0.0;3.0]	[0.0;4.0]	
>1 cDMARD concomitantly	175 (5.4)	141 (5.4)	34 (5.5)	580 (5.7)	-0.013
Hydroxychloroquine	178 (5.5)	139 (5.3)	39 (6.3)	489 (4.8)	0.032
Chloroquine	≤ 10	0 (0.0)	≤ 10	≤ 10	0.001
Azathioprine	13 (0.4)	≤ 10	≤ 10	33 (0.3)	0.013

Characteristics[a]	Baricitinib Any[d] n = 3242	Baricitinib 4 mg n = 2616	Baricitinib 2 mg n = 622	TNFi n = 10202	Std. Diff. (Any vs TNFi)
Leflunomide	410 (12.6)	345 (13.2)	65 (10.5)	1010 (9.9)	0.087
Methotrexate	1679 (51.8)	1390 (53.1)	287 (46.1)	6094 (59.7)	**-0.161**
Mycophenolate mofetil	≤ 10	≤ 10	0 (0.0)	≤ 10	0.001
Sulfasalazine	109 (3.4)	83 (3.2)	26 (4.2)	431 (4.2)	-0.045
Cyclosporin	≤ 10	≤ 10	≤ 10	≤ 10	0.021
Penicillamine	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.020
bDMARDs, during baseline period					
n, total (%)	1982 (61.1)	1661 (63.5)	317 (51.0)	2374 (23.3)	**0.830**
Mean (SD)	0.7 (0.6)	0.7 (0.6)	0.6 (0.6)	0.2 (0.5)	**0.817**
Median	1.0	1.0	1.0	0.0	
Min; Max	[0.0;3.0]	[0.0;3.0]	[0.0;3.0]	[0.0;3.0]	
cDMARDs, concomitant	1076 (33.2)	920 (35.2)	153 (24.6)	1304 (12.8)	**0.500**
Adalimumab[b]	253 (7.8)	221 (8.4)	32 (5.1)	408 (4.0)	**0.162**
Certolizumab pegol[b]	157 (4.8)	139 (5.3)	18 (2.9)	150 (1.5)	**0.194**
Etanercept[b]	359 (11.1)	305 (11.7)	53 (8.5)	664 (6.5)	**0.162**
Golimumab[b]	132 (4.1)	123 (4.7)	≤ 10	146 (1.4)	**0.162**
Infliximab[b]	92 (2.8)	82 (3.1)	≤ 10	185 (1.8)	0.068
Rituximab	122 (3.8)	96 (3.7)	26 (4.2)	38 (0.4)	**0.240**
Sarilumab	47 (1.4)	37 (1.4)	≤ 10	27 (0.3)	**0.129**
Abatacept	556 (17.1)	445 (17.0)	108 (17.4)	490 (4.8)	**0.403**
Tocilizumab	506 (15.6)	432 (16.5)	74 (11.9)	389 (3.8)	**0.407**
Anakinra	16 (0.5)	11 (0.4)	≤ 10	17 (0.2)	0.057

Characteristics[a]	Baricitinib Any[d] n = 3242	Baricitinib 4 mg n = 2616	Baricitinib 2 mg n = 622	TNFi n = 10202	Std. Diff. (Any vs TNFi)
TNFi naïve at baseline	2313 (71.3)	1806 (69.0)	506 (81.4)	8671 (85.0)	**-0.335**
Other prescription medications during baseline period, n (%)					
Antibiotics	1369 (42.2)	1073 (41.0)	294 (47.3)	3880 (38.0)	0.086
Antidiabetic agents	310 (9.6)	229 (8.8)	80 (12.9)	828 (8.1)	0.051
Insulins	118 (3.6)	87 (3.3)	31 (5.0)	299 (2.9)	0.040
Non-insulins	252 (7.8)	189 (7.2)	62 (10.0)	688 (6.7)	0.040
Cardiovascular					
Antithrombotic agents	506 (15.6)	340 (13.0)	165 (26.5)	1399 (13.7)	0.054
Anticoagulant	142 (4.4)	84 (3.2)	58 (9.3)	465 (4.6)	-0.009
Antiplatelet	396 (12.2)	272 (10.4)	123 (19.8)	1002 (9.8)	0.077
Antihypertensives	1119 (34.5)	770 (29.4)	347 (55.8)	2933 (28.7)	**0.124**
Angiotensin converting enzyme inhibitors (ACE)	287 (8.9)	200 (7.6)	87 (14.0)	843 (8.3)	0.021
Angiotensin receptor blockers (ARB)	425 (13.1)	290 (11.1)	135 (21.7)	1186 (11.6)	0.045
Beta blocker	489 (15.1)	326 (12.5)	162 (26.0)	1207 (11.8)	0.095
Calcium channel blocker	336 (10.4)	216 (8.3)	118 (19.0)	812 (8.0)	0.083
Nitrates	31 (1.0)	15 (0.6)	16 (2.6)	86 (0.8)	0.012
Acyclovir	15 (0.5)	≤ 10	≤ 10	59 (0.6)	-0.016
Valacyclovir	123 (3.8)	93 (3.6)	30 (4.8)	318 (3.1)	0.037
Hormonal	406 (12.5)	355 (13.6)	51 (8.2)	1498 (14.7)	-0.063
HRT	245 (7.6)	209 (8.0)	36 (5.8)	684 (6.7)	0.033
Oral Contraceptives	157 (4.8)	143 (5.5)	14 (2.3)	773 (7.6)	**-0.114**

Characteristics[a]	Baricitinib Any[d] n = 3242	Baricitinib 4 mg n = 2616	Baricitinib 2 mg n = 622	TNFi n = 10202	Std. Diff. (Any vs TNFi)
SERMs	≤ 10	≤ 10	≤ 10	34 (0.3)	-0.010
Topic with progestogens and/or estrogens	≤ 10	≤ 10	0 (0.0)	58 (0.6)	-0.051
Lipid-lowering agents	555 (17.1)	394 (15.1)	160 (25.7)	1383 (13.6)	0.099
HMG CoA reductase inhibitors	450 (13.9)	315 (12.0)	134 (21.5)	1118 (11.0)	0.089
Fibrates	43 (1.3)	30 (1.1)	13 (2.1)	113 (1.1)	0.02
Bile acid sequestrants	13 (0.4)	≤ 10	≤ 10	33 (0.3)	0.013
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Other lipid modifying agents	26 (0.8)	19 (0.7)	≤ 10	89 (0.9)	-0.008
Lipid modifying agents, combinations	46 (1.4)	37 (1.4)	≤ 10	100 (1.0)	0.040
Rheumatoid arthritis-related					
Aspirin	41 (1.3)	28 (1.1)	12 (1.9)	117 (1.1)	0.011
Cox-2 Inhibitor	178 (5.5)	156 (6.0)	21 (3.4)	641 (6.3)	-0.034
NSAIDs	1162 (35.8)	995 (38.0)	166 (26.7)	4186 (41.0)	**-0.107**
Glucocorticosteroid	2359 (72.8)	1882 (71.9)	474 (76.2)	6709 (65.8)	**0.152**
Vaccines	958 (29.5)	727 (27.8)	231 (37.1)	3796 (37.2)	**-0.163**
Antineoplastic agents	12 (0.4)	≤ 10	≤ 10	25 (0.2)	0.023

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; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; 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. = standardized difference; TB = tuberculosis; 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

[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

Table 6.7. Clinical characteristics at baseline - VTE cohort, Matched [SNDS]

Characteristics[b]	Baricitinib Any[e] n = 2859	Baricitinib 4 mg n = 2306	Baricitinib 2 mg n = 551	TNFi[a] n = 2859	Std. Diff. (Any vs TNFi)
Clinical conditions during baseline period, n (%)					
Cancer, excluding NMSC	88 (3.1)	63 (2.7)	25 (4.5)	94 (3.3)	-0.012
NMSC	≤ 10	≤ 10	≤ 10	≤ 10	-0.009
Chronic lung disease, excluding cystic fibrosis[d]	381 (13.3)	278 (12.1)	103 (18.7)	325 (11.4)	0.060
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	29 (1.0)	13 (0.6)	16 (2.9)	27 (0.9)	0.007
Cardiovascular revascularization procedure	≤ 10	≤ 10	≤ 10	≤ 10	-0.013
Congestive Heart Failure, hospitalized	12 (0.4)	≤ 10	≤ 10	13 (0.5)	-0.005
Coronary artery disease	127 (4.4)	83 (3.6)	44 (8.0)	121 (4.2)	0.010
Unstable angina	≤ 10	0 (0.0)	≤ 10	≤ 10	-0.043
Ventricular arrhythmia	17 (0.6)	≤ 10	≤ 10	24 (0.8)	-0.029
Stroke	25 (0.9)	17 (0.7)	≤ 10	22 (0.8)	0.012
Hemorrhagic	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.027
Ischemic	≤ 10	≤ 10	≤ 10	≤ 10	0.024
Unknown	21 (0.7)	15 (0.7)	≤ 10	17 (0.6)	0.017
TIA	≤ 10	0 (0.0)	≤ 10	≤ 10	0.000
Diabetes Mellitus[d]	283 (9.9)	205 (8.9)	77 (14.0)	271 (9.5)	0.014
Treated insulin dependent	N/A	N/A	N/A	N/A	
Treated non insulin dependent	N/A	N/A	N/A	N/A	
Dyslipidemia (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	

Characteristics[b]	Baricitinib Any[e] n = 2859	Baricitinib 4 mg n = 2306	Baricitinib 2 mg n = 551	TNFi[a] n = 2859	Std. Diff. (Any vs TNFi)
Current hypertension	N/A	N/A	N/A	N/A	
Immune disorders	104 (3.6)	74 (3.2)	30 (5.4)	108 (3.8)	-0.007
AIDS/HIV	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.053
Antiphospholipid syndrome	N/A	N/A	N/A	N/A	
SLE	27 (0.9)	24 (1.0)	≤ 10	17 (0.6)	0.040
Primary Sjogren Syndrome	83 (2.9)	55 (2.4)	28 (5.1)	92 (3.2)	-0.018
Liver or pancreatic disorder[d]	89 (3.1)	68 (2.9)	20 (3.6)	85 (3.0)	0.008
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)	12 (0.4)	-0.024
RA Severity (CIRAS Index)					0.029
Mean (± SD)	6.5 (1.4)	6.6 (1.3)	5.8 (1.4)	6.4 (1.4)	
Smoking (not available in SNDS)	N/A	N/A	N/A	N/A	
DMARDs, n (%)					
cDMARDs, during baseline period					
n, total (%)	1945 (68.0)	1606 (69.6)	337 (61.2)	1882 (65.8)	0.047
Mean (SD)	0.8 (0.6)	0.8 (0.6)	0.7 (0.7)	0.7 (0.6)	0.064
Median	1.0	1.0	1.0	1.0	
Min; Max	[0.0;4.0]	[0.0;4.0]	[0.0;3.0]	[0.0;3.0]	
>1 cDMARD concomitantly	163 (5.7)	132 (5.7)	31 (5.6)	125 (4.4)	0.061
Hydroxychloroquine	165 (5.8)	128 (5.6)	37 (6.7)	138 (4.8)	0.042
Chloroquine	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000

Characteristics[b]	Baricitinib Any[e] n = 2859	Baricitinib 4 mg n = 2306	Baricitinib 2 mg n = 551	TNFi[a] n = 2859	Std. Diff. (Any vs TNFi)
Azathioprin	≤ 10	≤ 10	≤ 10	≤ 10	-0.006
Leflunomid	361 (12.6)	299 (13.0)	62 (11.3)	310 (10.8)	0.055
Methotrexate	1523 (53.3)	1266 (54.9)	256 (46.5)	1486 (52.0)	0.026
Mycophenolate mofetil	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.015
Sulfasalazin	101 (3.5)	76 (3.3)	25 (4.5)	105 (3.7)	-0.008
Cyclosporin	≤ 10	≤ 10	≤ 10	≤ 10	0.015
Penicillamin	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.037
bDMARDs, during baseline period					
n, total (%)	1599 (55.9)	1351 (58.6)	246 (44.6)	1611 (56.3)	-0.009
Mean (SD)	0.6 (0.6)	0.6 (0.6)	0.5 (0.5)	0.6 (0.6)	-0.011
Median	1.0	1.0	0.0	1.0	
Min; Max	[0.0;3.0]	[0.0;3.0]	[0.0;3.0]	[0.0;3.0]	
cDMARDs, concomitant	910 (31.8)	784 (34.0)	124 (22.5)	847 (29.6)	0.048
Adalimumab[c]	212 (7.4)	182 (7.9)	30 (5.4)	228 (8.0)	-0.021
Certolizumab pegol[c]	119 (4.2)	106 (4.6)	13 (2.4)	122 (4.3)	-0.005
Etanercept[c]	329 (11.5)	279 (12.1)	50 (9.1)	353 (12.3)	-0.026
Golimumab[c]	101 (3.5)	93 (4.0)	≤ 10	109 (3.8)	-0.015
Infliximab[c]	81 (2.8)	72 (3.1)	≤ 10	87 (3.0)	-0.012
Rituximab	59 (2.1)	44 (1.9)	15 (2.7)	37 (1.3)	0.06
Sarilumab	23 (0.8)	17 (0.7)	≤ 10	25 (0.9)	-0.008
Abatacept	433 (15.1)	361 (15.7)	71 (12.9)	420 (14.7)	0.013
Tocilizumab	357 (12.5)	304 (13.2)	53 (9.6)	351 (12.3)	0.006
Anakinra	14 (0.5)	≤ 10	≤ 10	14 (0.5)	0

Characteristics[b]	Baricitinib Any[e] n = 2859	Baricitinib 4 mg n = 2306	Baricitinib 2 mg n = 551	TNFi[a] n = 2859	Std. Diff. (Any vs TNFi)
TNFi naïve at baseline	2054 (71.8)	1609 (69.8)	445 (80.8)	1979 (69.2)	0.058
Other prescription medications during baseline period, n (%)					
Antibiotics	1183 (41.4)	925 (40.1)	256 (46.5)	1147 (40.1)	0.026
Antidiabetic agents	276 (9.7)	203 (8.8)	72 (13.1)	253 (8.8)	0.028
Insulins	102 (3.6)	75 (3.3)	27 (4.9)	81 (2.8)	0.042
Non-insulins	224 (7.8)	168 (7.3)	55 (10.0)	210 (7.3)	0.019
Cardiovascular					
Antithrombotic agents	449 (15.7)	300 (13.0)	148 (26.9)	428 (15.0)	0.02
Anticoagulant	130 (4.5)	75 (3.3)	55 (10.0)	125 (4.4)	0.009
Antiplatelet	349 (12.2)	240 (10.4)	108 (19.6)	322 (11.3)	0.029
Antihypertensives	973 (34.0)	662 (28.7)	310 (56.3)	976 (34.1)	-0.002
Angiotensin converting enzyme inhibitors (ACE)	254 (8.9)	171 (7.4)	83 (15.1)	260 (9.1)	-0.007
Angiotensin receptor blockers (ARB)	362 (12.7)	245 (10.6)	117 (21.2)	420 (14.7)	-0.059
Beta blocker	427 (14.9)	284 (12.3)	142 (25.8)	413 (14.4)	0.014
Calcium channel blocker	286 (10.0)	180 (7.8)	105 (19.1)	282 (9.9)	0.005
Nitrates	25 (0.9)	11 (0.5)	14 (2.5)	32 (1.1)	-0.025
Acyclovir	14 (0.5)	≤ 10	≤ 10	20 (0.7)	-0.027
Valacyclovir	104 (3.6)	77 (3.3)	27 (4.9)	102 (3.6)	0.004
Hormonal	365 (12.8)	321 (13.9)	44 (8.0)	380 (13.3)	-0.016
HRT	213 (7.5)	183 (7.9)	30 (5.4)	218 (7.6)	-0.007
Oral Contraceptives	147 (5.1)	134 (5.8)	13 (2.4)	153 (5.4)	-0.009

Characteristics[b]	Baricitinib Any[e] n = 2859	Baricitinib 4 mg n = 2306	Baricitinib 2 mg n = 551	TNFi[a] n = 2859	Std. Diff. (Any vs TNFi)
SERMs	≤ 10	≤ 10	≤ 10	≤ 10	-0.006
Topic with progestogens and/or estrogens	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.013
Lipid-lowering agents	481 (16.8)	337 (14.6)	143 (26.0)	459 (16.1)	0.021
HMG CoA reductase inhibitors	394 (13.8)	273 (11.8)	120 (21.8)	372 (13.0)	0.023
Fibrates	37 (1.3)	24 (1.0)	13 (2.4)	43 (1.5)	-0.018
Bile acid sequestrants	11 (0.4)	≤ 10	≤ 10	≤ 10	0.032
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Other lipid modifying agents	23 (0.8)	16 (0.7)	≤ 10	27 (0.9)	-0.015
Lipid modifying agents, combinations	38 (1.3)	31 (1.3)	≤ 10	30 (1.0)	0.026
Rheumatoid arthritis-related					
Aspirin	37 (1.3)	25 (1.1)	11 (2.0)	35 (1.2)	0.006
Cox-2 Inhibitor	156 (5.5)	138 (6.0)	18 (3.3)	175 (6.1)	-0.029
NSAIDs	1041 (36.4)	885 (38.4)	156 (28.3)	1104 (38.6)	-0.046
Glucocorticosteroid	2026 (70.9)	1616 (70.1)	408 (74.0)	2002 (70.0)	0.018
Vaccines	855 (29.9)	649 (28.1)	206 (37.4)	830 (29.0)	0.019
Antineoplastic agents	11 (0.4)	≤ 10	≤ 10	12 (0.4)	-0.006

Abbreviations: 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=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 6.8. Clinical characteristics at baseline - MACE cohort, Matched [SNDS]

Characteristics[b]	Baricitinib Any[e] n = 2864	Baricitinib 4 mg n = 2314	Baricitinib 2 mg n = 548	TNFi[a] n = 2864	Std. Diff. (Any vs TNFi)
Clinical conditions during baseline period, n (%)					
Cancer, excluding NMSC	88 (3.1)	62 (2.7)	26 (4.7)	99 (3.5)	-0.022
NMSC	≤ 10	≤ 10	≤ 10	≤ 10	-0.014
Chronic lung disease, excluding cystic fibrosis[d]	392 (13.7)	288 (12.4)	104 (19.0)	334 (11.7)	0.061
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	30 (1.0)	14 (0.6)	16 (2.9)	11 (0.4)	0.079
Cardiovascular revascularization procedure	≤ 10	≤ 10	≤ 10	≤ 10	-0.034
Congestive Heart Failure, hospitalized	≤ 10	≤ 10	≤ 10	11 (0.4)	-0.006
Coronary artery disease	118 (4.1)	76 (3.3)	42 (7.7)	135 (4.7)	-0.029
Unstable angina	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.037
Ventricular arrhythmia	13 (0.5)	≤ 10	≤ 10	19 (0.7)	-0.028
Stroke (LTD or associated diagnosis)	23 (0.8)	17 (0.7)	≤ 10	16 (0.6)	0.030
Hemorrhagic	≤ 10	≤ 10	0 (0.0)	≤ 10	0.000
Ischemic	≤ 10	≤ 10	≤ 10	≤ 10	0.043
Unknown	18 (0.6)	14 (0.6)	≤ 10	14 (0.5)	0.019
TIA	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0.026
Diabetes Mellitus[d]	285 (10.0)	211 (9.1)	73 (13.3)	288 (10.1)	-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	
Dyslipidemia (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	

Characteristics[b]	Baricitinib Any[e] n = 2864	Baricitinib 4 mg n = 2314	Baricitinib 2 mg n = 548	TNFi[a] n = 2864	Std. Diff. (Any vs TNFi)
Current hypertension	N/A	N/A	N/A	N/A	
Immune disorders	100 (3.5)	70 (3.0)	30 (5.5)	112 (3.9)	-0.022
AIDS/HIV	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.037
Antiphospholipid syndrome	N/A	N/A	N/A	N/A	
SLE	25 (0.9)	22 (1.0)	≤ 10	11 (0.4)	0.062
Primary Sjogren Syndrome	80 (2.8)	52 (2.2)	28 (5.1)	101 (3.5)	-0.042
Liver or pancreatic disorder[d]	83 (2.9)	66 (2.9)	17 (3.1)	77 (2.7)	0.013
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)	24 (0.8)	-0.075
RA Severity (CIRAS Index)					0.014
Mean (± SD)	6.5 (1.4)	6.6 (1.3)	5.8 (1.4)	6.5 (1.4)	
Smoking (not available in SNDS)	N/A	N/A	N/A	N/A	
DMARDs, n (%)					
cDMARDs, during baseline period					
n, total (%)	1937 (67.6)	1600 (69.1)	335 (61.1)	1921 (67.1)	0.012
Mean (SD)	0.7 (0.6)	0.8 (0.6)	0.7 (0.6)	0.7 (0.6)	0.031
Median	1.0	1.0	1.0	1.0	
Min; Max	[0.0;4.0]	[0.0;4.0]	[0.0;3.0]	[0.0;4.0]	
>1 cDMARD concomitantly	160 (5.6)	128 (5.5)	32 (5.8)	126 (4.4)	0.055
Hydroxychloroquine	159 (5.6)	125 (5.4)	34 (6.2)	138 (4.8)	0.033
Chloroquine	≤ 10	0 (0.0)	≤ 10	≤ 10	0.000

Characteristics[b]	Baricitinib Any[e] n = 2864	Baricitinib 4 mg n = 2314	Baricitinib 2 mg n = 548	TNFi[a] n = 2864	Std. Diff. (Any vs TNFi)
Azathioprin	≤ 10	≤ 10	≤ 10	≤ 10	0.000
Leflunomid	351 (12.3)	297 (12.8)	54 (9.9)	342 (11.9)	0.010
Methotrexate	1523 (53.2)	1262 (54.5)	259 (47.3)	1509 (52.7)	0.010
Mycophenolate mofetil	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.015
Sulfasalazin	100 (3.5)	76 (3.3)	24 (4.4)	92 (3.2)	0.016
Cyclosporin	≤ 10	≤ 10	≤ 10	≤ 10	0.015
Penicillamin	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
bDMARDs, during baseline period					
n, total (%)	1605 (56.0)	1360 (58.8)	243 (44.3)	1620 (56.6)	-0.011
Mean (SD)	0.6 (0.6)	0.6 (0.6)	0.5 (0.6)	0.6 (0.6)	-0.020
Median	1.0	1.0	0.0	1.0	
Min; Max	[0.0;3.0]	[0.0;3.0]	[0.0;3.0]	[0.0;3.0]	
cDMARDs, concomitant	898 (31.4)	775 (33.5)	121 (22.1)	878 (30.7)	0.015
Adalimumab[c]	213 (7.4)	184 (8.0)	29 (5.3)	234 (8.2)	-0.027
Certolizumab pegol[c]	117 (4.1)	105 (4.5)	12 (2.2)	122 (4.3)	-0.009
Etanercept[c]	321 (11.2)	272 (11.8)	49 (8.9)	362 (12.6)	-0.044
Golimumab[c]	100 (3.5)	93 (4.0)	≤ 10	110 (3.8)	-0.019
Infliximab[c]	77 (2.7)	69 (3.0)	≤ 10	78 (2.7)	-0.002
Rituximab	63 (2.2)	48 (2.1)	15 (2.7)	36 (1.3)	0.072
Sarilumab	30 (1.0)	23 (1.0)	≤ 10	25 (0.9)	0.018
Abatacept	427 (14.9)	347 (15.0)	79 (14.4)	416 (14.5)	0.011
Tocilizumab	364 (12.7)	316 (13.7)	48 (8.8)	360 (12.6)	0.004
Anakinra	12 (0.4)	≤ 10	≤ 10	14 (0.5)	-0.01

Characteristics[b]	Baricitinib Any[e] n = 2864		Baricitinib 4 mg n = 2314		Baricitinib 2 mg n = 548		TNFi[a] n = 2864		Std. Diff. (Any vs TNFi)
TNFi naïve at baseline	2070	(72.3)	1622	(70.1)	447	(81.6)	1978	(69.1)	0.071
Other prescription medications during baseline period, n (%)									
Antibiotics	1193	(41.7)	931	(40.2)	261	(47.6)	1161	(40.5)	0.023
Antidiabetic agents	275	(9.6)	206	(8.9)	68	(12.4)	275	(9.6)	0.000
Insulins	107	(3.7)	78	(3.4)	29	(5.3)	91	(3.2)	0.031
Non-insulins	220	(7.7)	169	(7.3)	50	(9.1)	230	(8.0)	-0.013
Cardiovascular									
Antithrombotic agents	444	(15.5)	299	(12.9)	144	(26.3)	456	(15.9)	-0.012
Anticoagulant	128	(4.5)	74	(3.2)	54	(9.9)	109	(3.8)	0.033
Antiplatelet	345	(12.0)	238	(10.3)	106	(19.3)	367	(12.8)	-0.023
Antihypertensives	965	(33.7)	660	(28.5)	304	(55.5)	1022	(35.7)	-0.042
Angiotensin converting enzyme inhibitors (ACE)	249	(8.7)	172	(7.4)	77	(14.1)	264	(9.2)	-0.018
Angiotensin receptor blockers (ARB)	375	(13.1)	253	(10.9)	122	(22.3)	448	(15.6)	-0.073
Beta blocker	420	(14.7)	280	(12.1)	139	(25.4)	420	(14.7)	0.000
Calcium channel blocker	283	(9.9)	174	(7.5)	108	(19.7)	297	(10.4)	-0.016
Nitrates	23	(0.8)	11	(0.5)	12	(2.2)	36	(1.3)	-0.045
Acyclovir	13	(0.5)	≤ 10		≤ 10		25	(0.9)	-0.052
Valacyclovir	105	(3.7)	78	(3.4)	27	(4.9)	109	(3.8)	-0.007
Hormonal	349	(12.2)	305	(13.2)	44	(8.0)	399	(13.9)	-0.052
HRT	203	(7.1)	173	(7.5)	30	(5.5)	231	(8.1)	-0.037
Oral Contraceptives	142	(5.0)	129	(5.6)	13	(2.4)	157	(5.5)	-0.024

Characteristics[b]	Baricitinib Any[e] n = 2864	Baricitinib 4 mg n = 2314	Baricitinib 2 mg n = 548	TNFi[a] n = 2864	Std. Diff. (Any vs TNFi)
SERMs	≤ 10	≤ 10	≤ 10	≤ 10	-0.006
Topic with progestogens and/or estrogens	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.014
Lipid-lowering agents	478 (16.7)	336 (14.5)	141 (25.7)	498 (17.4)	-0.019
HMG CoA reductase inhibitors	394 (13.8)	275 (11.9)	118 (21.5)	410 (14.3)	-0.016
Fibrates	32 (1.1)	20 (0.9)	12 (2.2)	41 (1.4)	-0.028
Bile acid sequestrants	≤ 10	≤ 10	≤ 10	≤ 10	0.000
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Other lipid modifying agents	22 (0.8)	15 (0.6)	≤ 10	33 (1.2)	-0.039
Lipid modifying agents, combinations	41 (1.4)	33 (1.4)	≤ 10	37 (1.3)	0.012
Rheumatoid arthritis-related					
Aspirin	34 (1.2)	22 (1.0)	11 (2.0)	37 (1.3)	-0.01
Cox-2 Inhibitor	156 (5.4)	138 (6.0)	17 (3.1)	168 (5.9)	-0.018
NSAIDs	1047 (36.6)	894 (38.6)	153 (27.9)	1096 (38.3)	-0.035
Glucocorticosteroid	2034 (71.0)	1627 (70.3)	406 (74.1)	2033 (71.0)	0.001
Vaccines	864 (30.2)	658 (28.4)	206 (37.6)	857 (29.9)	0.005
Antineoplastic agents	12 (0.4)	≤ 10	≤ 10	12 (0.4)	0.000

Abbreviations: MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; N = number of patients in the specified category; Std. Diff = standardized difference; TNFi = tumor necrosis factor inhibitor; 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=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 6.9. Clinical Characteristics at baseline - Incident Serious Infection cohort, Matched [SNDS]

Characteristics[b]	Baricitinib Any[e] n = 2979	Baricitinib 4 mg n = 2385	Baricitinib 2 mg n = 591	TNFi[a] n = 2979	Std. Diff. (Any vs TNFi)
Clinical conditions during baseline period, n (%)					
Cancer, excluding NMSC	96 (3.2)	67 (2.8)	29 (4.9)	104 (3.5)	-0.015
NMSC	≤ 10	≤ 10	≤ 10	≤ 10	0.018
Chronic lung disease, excluding cystic fibrosis[d]	409 (13.7)	296 (12.4)	113 (19.1)	371 (12.5)	0.038
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	66 (2.2)	32 (1.3)	34 (5.8)	40 (1.3)	0.066
Cardiovascular revascularization procedure	≤ 10	≤ 10	≤ 10	≤ 10	-0.026
Congestive Heart Failure, hospitalized	16 (0.5)	≤ 10	11 (1.9)	11 (0.4)	0.025
Coronary artery disease	139 (4.7)	94 (3.9)	45 (7.6)	121 (4.1)	0.03
Unstable angina	≤ 10	0 (0.0)	≤ 10	≤ 10	-0.055
Ventricular arrhythmia	21 (0.7)	≤ 10	12 (2.0)	30 (1.0)	-0.033
Stroke	31 (1.0)	22 (0.9)	≤ 10	28 (0.9)	0.01
Hemorrhagic	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.015
Ischemic	≤ 10	≤ 10	≤ 10	≤ 10	0.012
Unknown	24 (0.8)	18 (0.8)	≤ 10	19 (0.6)	0.02
TIA	≤ 10	0 (0.0)	≤ 10	≤ 10	-0.015
Diabetes Mellitus[d]	299 (10.0)	213 (8.9)	85 (14.4)	296 (9.9)	0.003
Treated insulin dependent	N/A	N/A	N/A	N/A	
Treated non insulin dependent	N/A	N/A	N/A	N/A	
Dyslipidemia (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	

Characteristics[b]	Baricitinib Any[e] n = 2979	Baricitinib 4 mg n = 2385	Baricitinib 2 mg n = 591	TNFi[a] n = 2979	Std. Diff. (Any vs TNFi)
Current hypertension	N/A	N/A	N/A	N/A	
Immune disorders	114 (3.8)	82 (3.4)	32 (5.4)	109 (3.7)	0.009
AIDS/HIV	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.026
Antiphospholipid syndrome	N/A	N/A	N/A	N/A	
SLE	32 (1.1)	28 (1.2)	≤ 10	12 (0.4)	0.079
Primary Sjogren Syndrome	88 (3.0)	58 (2.4)	30 (5.1)	99 (3.3)	-0.021
Liver or pancreatic disorder[d]	90 (3.0)	68 (2.9)	21 (3.6)	93 (3.1)	-0.006
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)	21 (0.7)	-0.063
RA Severity (CIRAS Index)					-0.003
Mean (± SD)	6.4 (1.4)	6.6 (1.3)	5.7 (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 (%)	2015 (67.6)	1658 (69.5)	354 (59.9)	2005 (67.3)	0.007
Mean (SD)	0.8 (0.6)	0.8 (0.6)	0.7 (0.6)	0.7 (0.6)	0.026
Median	1.0	1.0	1.0	1.0	
Min; Max	[0.0;4.0]	[0.0;4.0]	[0.0;3.0]	[0.0;4.0]	
>1 cDMARD concomitantly	166 (5.6)	133 (5.6)	33 (5.6)	123 (4.1)	0.067
Hydroxychloroquine	170 (5.7)	131 (5.5)	39 (6.6)	120 (4.0)	0.078
Chloroquine	≤ 10	0 (0.0)	≤ 10	≤ 10	0.00

Characteristics[b]	Baricitinib Any[e] n = 2979	Baricitinib 4 mg n = 2385	Baricitinib 2 mg n = 591	TNFi[a] n = 2979	Std. Diff. (Any vs TNFi)
Azathioprin	12 (0.4)	≤ 10	≤ 10	≤ 10	0.011
Leflunomid	371 (12.5)	312 (13.1)	59 (10.0)	381 (12.8)	-0.01
Methotrexate	1575 (52.9)	1301 (54.5)	272 (46.0)	1585 (53.2)	-0.007
Mycophenolate mofetil	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.015
Sulfasalazin	105 (3.5)	80 (3.4)	25 (4.2)	91 (3.1)	0.026
Cyclosporin	≤ 10	≤ 10	≤ 10	0 (0.0)	0.037
Penicillamin	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.026
bDMARDs, during baseline period					
n, total (%)	1657 (55.6)	1397 (58.6)	257 (43.5)	1670 (56.1)	-0.009
Mean (SD)	0.6 (0.6)	0.6 (0.6)	0.5 (0.5)	0.6 (0.6)	-0.016
Median	1.0	1.0	0.0	1.0	
Min; Max	[0.0;3.0]	[0.0;3.0]	[0.0;2.0]	[0.0;3.0]	
cDMARDs, concomitant	946 (31.8)	815 (34.2)	128 (21.7)	921 (30.9)	0.018
Adalimumab[c]	222 (7.5)	195 (8.2)	27 (4.6)	241 (8.1)	-0.024
Certolizumab pegol[c]	114 (3.8)	101 (4.2)	13 (2.2)	124 (4.2)	-0.017
Etanercept[c]	329 (11.0)	281 (11.8)	48 (8.1)	357 (12.0)	-0.03
Golimumab[c]	108 (3.6)	100 (4.2)	≤ 10	107 (3.6)	0.002
Infliximab[c]	84 (2.8)	77 (3.2)	≤ 10	86 (2.9)	-0.004
Rituximab	53 (1.8)	40 (1.7)	13 (2.2)	36 (1.2)	0.047
Sarilumab	35 (1.2)	28 (1.2)	≤ 10	28 (0.9)	0.023
Abatacept	451 (15.1)	360 (15.1)	89 (15.1)	448 (15.0)	0.003
Tocilizumab	375 (12.6)	321 (13.5)	54 (9.1)	368 (12.4)	0.007
Anakinra	12 (0.4)	≤ 10	≤ 10	16 (0.5)	-0.02

Characteristics[b]	Baricitinib Any[e] n = 2979	Baricitinib 4 mg n = 2385	Baricitinib 2 mg n = 591	TNFi[a] n = 2979	Std. Diff. (Any vs TNFi)
TNFi naïve at baseline	2160 (72.5)	1668 (69.9)	491 (83.1)	2085 (70.0)	0.056
Other prescription medications during baseline period, n (%)					
Antibiotics	1260 (42.3)	973 (40.8)	285 (48.2)	1225 (41.1)	0.024
Antidiabetic agents	287 (9.6)	207 (8.7)	79 (13.4)	281 (9.4)	0.007
Insulins	113 (3.8)	81 (3.4)	32 (5.4)	103 (3.5)	0.018
Non-insulins	233 (7.8)	171 (7.2)	61 (10.3)	231 (7.8)	0.003
Cardiovascular					
Antithrombotic agents	575 (19.3)	377 (15.8)	197 (33.3)	517 (17.4)	0.050
Anticoagulant	257 (8.6)	154 (6.5)	103 (17.4)	223 (7.5)	0.042
Antiplatelet	367 (12.3)	249 (10.4)	117 (19.8)	329 (11.0)	0.040
Antihypertensives	1064 (35.7)	724 (30.4)	339 (57.4)	1043 (35.0)	0.015
Angiotensin converting enzyme inhibitors (ACE)	284 (9.5)	195 (8.2)	89 (15.1)	288 (9.7)	-0.005
Angiotensin receptor blockers (ARB)	403 (13.5)	273 (11.4)	130 (22.0)	430 (14.4)	-0.026
Beta blocker	483 (16.2)	314 (13.2)	168 (28.4)	440 (14.8)	0.040
Calcium channel blocker	298 (10.0)	187 (7.8)	110 (18.6)	295 (9.9)	0.003
Nitrates	29 (1.0)	13 (0.5)	16 (2.7)	28 (0.9)	0.003
Acyclovir	15 (0.5)	≤ 10	≤ 10	23 (0.8)	-0.034
Valacyclovir	108 (3.6)	82 (3.4)	26 (4.4)	109 (3.7)	-0.002
Hormonal	363 (12.2)	318 (13.3)	45 (7.6)	394 (13.2)	-0.031
HRT	210 (7.0)	180 (7.5)	30 (5.1)	220 (7.4)	-0.013
Oral Contraceptives	145 (4.9)	132 (5.5)	13 (2.2)	160 (5.4)	-0.023

Characteristics[b]	Baricitinib Any[e] n = 2979	Baricitinib 4 mg n = 2385	Baricitinib 2 mg n = 591	TNFi[a] n = 2979	Std. Diff. (Any vs TNFi)
SERMs	≤ 10	≤ 10	≤ 10	14 (0.5)	-0.027
Topic with progestogens and/or estrogens	≤ 10	≤ 10	≤ 10	≤ 10	0.000
Lipid-lowering agents	523 (17.6)	368 (15.4)	154 (26.1)	484 (16.2)	0.035
HMG CoA reductase inhibitors	426 (14.3)	294 (12.3)	131 (22.2)	396 (13.3)	0.029
Fibrates	41 (1.4)	28 (1.2)	13 (2.2)	40 (1.3)	0.003
Bile acid sequestrants	11 (0.4)	≤ 10	≤ 10	≤ 10	0.012
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Other lipid modifying agents	27 (0.9)	19 (0.8)	≤ 10	27 (0.9)	0.000
Lipid modifying agents, combinations	42 (1.4)	36 (1.5)	≤ 10	35 (1.2)	0.021
Rheumatoid arthritis-related					
Aspirin	36 (1.2)	24 (1.0)	11 (1.9)	40 (1.3)	-0.012
Cox-2 Inhibitor	155 (5.2)	135 (5.7)	19 (3.2)	175 (5.9)	-0.029
NSAIDs	1060 (35.6)	908 (38.1)	152 (25.7)	1133 (38.0)	-0.051
Glucocorticosteroid	2137 (71.7)	1687 (70.7)	448 (75.8)	2148 (72.1)	-0.008
Vaccines	913 (30.6)	683 (28.6)	230 (38.9)	910 (30.5)	0.002
Antineoplastic agents	11 (0.4)	≤ 10	≤ 10	12 (0.4)	-0.005

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 6.10. Clinical Characteristics during at baseline - Hospitalized Tuberculosis Cohort, Matched [SNDS]

Characteristics[b]	Baricitinib Any[e] n = 3005	Baricitinib 4 mg n = 2396	Baricitinib 2 mg n = 606	TNFi[b] n = 3005	Std. Diff. (Any vs TNFi)
Clinical conditions during baseline period, n (%)					
Cancer, excluding NMSC	99 (3.3)	69 (2.9)	30 (5.0)	101 (3.4)	-0.004
NMSC	≤ 10	≤ 10	≤ 10	≤ 10	-0.007
Chronic lung disease, excluding cystic fibrosis[d]	426 (14.2)	307 (12.8)	118 (19.5)	362 (12.0)	0.063
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	73 (2.4)	31 (1.3)	42 (6.9)	50 (1.7)	0.054
Cardiovascular revascularization procedure	≤ 10	≤ 10	≤ 10	11 (0.4)	-0.018
Congestive Heart Failure, hospitalized	17 (0.6)	≤ 10	12 (2.0)	22 (0.7)	-0.021
Coronary artery disease	139 (4.6)	91 (3.8)	48 (7.9)	144 (4.8)	-0.008
Unstable angina	≤ 10	0 (0.0)	≤ 10	≤ 10	-0.06
Ventricular arrhythmia	24 (0.8)	11 (0.5)	13 (2.1)	34 (1.1)	-0.034
Stroke (LTD or associated diagnosis)	31 (1.0)	21 (0.9)	≤ 10	28 (0.9)	0.01
Hemorrhagic	≤ 10	≤ 10	0 (0.0)	≤ 10	0.00
Ischemic	11 (0.4)	≤ 10	≤ 10	≤ 10	0.012
Unknown	25 (0.8)	19 (0.8)	≤ 10	19 (0.6)	0.023
TIA	≤ 10	0 (0.0)	≤ 10	≤ 10	-0.018
Diabetes Mellitus[d]	307 (10.2)	220 (9.2)	86 (14.2)	305 (10.1)	0.002
Treated insulin dependent	N/A	N/A	N/A	N/A	
Treated non insulin dependent	N/A	N/A	N/A	N/A	
Dyslipidemia (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	

Characteristics[b]	Baricitinib Any[e] n = 3005	Baricitinib 4 mg n = 2396	Baricitinib 2 mg n = 606	TNFi[b] n = 3005	Std. Diff. (Any vs TNFi)
Current hypertension	N/A	N/A	N/A	N/A	
Immune disorders	109 (3.6)	73 (3.0)	36 (5.9)	115 (3.8)	-0.011
AIDS/HIV	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.045
Antiphospholipid syndrome	N/A	N/A	N/A	N/A	
SLE	25 (0.8)	21 (0.9)	≤ 10	12 (0.4)	0.055
Primary Sjogren Syndrome	89 (3.0)	56 (2.3)	33 (5.4)	102 (3.4)	-0.025
Liver or pancreatic disorder[d]	97 (3.2)	72 (3.0)	25 (4.1)	82 (2.7)	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)	15 (0.5)	-0.038
RA Severity (CIRAS Index)					0.020
Mean (± SD)	6.4 (1.4)	6.6 (1.3)	5.7 (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 (%)	2033 (67.7)	1666 (69.5)	365 (60.2)	2019 (67.2)	0.010
Mean (SD)	0.7 (0.6)	0.8 (0.6)	0.7 (0.6)	0.7 (0.6)	0.026
Median	1.0	1.0	1.0	1.0	
Min; Max	[0.0;4.0]	[0.0;4.0]	[0.0;3.0]	[0.0;4.0]	
>1 cDMARD concomitantly	169 (5.6)	133 (5.6)	36 (5.9)	127 (4.2)	0.065
Hydroxychloroquine	169 (5.6)	130 (5.4)	39 (6.4)	128 (4.3)	0.063
Chloroquine	≤ 10	0 (0.0)	≤ 10	≤ 10	0.000

Characteristics[b]	Baricitinib Any[e] n = 3005	Baricitinib 4 mg n = 2396	Baricitinib 2 mg n = 606	TNFi[b] n = 3005	Std. Diff. (Any vs TNFi)
Azathioprin	≤ 10	≤ 10	≤ 10	13 (0.4)	-0.022
Leflunomid	376 (12.5)	314 (13.1)	62 (10.2)	368 (12.2)	0.008
Methotrexate	1586 (52.8)	1306 (54.5)	278 (45.9)	1609 (53.5)	-0.015
Mycophenolate mofetil	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.015
Sulfasalazin	106 (3.5)	81 (3.4)	25 (4.1)	82 (2.7)	0.046
Cyclosporin	≤ 10	≤ 10	≤ 10	0 (0.0)	0.037
Penicillamin	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.026
bDMARDs, during baseline period					
n, total (%)	1674 (55.7)	1406 (58.7)	265 (43.7)	1680 (55.9)	-0.004
Mean (SD)	0.6 (0.6)	0.6 (0.6)	0.5 (0.5)	0.6 (0.6)	-0.011
Median	1.0	1.0	0.0	1.0	
Min; Max	[0.0;3.0]	[0.0;3.0]	[0.0;2.0]	[0.0;3.0]	
cDMARDs, concomitant	956 (31.8)	821 (34.3)	133 (21.9)	914 (30.4)	0.030
Adalimumab[c]	226 (7.5)	194 (8.1)	32 (5.3)	244 (8.1)	-0.022
Certolizumab pegol[c]	115 (3.8)	102 (4.3)	13 (2.1)	121 (4.0)	-0.010
Etanercept[c]	332 (11.0)	279 (11.6)	52 (8.6)	372 (12.4)	-0.041
Golimumab[c]	113 (3.8)	105 (4.4)	≤ 10	109 (3.6)	0.007
Infliximab[c]	85 (2.8)	76 (3.2)	≤ 10	80 (2.7)	0.010
Rituximab	61 (2.0)	47 (2.0)	14 (2.3)	37 (1.2)	0.063
Sarilumab	25 (0.8)	20 (0.8)	≤ 10	25 (0.8)	0.000
Abatacept	449 (14.9)	361 (15.1)	86 (14.2)	445 (14.8)	0.004
Tocilizumab	381 (12.7)	326 (13.6)	55 (9.1)	372 (12.4)	0.009
Anakinra	15 (0.5)	≤ 10	≤ 10	16 (0.5)	-0.005

Characteristics[b]	Baricitinib Any[e] n = 3005	Baricitinib 4 mg n = 2396	Baricitinib 2 mg n = 606	TNFi[b] n = 3005	Std. Diff. (Any vs TNFi)
TNFi naïve at baseline	2173 (72.3)	1676 (69.9)	496 (81.8)	2100 (69.9)	0.054
Other prescription medications during baseline period, n (%)					
Antibiotics	1277 (42.5)	980 (40.9)	296 (48.8)	1254 (41.7)	0.016
Antidiabetic agents	298 (9.9)	218 (9.1)	79 (13.0)	283 (9.4)	0.017
Insulins	115 (3.8)	82 (3.4)	33 (5.4)	92 (3.1)	0.042
Non-insulins	241 (8.0)	180 (7.5)	60 (9.9)	241 (8.0)	0.000
Cardiovascular					
Antithrombotic agents	582 (19.4)	378 (15.8)	203 (33.5)	534 (17.8)	0.041
Anticoagulant	263 (8.8)	152 (6.3)	111 (18.3)	229 (7.6)	0.041
Antiplatelet	367 (12.2)	250 (10.4)	116 (19.1)	345 (11.5)	0.023
Antihypertensives	1075 (35.8)	729 (30.4)	344 (56.8)	1096 (36.5)	-0.015
Angiotensin converting enzyme inhibitors (ACE)	284 (9.5)	196 (8.2)	88 (14.5)	303 (10.1)	-0.021
Angiotensin receptor blockers (ARB)	397 (13.2)	268 (11.2)	129 (21.3)	451 (15.0)	-0.052
Beta blocker	492 (16.4)	316 (13.2)	175 (28.9)	478 (15.9)	0.013
Calcium channel blocker	318 (10.6)	194 (8.1)	122 (20.1)	320 (10.6)	-0.002
Nitrates	31 (1.0)	13 (0.5)	18 (3.0)	33 (1.1)	-0.007
Acyclovir	15 (0.5)	≤ 10	≤ 10	29 (1.0)	-0.055
Valacyclovir	107 (3.6)	80 (3.3)	27 (4.5)	109 (3.6)	-0.004
Hormonal	362 (12.0)	315 (13.1)	47 (7.8)	395 (13.1)	-0.033
HRT	211 (7.0)	179 (7.5)	32 (5.3)	227 (7.6)	-0.021
Oral Contraceptives	144 (4.8)	131 (5.5)	13 (2.1)	157 (5.2)	-0.020

Characteristics[b]	Baricitinib Any[e] n = 3005	Baricitinib 4 mg n = 2396	Baricitinib 2 mg n = 606	TNFi[b] n = 3005	Std. Diff. (Any vs TNFi)
SERMs	≤ 10	≤ 10	≤ 10	12 (0.4)	-0.023
Topic with progestogens and/or estrogens	≤ 10	≤ 10	≤ 10	≤ 10	-0.006
Lipid-lowering agents	531 (17.7)	370 (15.4)	160 (26.4)	527 (17.5)	0.004
HMG CoA reductase inhibitors	434 (14.4)	299 (12.5)	134 (22.1)	428 (14.2)	0.006
Fibrates	40 (1.3)	26 (1.1)	14 (2.3)	38 (1.3)	0.006
Bile acid sequestrants	13 (0.4)	≤ 10	≤ 10	14 (0.5)	-0.005
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Other lipid modifying agents	24 (0.8)	16 (0.7)	≤ 10	40 (1.3)	-0.052
Lipid modifying agents, combinations	43 (1.4)	36 (1.5)	≤ 10	38 (1.3)	0.014
Rheumatoid arthritis-related					
Aspirin	36 (1.2)	22 (0.9)	13 (2.1)	40 (1.3)	-0.012
Cox-2 Inhibitor	162 (5.4)	141 (5.9)	20 (3.3)	168 (5.6)	-0.009
NSAIDs	1066 (35.5)	912 (38.1)	153 (25.2)	1132 (37.7)	-0.046
Glucocorticosteroid	2148 (71.5)	1685 (70.3)	461 (76.1)	2135 (71.0)	0.010
Vaccines	933 (31.0)	693 (28.9)	240 (39.6)	925 (30.8)	0.006
Antineoplastic agents	11 (0.4)	≤ 10	≤ 10	11 (0.4)	0.000

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 6.11. Baseline healthcare resource utilization during baseline period - Unmatched cohort [SNDS]

Type of resource use during baseline period[a]	Baricitinib Any[c] n = 3242	Baricitinib 4 mg n = 2616	Baricitinib 2 mg n = 622	TNFi n = 10202	Std. Diff. (Any vs TNFi)
Physician Office Visits (rheumatologist visits excluded)					
n, patients (%)	1983 (61.2)	1553 (59.4)	430 (69.1)	6425 (63.0)	-0.037
n, events	5616	4291	1325	20308	
Mean (SD)	1.7 (2.6)	1.6 (2.6)	2.1 (2.6)	2.0 (3.1)	-0.091
Median	1.0	1.0	1.0	1.0	
Min; Max	[0.0;41.0]	[0.0;41.0]	[0.0;19.0]	[0.0;85.0]	
Rheumatologist Visits					
n, patients (%)	2052 (63.3)	1673 (64.0)	377 (60.6)	6519 (63.9)	-0.013
n, events	4585	3692	881	14757	
Mean (SD)	1.4 (1.5)	1.4 (1.5)	1.4 (1.6)	1.4 (1.5)	-0.021
Median	1.0	1.0	1.0	1.0	
Min; Max	[0.0;11.0]	[0.0;9.0]	[0.0;11.0]	[0.0;13.0]	
Other Outpatient Visits					
n, patients (%)	3024 (93.3)	2418 (92.4)	603 (96.9)	9311 (91.3)	0.075
n, events	64488	44196	20175	156961	
Mean (SD)	19.9 (33.3)	16.9 (28.3)	32.4 (47.0)	15.4 (26.3)	**0.15**
Median	8.0	7.0	15.0	7.0	
Min; Max	[0.0;322.0]	[0.0;322.0]	[0.0;266.0]	[0.0;283.0]	
Inpatient Visits[b]					
n, patients (%)	1593 (49.1)	1233 (47.1)	358 (57.6)	4802 (47.1)	0.041
n, events	3984	3099	875	8274	

Type of resource use during baseline period[a]	Baricitinib Any[c] n = 3242	Baricitinib 4 mg n = 2616	Baricitinib 2 mg n = 622	TNFi n = 10202	Std. Diff. (Any vs TNFi)
Mean (SD)	1.2 (1.9)	1.2 (1.8)	1.4 (1.9)	0.8 (1.6)	**0.238**
Median	0.0	0.0	1.0	0.0	
Min; Max	[0.0;14.0]	[0.0;14.0]	[0.0;12.0]	[0.0;76.0]	
ED Visits	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 6.12. Baseline healthcare resource utilization during baseline period - VTE cohort, Matched [SNDS]

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

Type of resource use during baseline period[b]	Baricitinib Any[d] n = 2859	Baricitinib 4 mg n = 2306	Baricitinib 2 mg n = 551	TNFi[a] n = 2859	Std. Diff. (Any vs TNFi)
Mean (SD)	1.1 (1.7)	1.0 (1.7)	1.3 (1.8)	1.1 (2.4)	0.010
Median	0.0	0.0	1.0	0.0	
Min; Max	[0.0;14.0]	[0.0;14.0]	[0.0;12.0]	[0.0;76.0]	
ED Visits	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=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 6.13. Baseline healthcare resource utilization during baseline period - MACE cohort, Matched [SNDS]

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

Type of resource use during baseline period[b]	Baricitinib Any[d] n = 2864	Baricitinib 4 mg n = 2314	Baricitinib 2 mg n = 548	TNFi[a] n = 2864	Std. Diff. (Any vs TNFi)
Mean (SD)	1.1 (1.8)	1.1 (1.7)	1.3 (1.8)	1.0 (2.0)	0.036
Median	0.0	0.0	1.0	0.0	
Min; Max	[0.0;14.0]	[0.0;14.0]	[0.0;12.0]	[0.0;56.0]	
ED Visits	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 6.14. Baseline healthcare resource utilization during baseline period – Incident Serious Infection Cohort, Matched [SNDS]

Type of resource use during baseline period[b]	Baricitinib Any[d] n = 2979	Baricitinib 4 mg n = 2385	Baricitinib 2 mg n = 591	TNFi[a] n = 2979	Std. Diff. (Any vs TNFi)
Physician Office Visits (rheumatologist visits excluded)					
n, patients (%)	1845 (61.9)	1438 (60.3)	407 (68.9)	1845 (61.9)	0.000
n, events	5348.0	4021.0	1327.0	5456.0	
Mean (SD)	1.8 (2.7)	1.7 (2.6)	2.2 (2.8)	1.8 (2.8)	-0.013
Median	1.0	1.0	1.0	1.0	
Min; Max	[0.0;41.0]	[0.0;41.0]	[0.0;20.0]	[0.0;47.0]	
Rheumatologist Visits					
n, patients (%)	1859 (62.4)	1513 (63.4)	345 (58.4)	1891 (63.5)	-0.022
n, events	4135.0	3354.0	775.0	4190.0	
Mean (SD)	1.4 (1.5)	1.4 (1.5)	1.3 (1.6)	1.4 (1.5)	-0.012
Median	1.0	1.0	1.0	1.0	
Min; Max	[0.0;11.0]	[0.0;9.0]	[0.0;11.0]	[0.0;13.0]	
Other Outpatient Visits					
n, patients (%)	2773 (93.1)	2200 (92.2)	571 (96.6)	2745 (92.1)	0.036
n, events	61251.0	40239.0	20897.0	53666.0	
Mean (SD)	20.6 (34.7)	16.9 (28.3)	35.4 (50.7)	18.0 (30.3)	0.078
Median	8.0	7.0	16.0	8.0	
Min; Max	[0.0;322.0]	[0.0;322.0]	[0.0;266.0]	[0.0;280.0]	
Inpatient Visits[c]					
n, patients (%)	1429 (48.0)	1085 (45.5)	342 (57.9)	1428 (47.9)	0.001
n, events	3383.0	2590.0	783.0	3156.0	

Type of resource use during baseline period[b]	Baricitinib Any[d] n = 2979	Baricitinib 4 mg n = 2385	Baricitinib 2 mg n = 591	TNFi[a] n = 2979	Std. Diff. (Any vs TNFi)
Mean (SD)	1.1 (1.8)	1.1 (1.8)	1.3 (1.8)	1.1 (1.9)	0.041
Median	0.0	0.0	1.0	0.0	
Min; Max	[0.0;14.0]	[0.0;14.0]	[0.0;12.0]	[0.0;51.0]	
ED Visits	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 6.15. Baseline healthcare resource utilization during baseline period - Hospitalized Tuberculosis Cohort, Matched [SNDS]

Type of resource use during baseline period[b]	Baricitinib Any[d] n = 3005	Baricitinib 4 mg n = 2396	Baricitinib 2 mg n = 606	TNFi[a] n = 3005	Std. Diff. (Any vs TNFi)
Physician Office Visits (rheumatologist visits excluded)					
n, patients (%)	1867 (62.1)	1445 (60.3)	422 (69.6)	1866 (62.1)	0.001
n, events	5378.0	4016.0	1362.0	5499.0	
Mean (SD)	1.8 (2.6)	1.7 (2.6)	2.2 (2.7)	1.8 (2.9)	-0.015
Median	1.0	1.0	1.0	1.0	
Min; Max	[0.0;41.0]	[0.0;41.0]	[0.0;19.0]	[0.0;47.0]	
Rheumatologist Visits					
n, patients (%)	1885 (62.7)	1525 (63.6)	358 (59.1)	1908 (63.5)	-0.016
n, events	4187.0	3363.0	812.0	4298.0	
Mean (SD)	1.4 (1.5)	1.4 (1.5)	1.3 (1.6)	1.4 (1.5)	-0.024
Median	1.0	1.0	1.0	1.0	
Min; Max	[0.0;9.0]	[0.0;9.0]	[0.0;8.0]	[0.0;13.0]	
Other Outpatient Visits					
n, patients (%)	2800 (93.2)	2212 (92.3)	586 (96.7)	2777 (92.4)	0.030
n, events	61941.0	41006.0	20894.0	55122.0	
Mean (SD)	20.6 (34.9)	17.1 (29.3)	34.5 (49.0)	18.3 (31.3)	0.069
Median	8.0	7.0	16.0	8.0	
Min; Max	[0.0;322.0]	[0.0;322.0]	[0.0;247.0]	[0.0;280.0]	
Inpatient Visits[c]					
n, patients (%)	1455 (48.4)	1101 (46.0)	353 (58.3)	1430 (47.6)	0.017

Type of resource use during baseline period[b]	Baricitinib Any[d] n = 3005	Baricitinib 4 mg n = 2396	Baricitinib 2 mg n = 606	TNFi[a] n = 3005	Std. Diff. (Any vs TNFi)
n, events	3474.0	2664.0	807.0	3171.0	
Mean (SD)	1.2 (1.8)	1.1 (1.8)	1.3 (1.8)	1.1 (1.9)	0.054
Median	0.0	0.0	1.0	0.0	
Min; Max	[0.0;14.0]	[0.0;14.0]	[0.0;12.0]	[0.0;51.0]	
ED Visits	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 6.16. 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	3244		2617		623		10212		
VTE, n events (%)	≤ 10		≤ 10		≤ 10		≤ 10		-0.013
MACE, N population	3244		2617		623		10212		
MACE, n events (%)	≤ 10		≤ 10		≤ 10		37	(0.4)	-0.021
Serious infection, N population	3398		2708		686		10515		
Serious infection, n events (%)	32	(0.9)	12	(0.4)	20	(2.9)	64	(0.6)	0.038
Hospitalized Tuberculosis, N population	3398		2708		686		10515		
Hospitalized Tuberculosis, n events (%)	0	(0.0)	0	(0.0)	0	(0.0)	≤ 10		-0.024

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

1.3 CHARACTERISTICS OF PATIENTS UNDER FOLLOW-UP

Table 6.17. Duration of follow-up period (in days) - Unmatched cohort [SNDS]

	Baricitinib [a] n = 3242	Baricitinib 4 mg n = 2616	Baricitinib 2 mg n = 622	TNFi n = 10202	Std. Diff. (Any vs TNFi)
Duration of follow-up period (in days)					
N (missing)	3242 (0)	2616 (0)	622 (0)	10202 (0)	
Mean (SD)	238.1 (196.5)	242.0 (197.6)	221.1 (190.7)	239.9 (204.7)	-0.009
Median	174.0	178.0	150.5	170.0	
Min; Max	[0.0;831.0]	[1.0;831.0]	[0.0;826.0]	[0.0;851.0]	
Reason for censoring, n (%)					
Switch	489 (15.1)	411 (15.7)	76 (12.2)	1522 (14.9)	0.005
Discontinuation	1096 (33.8)	855 (32.7)	240 (38.6)	4689 (46.0)	**-0.250**
Outcome	23 (0.7)	16 (0.6)	≤ 10	29 (0.3)	0.061
Death	11 (0.3)	≤ 10	≤ 10	15 (0.1)	0.039
End of study (31/12/2019)	1623 (50.1)	1329 (50.8)	293 (47.1)	3947 (38.7)	**0.230**

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 6.18. Duration of follow-up period (in days) - VTE cohort, Matched [SNDS]

	Baricitinib [b] n = 2859	Baricitinib 4 mg n = 2306	Baricitinib 2 mg n = 551	TNFi [a] n = 2859	Std. Diff. (Any vs TNFi)
Duration of follow-up period (in days)					
N (missing)	2859 (0)	2306 (0)	551 (0)	2859 (0)	
Mean (SD)	236.8 (195.2)	240.3 (195.8)	222.4 (192.3)	245.6 (206.4)	-0.043
Median	173.0	177.0	147.0	175.0	
Min; Max	[0.0;831.0]	[1.0;831.0]	[0.0;826.0]	[0.0;851.0]	
Reason for censoring, n (%)					
Switch	410 (14.3)	349 (15.1)	60 (10.9)	532 (18.6)	**-0.115**
Discontinuation	972 (34.0)	749 (32.5)	222 (40.3)	1238 (43.3)	**-0.192**
Outcome	20 (0.7)	14 (0.6)	≤ 10	13 (0.5)	0.032
Death	11 (0.4)	≤ 10	≤ 10	≤ 10	0.032
End of study (31/12/2019)	1446 (50.6)	1189 (51.6)	257 (46.6)	1070 (37.4)	**0.267**

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 6.19. Duration of follow-up period (in days) - Alternate VTE Cohort (Case Definition I), Matched [SNDS]

Not applicable for SNDS data

Table 6.20. Duration of follow-up period (in days) - Alternate VTE Cohort (Case Definition II), Matched [SNDS]

Not applicable for SNDS data

Table 6.21. Duration of follow-up period (in days) - MACE cohort, Matched [SNDS]

	Baricitinib [b] n = 2864	Baricitinib 4 mg n = 2314	Baricitinib 2 mg n = 548	TNFi [a] n = 2864	Std. Diff. (Any vs TNFi)
Duration of follow-up period (in days)					
N (missing)	2864 (0)	2314 (0)	548 (0)	2864 (0)	
Mean (SD)	235.6 (194.5)	239.9 (195.6)	217.3 (189.1)	241.6 (204.5)	-0.030
Median	173.0	176.0	147.5	168.0	
Min; Max	[0.0;831.0]	[1.0;831.0]	[0.0;826.0]	[0.0;851.0]	
Reason for censoring, n (%)					
Switch	412 (14.4)	348 (15.0)	63 (11.5)	541 (18.9)	**-0.121**
Discontinuation	984 (34.4)	767 (33.1)	216 (39.4)	1231 (43.0)	**-0.178**
Outcome	25 (0.9)	16 (0.7)	≤ 10	11 (0.4)	0.062
Death	≤ 10	≤ 10	≤ 10	≤ 10	-0.006
End of study (31/12/2019)	1434 (50.1)	1180 (51.0)	254 (46.4)	1071 (37.4)	**0.258**

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 6.22. Duration of follow-up period (in days) - Incident Serious Infection Cohort, Matched [SNDS]

	Baricitinib [b] n = 2979	Baricitinib 4 mg n = 2385	Baricitinib 2 mg n = 591	TNFi [a] n = 2979	Std. Diff. (Any vs TNFi)
Duration of follow-up period (in days)					
N (missing)	2979 (0)	2385 (0)	591 (0)	2979 (0)	
Mean (SD)	235.2 (193.9)	238.9 (194.4)	220.6 (191.8)	244.3 (205.7)	-0.045
Median	173.0	176.0	144.0	172.0	
Min; Max	[0.0;831.0]	[1.0;831.0]	[0.0;826.0]	[0.0;851.0]	
Reason for censoring, n (%)					
Switch	431 (14.5)	357 (15.0)	72 (12.2)	554 (18.6)	**-0.111**
Discontinuation	1011 (33.9)	779 (32.7)	231 (39.1)	1264 (42.4)	**-0.176**
Outcome	36 (1.2)	25 (1.0)	11 (1.9)	36 (1.2)	0.000
Death	≤ 10	≤ 10	≤ 10	≤ 10	0.007
End of study (31/12/2019)	1493 (50.1)	1221 (51.2)	272 (46.0)	1118 (37.5)	**0.256**

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 6.23. Duration of follow-up period (in days) - Hospitalized Tuberculosis Cohort, Matched [SNDS]

	Baricitinib [b] n = 3005	Baricitinib 4 mg n = 2396	Baricitinib 2 mg n = 606	TNFi [a] n = 3005	Std. Diff. (Any vs TNFi)
Duration of follow-up period (in days)					
N (missing)	3005 (0)	2396 (0)	606 (0)	3005 (0)	
Mean (SD)	237.4 (194.7)	241.2 (195.4)	221.7 (191.0)	246.3 (206.4)	-0.044
Median	174.0	178.0	147.0	176.0	
Min; Max	[0.0;831.0]	[1.0;831.0]	[0.0;826.0]	[0.0;851.0]	
Reason for censoring, n (%)					
Switch	417 (13.9)	343 (14.3)	73 (12.0)	537 (17.9)	**-0.109**
Discontinuation	1048 (34.9)	803 (33.5)	244 (40.3)	1328 (44.2)	**-0.191**
Outcome	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.026
Death	13 (0.4)	≤ 10	≤ 10	≤ 10	0.035
End of study (31/12/2019)	1527 (50.8)	1245 (52.0)	281 (46.4)	1132 (37.7)	**0.267**

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

1.4 CHARACTERISTICS OF PATIENTS BY EXPOSURE DURATION

1.4.1 BASELINE CHARACTERISTICS BY EXPOSURE DURATION

Table 6.24. 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 = 1686	TNFi n = 5372	Std. Diff.	Baricitinib n = 801	TNFi n = 2543	Std. Diff.	Baricitinib n = 676	TNFi n = 1910	Std. Diff.	Baricitinib n = 79	TNFi n = 377	Std. Diff.
Age [in years]			0.291			0.309			0.275			0.090
N (missing)	1686 (0)	5372 (0)		801 (0)	2543 (0)		676 (0)	1910 (0)		79 (0)	377 (0)	
Mean (SD)	58.4 (13.6)	54.3 (14.4)		59.6 (13.0)	55.4 (14.0)		59.2 (12.3)	55.6 (13.8)		57.8 (11.6)	56.7 (13.0)	
Median	59.0	55.0		60.0	56.0		60.0	57.0		60.0	57.0	
Min; Max	[18.0;90.0]	[18.0;94.0]		[19.0;89.0]	[18.0;91.0]		[20.0;92.0]	[18.0;93.0]		[30.0;77.0]	[19.0;84.0]	
Sex, n (%)			-0.173			-0.190			-0.043			-0.129
Male	310 (18.4)	1372 (25.5)		155 (19.4)	696 (27.4)		162 (24.0)	493 (25.8)		18 (22.8)	107 (28.4)	
Female	1376 (81.6)	4000 (74.5)		646 (80.6)	1847 (72.6)		514 (76.0)	1417 (74.2)		61 (77.2)	270 (71.6)	
Clinical conditions during baseline period, n (%)												
Cancer, excluding NMSC	54 (3.2)	147 (2.7)	0.028	22 (2.7)	82 (3.2)	-0.028	18 (2.7)	62 (3.2)	-0.035	≤ 10	≤ 10	-0.100
NMSC	≤ 10	≤ 10	-0.017	≤ 10	≤ 10	0.044	0 (0.0)	≤ 10	-0.065	0 (0.0)	≤ 10	-0.073
Chronic lung disease, excluding cystic fibrosis[c]	234 (13.9)	550 (10.2)	0.112	108 (13.5)	285 (11.2)	0.069	90 (13.3)	177 (9.3)	0.128	≤ 10	37 (9.8)	0.010
Cardiovascular conditions												

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1686	TNFi n = 5372	Std. Diff.	Baricitinib n = 801	TNFi n = 2543	Std. Diff.	Baricitinib n = 676	TNFi n = 1910	Std. Diff.	Baricitinib n = 79	TNFi n = 377	Std. Diff.
Atrial arrhythmia/fibrillation	18 (1.1)	28 (0.5)	0.062	≤ 10	12 (0.5)	0.073	≤ 10	12 (0.6)	0.045	0 (0.0)	≤ 10	-0.073
Cardiovascular revascularization	≤ 10	16 (0.3)	-0.012	≤ 10	≤ 10	-0.034	≤ 10	≤ 10	0.071	0 (0.0)	0 (0.0)	0.000
Congestive Heart Failure, hospitalized	≤ 10	16 (0.3)	0.029	≤ 10	≤ 10	0.010	≤ 10	≤ 10	0.041	0 (0.0)	0 (0.0)	0.000
Coronary artery disease	65 (3.9)	181 (3.4)	0.026	38 (4.7)	95 (3.7)	0.050	30 (4.4)	63 (3.3)	0.059	≤ 10	12 (3.2)	0.148
Unstable angina	≤ 10	≤ 10	-0.028	0 (0.0)	≤ 10	-0.056	0 (0.0)	≤ 10	-0.065	0 (0.0)	0 (0.0)	0.000
Ventricular arrhythmia	≤ 10	38 (0.7)	-0.03	≤ 10	14 (0.6)	0.025	≤ 10	13 (0.7)	0.007	0 (0.0)	≤ 10	-0.127
Stroke	12 (0.7)	28 (0.5)	0.024	≤ 10	19 (0.7)	0.039	≤ 10	12 (0.6)	0.059	0 (0.0)	≤ 10	-0.103
Hemorrhagic	≤ 10	≤ 10	0.01	≤ 10	≤ 10	0.002	0 (0.0)	≤ 10	-0.032	0 (0.0)	0 (0.0)	0.000
Ischemic	≤ 10	≤ 10	0.016	≤ 10	≤ 10	0.042	≤ 10	≤ 10	0.029	0 (0.0)	0 (0.0)	0.000
Unknown	≤ 10	19 (0.4)	0.019	≤ 10	14 (0.6)	0.051	≤ 10	≤ 10	0.058	0 (0.0)	≤ 10	-0.103
TIA	≤ 10	≤ 10	-0.012	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]	160 (9.5)	475 (8.8)	0.023	76 (9.5)	230 (9.0)	0.015	77 (11.4)	149 (7.8)	0.122	≤ 10	30 (8.0)	0.076
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 = 1686	TNFi n = 5372	Std. Diff.	Baricitinib n = 801	TNFi n = 2543	Std. Diff.	Baricitinib n = 676	TNFi n = 1910	Std. Diff.	Baricitinib n = 79	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	77 (4.6)	158 (2.9)	0.086	22 (2.7)	69 (2.7)	0.002	22 (3.3)	45 (2.4)	0.054	≤ 10	≤ 10	-0.008
AIDS/HIV	0 (0.0)	≤ 10	-0.051	0 (0.0)	≤ 10	-0.028	0 (0.0)	≤ 10	-0.046	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	23 (1.4)	35 (0.7)	0.071	≤ 10	≤ 10	0.010	≤ 10	≤ 10	0.041	≤ 10	≤ 10	0.047
Primary Sjogren Syndrome	59 (3.5)	122 (2.3)	0.073	20 (2.5)	61 (2.4)	0.006	19 (2.8)	38 (2.0)	0.054	≤ 10	≤ 10	-0.027
Liver or pancreatic disorder[c]	47 (2.8)	125 (2.3)	0.029	23 (2.9)	75 (2.9)	-0.005	26 (3.8)	47 (2.5)	0.079	≤ 10	≤ 10	0.137
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	77 (1.4)	-0.132	≤ 10	38 (1.5)	-0.117	≤ 10	26 (1.4)	-0.141	0 (0.0)	≤ 10	-0.127
RA Severity (CIRAS Index)			-0.181			-0.332			-0.286			-0.145
Mean (SD)	6.5 (1.4)	6.7 (1.6)		6.3 (1.3)	6.8 (1.6)		6.5 (1.3)	6.9 (1.5)		6.6 (1.4)	6.8 (1.5)	

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1686	TNFi n = 5372	Std. Diff.	Baricitinib n = 801	TNFi n = 2543	Std. Diff.	Baricitinib n = 676	TNFi n = 1910	Std. Diff.	Baricitinib n = 79	TNFi n = 377	Std. Diff.
Smoking (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
DMARDs, n (%)												
cDMARDs, during baseline period												
n, total (%)	1090 (64.7)	3627 (67.5)	-0.061	543 (67.8)	1895 (74.5)	-0.149	473 (70.0)	1478 (77.4)	-0.169	57 (72.2)	305 (80.9)	-0.208
Mean (SD)	0.7 (0.6)	0.7 (0.6)	-0.056	0.8 (0.6)	0.8 (0.6)	-0.117	0.8 (0.6)	0.9 (0.6)	-0.149	0.9 (0.7)	0.9 (0.5)	-0.041
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	83 (4.9)	261 (4.9)	0.003	45 (5.6)	147 (5.8)	-0.007	40 (5.9)	138 (7.2)	-0.053	≤ 10	34 (9.0)	-0.006
Hydroxychloroquine	81 (4.8)	240 (4.5)	0.016	50 (6.2)	120 (4.7)	0.067	39 (5.8)	104 (5.4)	0.014	≤ 10	25 (6.6)	0.126
Chloroquine	0 (0.0)	≤ 10	-0.033	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	≤ 10	0 (0.0)	0.16
Azathioprin	≤ 10	16 (0.3)	0.010	≤ 10	≤ 10	-0.019	≤ 10	≤ 10	0.024	≤ 10	0 (0.0)	0.16
Leflunomide	227 (13.5)	533 (9.9)	0.110	90 (11.2)	241 (9.5)	0.058	79 (11.7)	197 (10.3)	0.044	14 (17.7)	39 (10.3)	0.214
Methotrexate	830 (49.2)	2985 (55.6)	-0.127	435 (54.3)	1607 (63.2)	-0.181	375 (55.5)	1239 (64.9)	-0.193	39 (49.4)	263 (69.8)	-0.425
Mycophenolate mofetil	0 (0.0)	≤ 10	-0.027	0 (0.0)	≤ 10	-0.028	≤ 10	0 (0.0)	0.054	0 (0.0)	0 (0.0)	0
Sulfasalazin	53 (3.1)	216 (4.0)	-0.047	25 (3.1)	107 (4.2)	-0.058	25 (3.7)	96 (5.0)	-0.065	≤ 10	12 (3.2)	0.196
Cyclosporin	≤ 10	≤ 10	0.021	0 (0.0)	0 (0.0)	0.000	≤ 10	≤ 10	0.030	0 (0.0)	0 (0.0)	0
Penicillamin	0 (0.0)	0 (0.0)	0.000	0 (0.0)	≤ 10	-0.028	0 (0.0)	≤ 10	-0.032	0 (0.0)	0 (0.0)	0
bDMARDs, during baseline period												
n, total (%)	988 (58.6)	1210 (22.5)	0.790	499 (62.3)	616 (24.2)	0.832	441 (65.2)	444 (23.2)	0.933	54 (68.4)	104 (27.6)	0.894

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1686	TNFi n = 5372	Std. Diff.	Baricitinib n = 801	TNFi n = 2543	Std. Diff.	Baricitinib n = 676	TNFi n = 1910	Std. Diff.	Baricitinib n = 79	TNFi n = 377	Std. Diff.
Mean (SD)	0.7 (0.6)	0.2 (0.5)	0.779	0.7 (0.6)	0.3 (0.5)	0.814	0.7 (0.6)	0.2 (0.5)	0.917	0.8 (0.7)	0.3 (0.5)	0.928
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;3.0]		[0.0;3.0]	[0.0;2.0]		[0.0;3.0]	[0.0;2.0]		[0.0;2.0]	[0.0;2.0]	
cDMARDs, concomitant	508 (30.1)	628 (11.7)	0.466	289 (36.1)	347 (13.6)	0.538	247 (36.5)	259 (13.6)	0.55	32 (40.5)	70 (18.6)	0.495
Adalimumab[b]	129 (7.7)	195 (3.6)	0.175	57 (7.1)	107 (4.2)	0.126	59 (8.7)	76 (4.0)	0.196	≤ 10	30 (8.0)	0.076
Certolizumab pegol[b]	75 (4.4)	75 (1.4)	0.182	43 (5.4)	40 (1.6)	0.209	31 (4.6)	26 (1.4)	0.191	≤ 10	≤ 10	0.324
Etanercept[b]	200 (11.9)	348 (6.5)	0.187	92 (11.5)	173 (6.8)	0.163	64 (9.5)	118 (6.2)	0.123	≤ 10	25 (6.6)	-0.128
Golimumab[b]	66 (3.9)	79 (1.5)	0.151	33 (4.1)	29 (1.1)	0.187	30 (4.4)	29 (1.5)	0.172	≤ 10	≤ 10	0.082
Infliximab[b]	48 (2.8)	96 (1.8)	0.071	24 (3.0)	44 (1.7)	0.083	18 (2.7)	35 (1.8)	0.056	≤ 10	≤ 10	-0.008
Rituximab	47 (2.8)	18 (0.3)	0.199	31 (3.9)	15 (0.6)	0.224	33 (4.9)	≤ 10	0.310	11 (13.9)	≤ 10	0.52
Sarilumab	33 (2.0)	18 (0.3)	0.153	14 (1.7)	≤ 10	0.137	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Abatacept	262 (15.5)	247 (4.6)	0.370	148 (18.5)	131 (5.2)	0.422	129 (19.1)	100 (5.2)	0.434	17 (21.5)	12 (3.2)	0.580
Tocilizumab	242 (14.4)	198 (3.7)	0.379	123 (15.4)	104 (4.1)	0.387	127 (18.8)	75 (3.9)	0.482	14 (17.7)	12 (3.2)	0.489
Anakinra	≤ 10	≤ 10	0.063	≤ 10	≤ 10	0.066	≤ 10	≤ 10	0.029	0 (0.0)	0 (0.0)	0.000
TNFi naïve at baseline	1199 (71.1)	4590 (85.4)	-0.353	570 (71.2)	2154 (84.7)	-0.331	486 (71.9)	1630 (85.3)	-0.333	58 (73.4)	297 (78.8)	-0.126
Other prescription medications during baseline period, n (%)												
Antibiotics	695 (41.2)	2046 (38.1)	0.064	344 (42.9)	1018 (40.0)	0.059	296 (43.8)	708 (37.1)	0.137	34 (43.0)	108 (28.6)	0.304
Antidiabetic agents	154 (9.1)	439 (8.2)	0.034	73 (9.1)	211 (8.3)	0.029	73 (10.8)	146 (7.6)	0.109	≤ 10	32 (8.5)	0.136

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1686	TNFi n = 5372	Std. Diff.	Baricitinib n = 801	TNFi n = 2543	Std. Diff.	Baricitinib n = 676	TNFi n = 1910	Std. Diff.	Baricitinib n = 79	TNFi n = 377	Std. Diff.
Insulins	64 (3.8)	175 (3.3)	0.029	30 (3.7)	68 (2.7)	0.061	21 (3.1)	45 (2.4)	0.046	≤ 10	11 (2.9)	0.049
Non-insulins	120 (7.1)	359 (6.7)	0.017	62 (7.7)	179 (7.0)	0.027	61 (9.0)	122 (6.4)	0.099	≤ 10	28 (7.4)	0.136
Cardiovascular												
Antithrombotic agents	251 (14.9)	755 (14.1)	0.024	134 (16.7)	342 (13.4)	0.092	102 (15.1)	239 (12.5)	0.075	19 (24.1)	63 (16.7)	0.183
Anticoagulant	76 (4.5)	255 (4.7)	-0.011	41 (5.1)	110 (4.3)	0.037	22 (3.3)	74 (3.9)	-0.033	≤ 10	26 (6.9)	-0.138
Antiplatelet	193 (11.4)	540 (10.1)	0.045	104 (13.0)	247 (9.7)	0.103	82 (12.1)	172 (9.0)	0.102	17 (21.5)	43 (11.4)	0.275
Antihypertensives	542 (32.1)	1513 (28.2)	0.087	286 (35.7)	740 (29.1)	0.142	255 (37.7)	576 (30.2)	0.160	36 (45.6)	104 (27.6)	0.380
Angiotensin converting enzyme inhibitors (ACE)	135 (8.0)	461 (8.6)	-0.021	67 (8.4)	208 (8.2)	0.007	72 (10.7)	146 (7.6)	0.104	13 (16.5)	28 (7.4)	0.281
Angiotensin receptor blockers (ARB)	216 (12.8)	575 (10.7)	0.066	115 (14.4)	323 (12.7)	0.048	86 (12.7)	244 (12.8)	-0.002	≤ 10	44 (11.7)	-0.050
Beta blocker	240 (14.2)	632 (11.8)	0.074	116 (14.5)	292 (11.5)	0.089	115 (17.0)	237 (12.4)	0.130	18 (22.8)	46 (12.2)	0.281
Calcium channel blocker	146 (8.7)	416 (7.7)	0.033	91 (11.4)	212 (8.3)	0.102	88 (13.0)	155 (8.1)	0.160	11 (13.9)	29 (7.7)	0.202
Nitrates	15 (0.9)	45 (0.8)	0.006	≤ 10	21 (0.8)	-0.059	12 (1.8)	19 (1.0)	0.067	≤ 10	≤ 10	0.115
Acyclovir	≤ 10	32 (0.6)	0.000	≤ 10	18 (0.7)	-0.045	≤ 10	≤ 10	0.007	0 (0.0)	≤ 10	-0.147
Valacyclovir	56 (3.3)	172 (3.2)	0.007	30 (3.7)	80 (3.1)	0.033	36 (5.3)	53 (2.8)	0.130	≤ 10	13 (3.4)	-0.144
Hormonal	200 (11.9)	807 (15.0)	-0.093	113 (14.1)	373 (14.7)	-0.016	81 (12.0)	262 (13.7)	-0.052	12 (15.2)	56 (14.9)	0.009
HRT	122 (7.2)	383 (7.1)	0.004	63 (7.9)	156 (6.1)	0.068	53 (7.8)	120 (6.3)	0.061	≤ 10	25 (6.6)	0.084

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1686	TNFi n = 5372	Std. Diff.	Baricitinib n = 801	TNFi n = 2543	Std. Diff.	Baricitinib n = 676	TNFi n = 1910	Std. Diff.	Baricitinib n = 79	TNFi n = 377	Std. Diff.
Oral Contraceptives	76 (4.5)	411 (7.7)	-0.132	50 (6.2)	191 (7.5)	-0.05	26 (3.8)	140 (7.3)	-0.152	≤ 10	31 (8.2)	-0.073
SERMs	≤ 10	≤ 10	-0.002	≤ 10	16 (0.6)	-0.057	≤ 10	≤ 10	0.004	≤ 10	0 (0.0)	0.160
Topic with progestogens and/or estrogens	≤ 10	30 (0.6)	-0.063	≤ 10	19 (0.7)	-0.071	≤ 10	≤ 10	0.012	0 (0.0)	≤ 10	-0.103
Lipid-lowering agents	272 (16.1)	720 (13.4)	0.077	138 (17.2)	339 (13.3)	0.109	127 (18.8)	268 (14.0)	0.129	18 (22.8)	56 (14.9)	0.204
HMG CoA reductase inhibitors	220 (13.0)	580 (10.8)	0.070	116 (14.5)	280 (11.0)	0.104	99 (14.6)	213 (11.2)	0.104	15 (19.0)	45 (11.9)	0.196
Fibrates	20 (1.2)	61 (1.1)	0.005	≤ 10	23 (0.9)	0.022	14 (2.1)	25 (1.3)	0.059	0 (0.0)	≤ 10	-0.147
Bile acid sequestrants	≤ 10	17 (0.3)	0.025	≤ 10	≤ 10	-0.003	≤ 10	≤ 10	0.007	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	14 (0.8)	57 (1.1)	-0.024	≤ 10	16 (0.6)	-0.001	≤ 10	15 (0.8)	0.026	0 (0.0)	≤ 10	-0.073
Lipid modifying agents, combinations	20 (1.2)	49 (0.9)	0.027	11 (1.4)	21 (0.8)	0.053	12 (1.8)	25 (1.3)	0.038	≤ 10	≤ 10	0.157
Rheumatoid arthritis-related												
Aspirin	19 (1.1)	63 (1.2)	-0.004	≤ 10	35 (1.4)	-0.048	13 (1.9)	16 (0.8)	0.093	≤ 10	≤ 10	0.136
Cox-2 Inhibitor	90 (5.3)	329 (6.1)	-0.034	44 (5.5)	157 (6.2)	-0.029	41 (6.1)	121 (6.3)	-0.011	≤ 10	34 (9.0)	-0.214
NSAIDs	616 (36.5)	2130 (39.7)	-0.064	287 (35.8)	1079 (42.4)	-0.136	233 (34.5)	832 (43.6)	-0.187	26 (32.9)	145 (38.5)	-0.116
Glucocorticosteroid	1238 (73.4)	3414 (63.6)	0.214	597 (74.5)	1748 (68.7)	0.129	469 (69.4)	1300 (68.1)	0.028	55 (69.6)	247 (65.5)	0.088
Vaccines	472 (28.0)	1829 (34.0)	-0.131	267 (33.3)	1035 (40.7)	-0.153	196 (29.0)	800 (41.9)	-0.272	23 (29.1)	132 (35.0)	-0.127

Characteristics[a]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1686	TNFi n = 5372	Std. Diff.	Baricitinib n = 801	TNFi n = 2543	Std. Diff.	Baricitinib n = 676	TNFi n = 1910	Std. Diff.	Baricitinib n = 79	TNFi n = 377	Std. Diff.
Antineoplastic agents	≤ 10	17 (0.3)	0.016	≤ 10	≤ 10	0.042	≤ 10	≤ 10	-0.015	≤ 10	0 (0.0)	0.160

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 6.24. (continued). Baseline characteristics by exposure duration and dose of baricitinib - Unmatched cohort [SNDS]

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1336	Bari. 2 mg n = 349	Bari. 4 mg n = 652	Bari. 2 mg n = 147	Bari. 4 mg n = 562	Bari. 2 mg n = 113	Bari. 4 mg n = 66	Bari. 2 mg n = 13
Age [in years]								
N (missing)	1336 (0)	349 (0)	652 (0)	147 (0)	562 (0)	113 (0)	66 (0)	13 (0)
Mean (SD)	55.6 (12.3)	69.2 (12.9)	57.2 (11.9)	70.1 (12.6)	57.3 (11.4)	68.6 (12.7)	56.6 (11.8)	63.9 (8.0)
Median	57.0	72.0	58.0	73.0	59.0	71.0	58.5	65.0
Min; Max	[18.0;90.0]	[25.0;89.0]	[19.0;86.0]	[20.0;89.0]	[20.0;82.0]	[30.0;92.0]	[30.0;76.0]	[49.0;77.0]
Sex, n (%)								
Male	253 (18.9)	57 (16.3)	133 (20.4)	22 (15.0)	135 (24.0)	27 (23.9)	15 (22.7)	≤ 10
Female	1083 (81.1)	292 (83.7)	519 (79.6)	125 (85.0)	427 (76.0)	86 (76.1)	51 (77.3)	≤ 10
Clinical conditions during baseline period, n (%)								
Cancer, excluding NMSC	37 (2.8)	17 (4.9)	16 (2.5)	≤ 10	15 (2.7)	≤ 10	≤ 10	0 (0.0)
NMSC	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chronic lung disease, excluding cystic fibrosis[c]	173 (12.9)	61 (17.5)	81 (12.4)	27 (18.4)	59 (10.5)	30 (26.5)	≤ 10	≤ 10
Cardiovascular conditions								
Atrial arrhythmia/fibrillation	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Cardiovascular revascularization	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1336	Bari. 2 mg n = 349	Bari. 4 mg n = 652	Bari. 2 mg n = 147	Bari. 4 mg n = 562	Bari. 2 mg n = 113	Bari. 4 mg n = 66	Bari. 2 mg n = 13
Congestive Heart Failure, hospitalized	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Coronary artery disease	43 (3.2)	22 (6.3)	25 (3.8)	13 (8.8)	19 (3.4)	11 (9.7)	≤ 10	≤ 10
Unstable angina	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ventricular arrhythmia	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Stroke	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Hemorrhagic	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ischemic	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Unknown	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
TIA	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Diabetes Mellitus[c]	112 (8.4)	48 (13.8)	58 (8.9)	17 (11.6)	57 (10.1)	20 (17.7)	≤ 10	≤ 10
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

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1336	Bari. 2 mg n = 349	Bari. 4 mg n = 652	Bari. 2 mg n = 147	Bari. 4 mg n = 562	Bari. 2 mg n = 113	Bari. 4 mg n = 66	Bari. 2 mg n = 13
Immune disorders	55 (4.1)	22 (6.3)	16 (2.5)	≤ 10	16 (2.8)	≤ 10	≤ 10	≤ 10
AIDS/HIV	0 (0.0)	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	19 (1.4)	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)
Primary Sjogren Syndrome	39 (2.9)	20 (5.7)	15 (2.3)	≤ 10	13 (2.3)	≤ 10	0 (0.0)	≤ 10
Liver or pancreatic disorder[e]	35 (2.6)	11 (3.2)	16 (2.5)	≤ 10	22 (3.9)	≤ 10	≤ 10	≤ 10
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	0 (0.0)	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
RA Severity (CIRAS Index)								
Mean (± SD)	6.7 (1.4)	5.7 (1.4)	6.5 (1.2)	5.8 (1.4)	6.6 (1.3)	5.9 (1.4)	6.7 (1.4)	6.0 (1.1)
Smoking (not available in SNDS)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
DMARDs, n (%)								
cDMARDs, during baseline period								
n, total (%)	877 (65.6)	212 (60.7)	450 (69.0)	91 (61.9)	407 (72.4)	66 (58.4)	48 (72.7)	≤ 10
Mean (SD)	0.7 (0.6)	0.7 (0.6)	0.8 (0.6)	0.7 (0.7)	0.8 (0.6)	0.6 (0.6)	0.8 (0.7)	1.0 (1.0)

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1336	Bari. 2 mg n = 349	Bari. 4 mg n = 652	Bari. 2 mg n = 147	Bari. 4 mg n = 562	Bari. 2 mg n = 113	Bari. 4 mg n = 66	Bari. 2 mg n = 13
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	65 (4.9)	18 (5.2)	35 (5.4)	≤ 10	36 (6.4)	≤ 10	≤ 10	≤ 10
Hydroxychloroquine	63 (4.7)	18 (5.2)	35 (5.4)	15 (10.2)	35 (6.2)	≤ 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)	≤ 10
Azathioprin	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)
Leflunomide	186 (13.9)	41 (11.7)	81 (12.4)	≤ 10	68 (12.1)	11 (9.7)	≤ 10	≤ 10
Methotrexate	673 (50.4)	157 (45.0)	358 (54.9)	75 (51.0)	324 (57.7)	51 (45.1)	35 (53.0)	≤ 10
Mycophenolate mofetil	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Sulfasalazin	40 (3.0)	13 (3.7)	20 (3.1)	≤ 10	19 (3.4)	≤ 10	≤ 10	≤ 10
Cyclosporin	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	≤ 10	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 (%)	821 (61.5)	166 (47.6)	421 (64.6)	76 (51.7)	372 (66.2)	68 (60.2)	47 (71.2)	≤ 10
Mean (SD)	0.7 (0.6)	0.5 (0.6)	0.7 (0.6)	0.6 (0.6)	0.7 (0.6)	0.6 (0.6)	0.9 (0.7)	0.6 (0.7)
Median	1.0	0.0	1.0	1.0	1.0	1.0	1.0	1.0
Min; Max	[0.0;3.0]	[0.0;2.0]	[0.0;3.0]	[0.0;2.0]	[0.0;3.0]	[0.0;3.0]	[0.0;2.0]	[0.0;2.0]
cDMARDs, concomitant	432 (32.3)	75 (21.5)	243 (37.3)	44 (29.9)	217 (38.6)	30 (26.5)	28 (42.4)	≤ 10
Adalimumab[b]	110 (8.2)	19 (5.4)	49 (7.5)	≤ 10	55 (9.8)	≤ 10	≤ 10	≤ 10
Certolizumab pegol[b]	66 (4.9)	≤ 10	38 (5.8)	≤ 10	28 (5.0)	≤ 10	≤ 10	≤ 10

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1336	Bari. 2 mg n = 349	Bari. 4 mg n = 652	Bari. 2 mg n = 147	Bari. 4 mg n = 562	Bari. 2 mg n = 113	Bari. 4 mg n = 66	Bari. 2 mg n = 13
Etanercept[b]	169 (12.6)	31 (8.9)	80 (12.3)	12 (8.2)	53 (9.4)	≤ 10	≤ 10	0 (0.0)
Golimumab[b]	62 (4.6)	≤ 10	32 (4.9)	0 (0.0)	27 (4.8)	≤ 10	≤ 10	≤ 10
Infliximab[b]	42 (3.1)	≤ 10	21 (3.2)	≤ 10	17 (3.0)	≤ 10	≤ 10	0 (0.0)
Rituximab	38 (2.8)	≤ 10	25 (3.8)	≤ 10	23 (4.1)	≤ 10	≤ 10	≤ 10
Sarilumab	26 (1.9)	≤ 10	11 (1.7)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abatacept	209 (15.6)	52 (14.9)	119 (18.3)	28 (19.0)	102 (18.1)	26 (23.0)	15 (22.7)	≤ 10
Tocilizumab	203 (15.2)	39 (11.2)	105 (16.1)	18 (12.2)	112 (19.9)	15 (13.3)	12 (18.2)	≤ 10
Anakinra	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
TNFi naïve at baseline	917 (68.6)	282 (80.8)	448 (68.7)	121 (82.3)	393 (69.9)	93 (82.3)	48 (72.7)	≤ 10
Other prescription medications during baseline period, n (%)								
Antibiotics	535 (40.0)	159 (45.6)	270 (41.4)	73 (49.7)	238 (42.3)	58 (51.3)	30 (45.5)	≤ 10
Antidiabetic agents	110 (8.2)	44 (12.6)	57 (8.7)	15 (10.2)	54 (9.6)	19 (16.8)	≤ 10	≤ 10
Insulins	45 (3.4)	19 (5.4)	24 (3.7)	≤ 10	15 (2.7)	≤ 10	≤ 10	0 (0.0)
Non-insulins	89 (6.7)	31 (8.9)	48 (7.4)	13 (8.8)	45 (8.0)	16 (14.2)	≤ 10	≤ 10
Cardiovascular								
Antithrombotic agents	160 (12.0)	91 (26.1)	91 (14.0)	42 (28.6)	75 (13.3)	27 (23.9)	14 (21.2)	≤ 10
Anticoagulant	40 (3.0)	36 (10.3)	26 (4.0)	15 (10.2)	17 (3.0)	≤ 10	≤ 10	≤ 10
Antiplatelet	130 (9.7)	63 (18.1)	70 (10.7)	33 (22.4)	59 (10.5)	23 (20.4)	13 (19.7)	≤ 10
Antihypertensives	354 (26.5)	188 (53.9)	206 (31.6)	79 (53.7)	184 (32.7)	70 (61.9)	26 (39.4)	≤ 10

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1336	Bari. 2 mg n = 349	Bari. 4 mg n = 652	Bari. 2 mg n = 147	Bari. 4 mg n = 562	Bari. 2 mg n = 113	Bari. 4 mg n = 66	Bari. 2 mg n = 13
Angiotensin converting enzyme inhibitors (ACE)	93 (7.0)	42 (12.0)	47 (7.2)	20 (13.6)	50 (8.9)	22 (19.5)	≤ 10	≤ 10
Angiotensin receptor blockers (ARB)	134 (10.0)	82 (23.5)	86 (13.2)	29 (19.7)	66 (11.7)	20 (17.7)	≤ 10	≤ 10
Beta blocker	154 (11.5)	86 (24.6)	79 (12.1)	36 (24.5)	81 (14.4)	34 (30.1)	12 (18.2)	≤ 10
Calcium channel blocker	81 (6.1)	65 (18.6)	69 (10.6)	21 (14.3)	58 (10.3)	29 (25.7)	≤ 10	≤ 10
Nitrates	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)
Acyclovir	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Valacyclovir	38 (2.8)	18 (5.2)	26 (4.0)	≤ 10	28 (5.0)	≤ 10	≤ 10	0 (0.0)
Hormonal	175 (13.1)	25 (7.2)	96 (14.7)	17 (11.6)	74 (13.2)	≤ 10	≤ 10	≤ 10
HRT	103 (7.7)	19 (5.4)	51 (7.8)	12 (8.2)	50 (8.9)	≤ 10	≤ 10	≤ 10
Oral Contraceptives	70 (5.2)	≤ 10	45 (6.9)	≤ 10	23 (4.1)	≤ 10	≤ 10	0 (0.0)
SERMs	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)
Topic with progestogens and/or estrogens	≤ 10	0 (0.0)	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Lipid-lowering agents	180 (13.5)	92 (26.4)	105 (16.1)	32 (21.8)	93 (16.5)	34 (30.1)	16 (24.2)	≤ 10
HMG CoA reductase inhibitors	143 (10.7)	77 (22.1)	86 (13.2)	29 (19.7)	73 (13.0)	26 (23.0)	13 (19.7)	≤ 10
Fibrates	14 (1.0)	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1336	Bari. 2 mg n = 349	Bari. 4 mg n = 652	Bari. 2 mg n = 147	Bari. 4 mg n = 562	Bari. 2 mg n = 113	Bari. 4 mg n = 66	Bari. 2 mg n = 13
Bile acid sequestrants	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other lipid modifying agents	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Lipid modifying agents, combinations	15 (1.1)	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)
Rheumatoid arthritis-related								
Aspirin	13 (1.0)	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
Cox-2 Inhibitor	77 (5.8)	13 (3.7)	38 (5.8)	≤ 10	38 (6.8)	≤ 10	≤ 10	0 (0.0)
NSAIDs	519 (38.8)	97 (27.8)	249 (38.2)	38 (25.9)	204 (36.3)	28 (24.8)	23 (34.8)	≤ 10
Glucocorticosteroid	971 (72.7)	266 (76.2)	472 (72.4)	124 (84.4)	392 (69.8)	76 (67.3)	47 (71.2)	≤ 10
Vaccines	357 (26.7)	115 (33.0)	205 (31.4)	62 (42.2)	146 (26.0)	50 (44.2)	19 (28.8)	≤ 10
Antineoplastic agents	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)	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] 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 6.25. Baseline characteristics by exposure duration - VTE cohort, Matched [SNDS]

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1496	TNFi[a] n = 1472	Std. Diff.	Baricitinib n = 701	TNFi[a] n = 734	Std. Diff.	Baricitinib n = 598	TNFi[a] n = 534	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 119	Std. Diff.
Age [in years]			-0.002			0.036			-0.01			-0.275
N (missing)	1496 (0)	1472 (0)		701 (0)	734 (0)		598 (0)	534 (0)		64 (0)	119 (0)	
Mean (SD)	57.9 (13.6)	57.9 (13.5)		59.2 (13.0)	58.7 (13.7)		59.0 (12.4)	59.1 (12.6)		56.4 (11.8)	59.5 (11.1)	
Median	58.0	59.0		59.0	60.0		60.0	60.0		58.5	60.0	
Min; Max	[18.0;90.0]	[19.0;94.0]		[19.0;88.0]	[18.0;91.0]		[20.0;92.0]	[18.0;90.0]		[30.0;76.0]	[34.0;84.0]	
Sex, n (%)			0.016			-0.018			0.116			0.079
Male	286 (19.1)	272 (18.5)		140 (20.0)	152 (20.7)		150 (25.1)	108 (20.2)		15 (23.4)	24 (20.2)	
Female	1210 (80.9)	1200 (81.5)		561 (80.0)	582 (79.3)		448 (74.9)	426 (79.8)		49 (76.6)	95 (79.8)	
Clinical conditions during baseline period, n (%)												
Cancer, excluding NMSC	51 (3.4)	45 (3.1)	0.020	19 (2.7)	27 (3.7)	-0.055	17 (2.8)	20 (3.7)	-0.051	≤ 10	≤ 10	-0.009
NMSC	≤ 10	≤ 10	-0.001	≤ 10	≤ 10	0.002	0 (0.0)	0 (0.0)	0.000	0 (0.0)	≤ 10	-0.130
Chronic lung disease, excluding cystic fibrosis[d]	205 (13.7)	168 (11.4)	0.069	91 (13.0)	86 (11.7)	0.039	79 (13.2)	60 (11.2)	0.060	≤ 10	11 (9.2)	0.005
Cardiovascular conditions												
Atrial arrhythmia/fibrillation	15 (1.0)	11 (0.7)	0.027	≤ 10	≤ 10	0.005	≤ 10	≤ 10	-0.029	0 (0.0)	≤ 10	-0.130

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1496	TNFi[a] n = 1472	Std. Diff.	Baricitinib n = 701	TNFi[a] n = 734	Std. Diff.	Baricitinib n = 598	TNFi[a] n = 534	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 119	Std. Diff.
Cardiovascular revascularization	≤ 10	≤ 10	-0.027	≤ 10	≤ 10	-0.051	≤ 10	≤ 10	0.054	0 (0.0)	0 (0.0)	0.000
Congestive Heart Failure, hospitalized	≤ 10	≤ 10	-0.022	≤ 10	≤ 10	0.003	≤ 10	≤ 10	0.014	0 (0.0)	0 (0.0)	0.000
Coronary artery disease	62 (4.1)	54 (3.7)	0.025	35 (5.0)	40 (5.4)	-0.021	27 (4.5)	25 (4.7)	-0.008	≤ 10	≤ 10	0.172
Unstable angina	≤ 10	≤ 10	0.000	0 (0.0)	≤ 10	-0.074	0 (0.0)	≤ 10	-0.087	0 (0.0)	0 (0.0)	0.000
Ventricular arrhythmia	≤ 10	14 (1.0)	-0.058	≤ 10	≤ 10	0.021	≤ 10	≤ 10	-0.011	0 (0.0)	≤ 10	-0.13
Stroke	≤ 10	≤ 10	-0.001	≤ 10	≤ 10	0.018	≤ 10	≤ 10	0.023	0 (0.0)	0 (0.0)	0.000
Hemorrhagic	0 (0.0)	0 (0.0)	0.000	≤ 10	≤ 10	-0.029	0 (0.0)	≤ 10	-0.061	0 (0.0)	0 (0.0)	0.000
Ischemic	≤ 10	≤ 10	0.029	≤ 10	≤ 10	0.033	≤ 10	≤ 10	-0.005	0 (0.0)	0 (0.0)	0.000
Unknown	≤ 10	≤ 10	-0.020	≤ 10	≤ 10	0.048	≤ 10	≤ 10	0.050	0 (0.0)	0 (0.0)	0.000
TIA	≤ 10	≤ 10	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
Diabetes Mellitus[d]	142 (9.5)	149 (10.1)	-0.021	66 (9.4)	69 (9.4)	0.001	69 (11.5)	41 (7.7)	0.131	≤ 10	12 (10.1)	-0.024
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)												

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1496	TNFi[a] n = 1472	Std. Diff.	Baricitinib n = 701	TNFi[a] n = 734	Std. Diff.	Baricitinib n = 598	TNFi[a] n = 534	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 119	Std. Diff.
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	65 (4.3)	57 (3.9)	0.024	17 (2.4)	29 (4.0)	-0.087	20 (3.3)	18 (3.4)	-0.002	≤ 10	≤ 10	-0.013
AIDS/HIV	0 (0.0)	≤ 10	-0.052	0 (0.0)	0 (0.0)	0.000	0 (0.0)	≤ 10	-0.087	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	20 (1.3)	≤ 10	0.066	≤ 10	≤ 10	-0.021	≤ 10	≤ 10	0.041	≤ 10	≤ 10	-0.009
Primary Sjogren Syndrome	49 (3.3)	48 (3.3)	0.001	16 (2.3)	27 (3.7)	-0.082	17 (2.8)	15 (2.8)	0.002	≤ 10	≤ 10	-0.009
Liver or pancreatic disorder[d]	43 (2.9)	40 (2.7)	0.010	21 (3.0)	23 (3.1)	-0.008	22 (3.7)	20 (3.7)	-0.004	≤ 10	≤ 10	0.172
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	-0.024	≤ 10	≤ 10	-0.017	≤ 10	≤ 10	-0.040	0 (0.0)	0 (0.0)	0.000
RA Severity (CIRAS Index)			0.057			-0.045			0.032			0.134
Mean (± SD)	6.5 (1.4)	6.4 (1.4)		6.4 (1.3)	6.4 (1.4)		6.5 (1.3)	6.5 (1.4)		6.7 (1.4)	6.5 (1.4)	
Smoking (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1496	TNFi[a] n = 1472	Std. Diff.	Baricitinib n = 701	TNFi[a] n = 734	Std. Diff.	Baricitinib n = 598	TNFi[a] n = 534	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 119	Std. Diff.
DMARDs, n (%)												
cDMARDs, during baseline period												
n, total (%)	988 (66.0)	926 (62.9)	0.066	485 (69.2)	493 (67.2)	0.043	426 (71.2)	372 (69.7)	0.035	46 (71.9)	91 (76.5)	-0.105
Mean (SD)	0.7 (0.6)	0.7 (0.6)	0.073	0.8 (0.6)	0.7 (0.6)	0.065	0.8 (0.6)	0.8 (0.6)	0.056	0.9 (0.8)	0.9 (0.6)	0.072
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	78 (5.2)	58 (3.9)	0.061	40 (5.7)	33 (4.5)	0.055	38 (6.4)	23 (4.3)	0.091	≤ 10	11 (9.2)	0.056
Hydroxychloroquine	76 (5.1)	70 (4.8)	0.015	46 (6.6)	35 (4.8)	0.078	35 (5.9)	25 (4.7)	0.052	≤ 10	≤ 10	0.197
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)	0.000
Azathioprin	≤ 10	≤ 10	-0.001	≤ 10	≤ 10	0.002	≤ 10	≤ 10	-0.034	0 (0.0)	0 (0.0)	0.000
Leflunomide	198 (13.2)	160 (10.9)	0.073	82 (11.7)	75 (10.2)	0.047	68 (11.4)	64 (12.0)	-0.019	13 (20.3)	11 (9.2)	0.316
Methotrexate	763 (51.0)	715 (48.6)	0.049	387 (55.2)	401 (54.6)	0.012	342 (57.2)	291 (54.5)	0.054	31 (48.4)	79 (66.4)	-0.369
Mycophenolate mofetil	0 (0.0)	≤ 10	-0.037	0 (0.0)	≤ 10	-0.052	≤ 10	0 (0.0)	0.058	0 (0.0)	0 (0.0)	0.000
Sulfasalazin	49 (3.3)	60 (4.1)	-0.043	22 (3.1)	21 (2.9)	0.016	24 (4.0)	20 (3.7)	0.014	≤ 10	≤ 10	0.248
Cyclosporin	≤ 10	0 (0.0)	0.037	0 (0.0)	0 (0.0)	0.000	≤ 10	≤ 10	-0.005	0 (0.0)	0 (0.0)	0.000
Penicillamin	0 (0.0)	0 (0.0)	0.000	0 (0.0)	≤ 10	-0.052	0 (0.0)	≤ 10	-0.061	0 (0.0)	0 (0.0)	0.000
bDMARDs, during baseline period												
n, total (%)	798 (53.3)	798 (54.2)	-0.017	399 (56.9)	433 (59.0)	-0.042	363 (60.7)	311 (58.2)	0.050	39 (60.9)	69 (58.0)	0.060
Mean (SD)	0.6 (0.6)	0.6 (0.6)	-0.033	0.6 (0.6)	0.6 (0.6)	-0.043	0.7 (0.6)	0.6 (0.6)	0.072	0.7 (0.7)	0.6 (0.6)	0.143

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1496	TNFi[a] n = 1472	Std. Diff.	Baricitinib n = 701	TNFi[a] n = 734	Std. Diff.	Baricitinib n = 598	TNFi[a] n = 534	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 119	Std. Diff.
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;3.0]	[0.0;2.0]		[0.0;2.0]	[0.0;2.0]	
cDMARDs, concomitant	431 (28.8)	396 (26.9)	0.043	244 (34.8)	232 (31.6)	0.068	212 (35.5)	174 (32.6)	0.061	23 (35.9)	45 (37.8)	-0.039
Adalimumab[c]	106 (7.1)	100 (6.8)	0.012	49 (7.0)	61 (8.3)	-0.050	51 (8.5)	47 (8.8)	-0.010	≤ 10	20 (16.8)	-0.222
Certolizumab pegol[c]	55 (3.7)	64 (4.3)	-0.034	33 (4.7)	30 (4.1)	0.030	26 (4.3)	21 (3.9)	0.021	≤ 10	≤ 10	0.077
Etanercept[c]	185 (12.4)	178 (12.1)	0.008	83 (11.8)	95 (12.9)	-0.034	59 (9.9)	68 (12.7)	-0.091	≤ 10	12 (10.1)	-0.283
Golimumab[c]	50 (3.3)	58 (3.9)	-0.032	23 (3.3)	24 (3.3)	0.001	25 (4.2)	20 (3.7)	0.022	≤ 10	≤ 10	-0.053
Infliximab[c]	43 (2.9)	48 (3.3)	-0.022	21 (3.0)	21 (2.9)	0.008	15 (2.5)	15 (2.8)	-0.019	≤ 10	≤ 10	0.037
Rituximab	26 (1.7)	17 (1.2)	0.049	12 (1.7)	15 (2.0)	-0.024	17 (2.8)	≤ 10	0.197	≤ 10	≤ 10	0.183
Sarilumab	17 (1.1)	17 (1.2)	-0.002	≤ 10	≤ 10	-0.024	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Abatacept	189 (12.6)	208 (14.1)	-0.044	118 (16.8)	117 (15.9)	0.024	112 (18.7)	83 (15.5)	0.085	14 (21.9)	12 (10.1)	0.326
Tocilizumab	175 (11.7)	172 (11.7)	0.000	85 (12.1)	97 (13.2)	-0.033	87 (14.5)	71 (13.3)	0.036	≤ 10	11 (9.2)	0.194
Anakinra	≤ 10	≤ 10	0.020	≤ 10	≤ 10	-0.012	≤ 10	≤ 10	-0.034	0 (0.0)	0 (0.0)	0.000
TNFi naïve at baseline	1072 (71.7)	1035 (70.3)	0.030	504 (71.9)	505 (68.8)	0.068	431 (72.1)	366 (68.5)	0.077	47 (73.4)	73 (61.3)	0.260
Other prescription medications during baseline period, n (%)												
Antibiotics	613 (41.0)	587 (39.9)	0.022	287 (40.9)	324 (44.1)	-0.065	257 (43.0)	203 (38.0)	0.101	26 (40.6)	33 (27.7)	0.274
Antidiabetic agents	136 (9.1)	137 (9.3)	-0.008	62 (8.8)	62 (8.4)	0.014	69 (11.5)	42 (7.9)	0.124	≤ 10	12 (10.1)	0.122

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1496	TNFi[a] n = 1472	Std. Diff.	Baricitinib n = 701	TNFi[a] n = 734	Std. Diff.	Baricitinib n = 598	TNFi[a] n = 534	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 119	Std. Diff.
Insulins	55 (3.7)	49 (3.3)	0.019	25 (3.6)	20 (2.7)	0.048	19 (3.2)	≤ 10	0.083	≤ 10	≤ 10	0.172
Non-insulins	105 (7.0)	109 (7.4)	-0.015	53 (7.6)	51 (6.9)	0.024	58 (9.7)	38 (7.1)	0.093	≤ 10	12 (10.1)	0.076
Cardiovascular												
Antithrombotic agents	226 (15.1)	222 (15.1)	0.001	116 (16.5)	114 (15.5)	0.028	91 (15.2)	73 (13.7)	0.044	16 (25.0)	19 (16.0)	0.225
Anticoagulant	69 (4.6)	67 (4.6)	0.003	37 (5.3)	31 (4.2)	0.050	21 (3.5)	20 (3.7)	-0.013	≤ 10	≤ 10	-0.053
Antiplatelet	174 (11.6)	164 (11.1)	0.015	89 (12.7)	87 (11.9)	0.026	72 (12.0)	57 (10.7)	0.043	14 (21.9)	14 (11.8)	0.273
Antihypertensives	469 (31.4)	471 (32.0)	-0.014	250 (35.7)	263 (35.8)	-0.004	227 (38.0)	199 (37.3)	0.014	27 (42.2)	43 (36.1)	0.124
Angiotensin converting enzyme inhibitors (ACE)	121 (8.1)	142 (9.6)	-0.055	60 (8.6)	64 (8.7)	-0.006	63 (10.5)	47 (8.8)	0.059	≤ 10	≤ 10	0.318
Angiotensin receptor blockers (ARB)	182 (12.2)	194 (13.2)	-0.031	97 (13.8)	115 (15.7)	-0.052	77 (12.9)	87 (16.3)	-0.097	≤ 10	24 (20.2)	-0.308
Beta blocker	207 (13.8)	198 (13.5)	0.011	103 (14.7)	110 (15.0)	-0.008	103 (17.2)	92 (17.2)	0.000	14 (21.9)	13 (10.9)	0.299
Calcium channel blocker	122 (8.2)	131 (8.9)	-0.027	79 (11.3)	86 (11.7)	-0.014	79 (13.2)	49 (9.2)	0.128	≤ 10	16 (13.4)	-0.128
Nitrates	12 (0.8)	15 (1.0)	-0.023	≤ 10	≤ 10	-0.142	11 (1.8)	≤ 10	0.043	≤ 10	0 (0.0)	0.178
Acyclovir	≤ 10	11 (0.7)	-0.009	≤ 10	≤ 10	-0.064	≤ 10	≤ 10	-0.005	0 (0.0)	≤ 10	-0.130
Valacyclovir	47 (3.1)	55 (3.7)	-0.033	27 (3.9)	27 (3.7)	0.009	29 (4.8)	19 (3.6)	0.064	≤ 10	≤ 10	0.066
Hormonal	180 (12.0)	208 (14.1)	-0.062	104 (14.8)	98 (13.4)	0.043	70 (11.7)	57 (10.7)	0.033	11 (17.2)	17 (14.3)	0.080

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1496	TNFi[a] n = 1472	Std. Diff.	Baricitinib n = 701	TNFi[a] n = 734	Std. Diff.	Baricitinib n = 598	TNFi[a] n = 534	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 119	Std. Diff.
HRT	106 (7.1)	125 (8.5)	-0.053	57 (8.1)	50 (6.8)	0.050	44 (7.4)	32 (6.0)	0.055	≤ 10	11 (9.2)	0.005
Oral Contraceptives	71 (4.7)	85 (5.8)	-0.046	47 (6.7)	38 (5.2)	0.065	24 (4.0)	23 (4.3)	-0.015	≤ 10	≤ 10	0.077
SERMs	≤ 10	≤ 10	0.036	≤ 10	≤ 10	-0.072	≤ 10	≤ 10	-0.008	≤ 10	0 (0.0)	0.178
Topic with progestogens and/or estrogens	≤ 10	≤ 10	-0.038	≤ 10	≤ 10	-0.040	≤ 10	0 (0.0)	0.100	0 (0.0)	0 (0.0)	0.000
Lipid-lowering agents	244 (16.3)	235 (16.0)	0.009	115 (16.4)	117 (15.9)	0.013	109 (18.2)	85 (15.9)	0.061	13 (20.3)	22 (18.5)	0.046
HMG CoA reductase inhibitors	199 (13.3)	194 (13.2)	0.004	97 (13.8)	94 (12.8)	0.030	86 (14.4)	64 (12.0)	0.071	12 (18.8)	20 (16.8)	0.051
Fibrates	18 (1.2)	25 (1.7)	-0.041	≤ 10	≤ 10	0.005	12 (2.0)	11 (2.1)	-0.004	0 (0.0)	0 (0.0)	0.000
Bile acid sequestrants	≤ 10	≤ 10	0.046	≤ 10	≤ 10	0.026	≤ 10	≤ 10	-0.005	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	12 (0.8)	15 (1.0)	-0.023	≤ 10	≤ 10	-0.044	≤ 10	≤ 10	0.023	0 (0.0)	0 (0.0)	0.000
Lipid modifying agents, combinations	17 (1.1)	≤ 10	0.048	≤ 10	≤ 10	0.030	≤ 10	≤ 10	-0.015	≤ 10	≤ 10	-0.009
Rheumatoid arthritis-related												
Aspirin	17 (1.1)	16 (1.1)	0.005	≤ 10	≤ 10	-0.034	11 (1.8)	≤ 10	0.027	≤ 10	≤ 10	0.164
Cox-2 Inhibitor	78 (5.2)	93 (6.3)	-0.047	40 (5.7)	37 (5.0)	0.030	35 (5.9)	37 (6.9)	-0.044	≤ 10	≤ 10	-0.088

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1496	TNFi[a] n = 1472	Std. Diff.	Baricitinib n = 701	TNFi[a] n = 734	Std. Diff.	Baricitinib n = 598	TNFi[a] n = 534	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 119	Std. Diff.
NSAIDs	556 (37.2)	564 (38.3)	-0.024	256 (36.5)	282 (38.4)	-0.039	204 (34.1)	215 (40.3)	-0.128	25 (39.1)	43 (36.1)	0.061
Glucocorticosteroid	1069 (71.5)	1020 (69.3)	0.047	509 (72.6)	528 (71.9)	0.015	407 (68.1)	382 (71.5)	-0.076	41 (64.1)	72 (60.5)	0.074
Vaccines	424 (28.3)	384 (26.1)	0.051	236 (33.7)	244 (33.2)	0.009	179 (29.9)	169 (31.6)	-0.037	16 (25.0)	33 (27.7)	-0.062
Antineoplastic agents	≤ 10	≤ 10	-0.028	≤ 10	≤ 10	0.033	≤ 10	≤ 10	-0.005	≤ 10	0 (0.0)	0.178

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 6.25. (continued) Baseline characteristics by exposure duration and dose of baricitinib - VTE cohort, Matched [SNDS]

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1183	Bari. 2 mg n = 312	Bari. 4 mg n = 574	Bari. 2 mg n = 126	Bari. 4 mg n = 497	Bari. 2 mg n = 101	Bari. 4 mg n = 52	Bari. 2 mg n = 12
Age [in years]								
N (missing)	1183 (0)	312 (0)	574 (0)	126 (0)	497 (0)	101 (0)	52 (0)	12 (0)
Mean (SD)	55.0 (12.2)	68.8 (13.1)	57.0 (11.9)	69.2 (13.1)	57.1 (11.5)	68.4 (12.6)	54.9 (12.1)	62.8 (7.3)
Median	56.0	71.5	58.0	71.5	58.0	71.0	56.5	65.0
Min; Max	[18.0;90.0]	[25.0;89.0]	[19.0;86.0]	[20.0;88.0]	[20.0;82.0]	[30.0;92.0]	[30.0;76.0]	[49.0;76.0]
Sex, n (%)								
Male	231 (19.5)	55 (17.6)	119 (20.7)	21 (16.7)	125 (25.2)	25 (24.8)	12 (23.1)	≤ 10
Female	952 (80.5)	257 (82.4)	455 (79.3)	105 (83.3)	372 (74.8)	76 (75.2)	40 (76.9)	≤ 10
Clinical conditions during baseline period, n (%)								
Cancer, excluding NMSC	34 (2.9)	17 (5.4)	14 (2.4)	≤ 10	14 (2.8)	≤ 10	≤ 10	0 (0.0)
NMSC	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chronic lung disease, excluding cystic fibrosis[c]	150 (12.7)	55 (17.6)	71 (12.4)	20 (15.9)	52 (10.5)	27 (26.7)	≤ 10	≤ 10
Cardiovascular conditions								
Atrial arrhythmia/fibrillation	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Cardiovascular revascularization	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1183	Bari. 2 mg n = 312	Bari. 4 mg n = 574	Bari. 2 mg n = 126	Bari. 4 mg n = 497	Bari. 2 mg n = 101	Bari. 4 mg n = 52	Bari. 2 mg n = 12
Congestive Heart Failure, hospitalized	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Coronary artery disease	41 (3.5)	21 (6.7)	24 (4.2)	11 (8.7)	17 (3.4)	≤ 10	≤ 10	≤ 10
Unstable angina	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ventricular arrhythmia	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Stroke	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Hemorrhagic	0 (0.0)	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ischemic	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Unknown	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
TIA	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Diabetes Mellitus[c]	97 (8.2)	45 (14.4)	51 (8.9)	14 (11.1)	52 (10.5)	17 (16.8)	≤ 10	≤ 10
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	
	Bari. 4 mg n = 1183	Bari. 2 mg n = 312	Bari. 4 mg n = 574	Bari. 2 mg n = 126	Bari. 4 mg n = 497	Bari. 2 mg n = 101	Bari. 4 mg n = 52	Bari. 2 mg n = 12
Current hypertension	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Immune disorders	47 (4.0)	18 (5.8)	11 (1.9)	≤ 10	15 (3.0)	≤ 10	≤ 10	≤ 10
AIDS/HIV	0 (0.0)	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	18 (1.5)	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)
Primary Sjogren Syndrome	32 (2.7)	17 (5.4)	11 (1.9)	≤ 10	12 (2.4)	≤ 10	0 (0.0)	≤ 10
Liver or pancreatic disorder[c]	33 (2.8)	≤ 10	14 (2.4)	≤ 10	19 (3.8)	≤ 10	≤ 10	≤ 10
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	0 (0.0)	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
RA Severity (CIRAS Index)								
Mean (± SD)	6.7 (1.3)	5.8 (1.4)	6.5 (1.3)	5.8 (1.4)	6.6 (1.3)	5.9 (1.4)	6.8 (1.4)	6.2 (1.1)
DMARDs, n (%)								
cDMARDs, during baseline period								
n, total (%)	797 (67.4)	190 (60.9)	404 (70.4)	80 (63.5)	367 (73.8)	59 (58.4)	38 (73.1)	≤ 10

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1183	Bari. 2 mg n = 312	Bari. 4 mg n = 574	Bari. 2 mg n = 126	Bari. 4 mg n = 497	Bari. 2 mg n = 101	Bari. 4 mg n = 52	Bari. 2 mg n = 12
Mean (SD)	0.7 (0.6)	0.7 (0.6)	0.8 (0.6)	0.7 (0.7)	0.8 (0.6)	0.7 (0.6)	0.9 (0.7)	1.0 (1.0)
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	61 (5.2)	17 (5.4)	32 (5.6)	≤ 10	34 (6.8)	≤ 10	≤ 10	≤ 10
Hydroxychloroquine	60 (5.1)	16 (5.1)	31 (5.4)	15 (11.9)	31 (6.2)	≤ 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	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Leflunomide	159 (13.4)	39 (12.5)	73 (12.7)	≤ 10	58 (11.7)	≤ 10	≤ 10	≤ 10
Methotrexate	621 (52.5)	142 (45.5)	322 (56.1)	64 (50.8)	296 (59.6)	46 (45.5)	27 (51.9)	≤ 10
Mycophenolate mofetil	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Sulfasalazin	37 (3.1)	12 (3.8)	17 (3.0)	≤ 10	18 (3.6)	≤ 10	≤ 10	≤ 10
Cyclosporin	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	≤ 10	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 (%)	668 (56.5)	129 (41.3)	343 (59.8)	55 (43.7)	307 (61.8)	56 (55.4)	33 (63.5)	≤ 10
Mean (SD)	0.6 (0.6)	0.4 (0.5)	0.7 (0.6)	0.5 (0.6)	0.7 (0.6)	0.6 (0.6)	0.8 (0.7)	0.6 (0.7)
Median	1.0	0.0	1.0	0.0	1.0	1.0	1.0	0.5
Min; Max	[0.0;3.0]	[0.0;2.0]	[0.0;3.0]	[0.0;2.0]	[0.0;2.0]	[0.0;3.0]	[0.0;2.0]	[0.0;2.0]
cDMARDs, concomitant	370 (31.3)	60 (19.2)	208 (36.2)	35 (27.8)	187 (37.6)	25 (24.8)	19 (36.5)	≤ 10

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1183	Bari. 2 mg n = 312	Bari. 4 mg n = 574	Bari. 2 mg n = 126	Bari. 4 mg n = 497	Bari. 2 mg n = 101	Bari. 4 mg n = 52	Bari. 2 mg n = 12
Adalimumab[b]	88 (7.4)	18 (5.8)	42 (7.3)	≤ 10	47 (9.5)	≤ 10	≤ 10	≤ 10
Certolizumab pegol[b]	50 (4.2)	≤ 10	29 (5.1)	≤ 10	23 (4.6)	≤ 10	≤ 10	≤ 10
Etanercept[b]	156 (13.2)	29 (9.3)	72 (12.5)	11 (8.7)	49 (9.9)	≤ 10	≤ 10	0 (0.0)
Golimumab[b]	47 (4.0)	≤ 10	22 (3.8)	0 (0.0)	22 (4.4)	≤ 10	≤ 10	≤ 10
Infliximab[b]	37 (3.1)	≤ 10	19 (3.3)	≤ 10	14 (2.8)	≤ 10	≤ 10	0 (0.0)
Rituximab	19 (1.6)	≤ 10	11 (1.9)	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)
Sarilumab	13 (1.1)	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abatacept	158 (13.4)	30 (9.6)	98 (17.1)	20 (15.9)	93 (18.7)	19 (18.8)	12 (23.1)	≤ 10
Tocilizumab	147 (12.4)	28 (9.0)	74 (12.9)	11 (8.7)	75 (15.1)	12 (11.9)	≤ 10	≤ 10
Anakinra	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
TNFi naïve at baseline	820 (69.3)	252 (80.8)	401 (69.9)	103 (81.7)	350 (70.4)	81 (80.2)	38 (73.1)	≤ 10
Other prescription medications during baseline period, n (%)								
Antibiotics	472 (39.9)	140 (44.9)	225 (39.2)	61 (48.4)	206 (41.4)	51 (50.5)	22 (42.3)	≤ 10
Antidiabetic agents	95 (8.0)	41 (13.1)	49 (8.5)	12 (9.5)	52 (10.5)	17 (16.8)	≤ 10	≤ 10
Insulins	37 (3.1)	18 (5.8)	21 (3.7)	≤ 10	14 (2.8)	≤ 10	≤ 10	0 (0.0)
Non-insulins	76 (6.4)	29 (9.3)	42 (7.3)	≤ 10	44 (8.9)	14 (13.9)	≤ 10	≤ 10
Cardiovascular								
Antithrombotic agents	139 (11.7)	87 (27.9)	80 (13.9)	35 (27.8)	69 (13.9)	22 (21.8)	12 (23.1)	≤ 10

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1183	Bari. 2 mg n = 312	Bari. 4 mg n = 574	Bari. 2 mg n = 126	Bari. 4 mg n = 497	Bari. 2 mg n = 101	Bari. 4 mg n = 52	Bari. 2 mg n = 12
Anticoagulant	34 (2.9)	35 (11.2)	23 (4.0)	14 (11.1)	17 (3.4)	≤ 10	≤ 10	≤ 10
Antiplatelet	114 (9.6)	60 (19.2)	62 (10.8)	26 (20.6)	53 (10.7)	19 (18.8)	11 (21.2)	≤ 10
Antihypertensives	303 (25.6)	166 (53.2)	176 (30.7)	73 (57.9)	165 (33.2)	62 (61.4)	18 (34.6)	≤ 10
Angiotensin converting enzyme inhibitors (ACE)	81 (6.8)	40 (12.8)	41 (7.1)	19 (15.1)	42 (8.5)	21 (20.8)	≤ 10	≤ 10
Angiotensin receptor blockers (ARB)	114 (9.6)	68 (21.8)	69 (12.0)	28 (22.2)	60 (12.1)	17 (16.8)	≤ 10	≤ 10
Beta blocker	132 (11.2)	75 (24.0)	69 (12.0)	33 (26.2)	75 (15.1)	28 (27.7)	≤ 10	≤ 10
Calcium channel blocker	64 (5.4)	58 (18.6)	60 (10.5)	18 (14.3)	52 (10.5)	27 (26.7)	≤ 10	≤ 10
Nitrates	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)
Acyclovir	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Valacyclovir	31 (2.6)	16 (5.1)	23 (4.0)	≤ 10	22 (4.4)	≤ 10	≤ 10	0 (0.0)
Hormonal	158 (13.4)	22 (7.1)	90 (15.7)	14 (11.1)	64 (12.9)	≤ 10	≤ 10	≤ 10
HRT	90 (7.6)	16 (5.1)	48 (8.4)	≤ 10	41 (8.2)	≤ 10	≤ 10	≤ 10
Oral Contraceptives	65 (5.5)	≤ 10	42 (7.3)	≤ 10	22 (4.4)	≤ 10	≤ 10	0 (0.0)
SERMs	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)
Topic with progestogens and/or estrogens	≤ 10	0 (0.0)	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1183	Bari. 2 mg n = 312	Bari. 4 mg n = 574	Bari. 2 mg n = 126	Bari. 4 mg n = 497	Bari. 2 mg n = 101	Bari. 4 mg n = 52	Bari. 2 mg n = 12
Lipid-lowering agents	158 (13.4)	86 (27.6)	88 (15.3)	26 (20.6)	80 (16.1)	29 (28.7)	11 (21.2)	≤ 10
HMG CoA reductase inhibitors	125 (10.6)	74 (23.7)	73 (12.7)	23 (18.3)	65 (13.1)	21 (20.8)	≤ 10	≤ 10
Fibrates	12 (1.0)	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Bile acid sequestrants	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other lipid modifying agents	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Lipid modifying agents, combinations	14 (1.2)	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)
Rheumatoid arthritis-related								
Aspirin	11 (0.9)	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
Cox-2 Inhibitor	67 (5.7)	11 (3.5)	36 (6.3)	≤ 10	32 (6.4)	≤ 10	≤ 10	0 (0.0)
NSAIDs	467 (39.5)	89 (28.5)	219 (38.2)	37 (29.4)	177 (35.6)	27 (26.7)	22 (42.3)	≤ 10
Glucocorticosteroid	838 (70.8)	230 (73.7)	404 (70.4)	104 (82.5)	340 (68.4)	67 (66.3)	34 (65.4)	≤ 10
Vaccines	319 (27.0)	105 (33.7)	182 (31.7)	54 (42.9)	136 (27.4)	43 (42.6)	12 (23.1)	≤ 10
Antineoplastic agents	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)	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] 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 6.26. Baseline characteristics by exposure duration - Alternate VTE Cohort (Case Definition I), Matched [SNDS]

Not applicable for SNDS data

Table 6.27. Baseline characteristics by exposure duration - Alternate VTE Cohort (Case Definition II), Matched [SNDS]

Not applicable for SNDS data

Table 6.28. Baseline characteristics by exposure duration - MACE cohort, Matched [SNDS]

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1505	TNFi[a] n = 1521	Std. Diff.	Baricitinib n = 703	TNFi[a] n = 705	Std. Diff.	Baricitinib n = 592	TNFi[a] n = 527	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 111	Std. Diff.
Age [in years]			0.018			0.050			-0.017			-0.299
N (missing)	1505 (0)	1521 (0)		703 (0)	705 (0)		592 (0)	527 (0)		64 (0)	111 (0)	
Mean (SD)	58.1 (13.7)	57.9 (13.6)		59.2 (13.1)	58.5 (13.2)		59.0 (12.4)	59.3 (12.4)		56.5 (11.8)	59.9 (11.0)	
Median	58.0	59.0		59.0	59.0		60.0	60.0		58.0	59.0	
Min; Max	[18.0;90.0]	[18.0;92.0]		[19.0;88.0]	[19.0;91.0]		[20.0;86.0]	[24.0;92.0]		[30.0;77.0]	[37.0;83.0]	
Sex, n (%)			-0.02			0.048			0.093			-0.117
Male	288 (19.1)	303 (19.9)		141 (20.1)	128 (18.2)		143 (24.2)	107 (20.3)		13 (20.3)	28 (25.2)	
Female	1217 (80.9)	1218 (80.1)		562 (79.9)	577 (81.8)		449 (75.8)	420 (79.7)		51 (79.7)	83 (74.8)	
Clinical conditions during baseline period, n (%)												
Cancer, excluding NMSC	51 (3.4)	46 (3.0)	0.021	19 (2.7)	30 (4.3)	-0.085	17 (2.9)	18 (3.4)	-0.031	≤ 10	≤ 10	-0.172
NMSC	≤ 10	≤ 10	-0.051	≤ 10	≤ 10	0.072	0 (0.0)	0 (0.0)	0.000	0 (0.0)	≤ 10	-0.135
Chronic lung disease, excluding cystic fibrosis[d]	213 (14.2)	181 (11.9)	0.067	92 (13.1)	79 (11.2)	0.058	80 (13.5)	63 (12.0)	0.047	≤ 10	11 (9.9)	0.034
Cardiovascular conditions												
Atrial arrhythmia/fibrillation	15 (1.0)	≤ 10	0.093	≤ 10	≤ 10	0.086	≤ 10	≤ 10	0.033	0 (0.0)	0 (0.0)	0.000
Cardiovascular revascularization	≤ 10	≤ 10	-0.036	0 (0.0)	≤ 10	-0.075	≤ 10	≤ 10	-0.007	0 (0.0)	0 (0.0)	0.000

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1505	TNFi[a] n = 1521	Std. Diff.	Baricitinib n = 703	TNFi[a] n = 705	Std. Diff.	Baricitinib n = 592	TNFi[a] n = 527	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 111	Std. Diff.
Congestive Heart Failure, hospitalized	≤ 10	≤ 10	0.013	≤ 10	≤ 10	-0.060	≤ 10	≤ 10	0.019	0 (0.0)	0 (0.0)	0.000
Coronary artery disease	59 (3.9)	75 (4.9)	-0.049	31 (4.4)	35 (5.0)	-0.026	26 (4.4)	21 (4.0)	0.02	≤ 10	≤ 10	-0.027
Unstable angina	0 (0.0)	0 (0.0)	0.000	0 (0.0)	≤ 10	-0.053	0 (0.0)	≤ 10	-0.062	0 (0.0)	0 (0.0)	0.000
Ventricular arrhythmia	≤ 10	≤ 10	-0.036	≤ 10	≤ 10	-0.020	≤ 10	≤ 10	-0.030	0 (0.0)	0 (0.0)	0.000
Stroke	≤ 10	≤ 10	0.027	≤ 10	≤ 10	0.034	≤ 10	≤ 10	0.023	0 (0.0)	0 (0.0)	0.000
Hemorrhagic	≤ 10	0 (0.0)	0.037	0 (0.0)	≤ 10	-0.053	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Ischemic	≤ 10	0 (0.0)	0.052	≤ 10	0 (0.0)	0.076	≤ 10	≤ 10	-0.005	0 (0.0)	0 (0.0)	0.000
Unknown	≤ 10	≤ 10	0.001	≤ 10	≤ 10	0.038	≤ 10	≤ 10	0.027	0 (0.0)	0 (0.0)	0.000
TIA	≤ 10	0 (0.0)	0.037	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[d]	148 (9.8)	145 (9.5)	0.010	66 (9.4)	74 (10.5)	-0.037	63 (10.6)	56 (10.6)	0.001	≤ 10	13 (11.7)	0.024
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[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1505	TNFi[a] n = 1521	Std. Diff.	Baricitinib n = 703	TNFi[a] n = 705	Std. Diff.	Baricitinib n = 592	TNFi[a] n = 527	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 111	Std. Diff.
Current hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Immune disorders	63 (4.2)	56 (3.7)	0.026	16 (2.3)	33 (4.7)	-0.132	19 (3.2)	20 (3.8)	-0.032	≤ 10	≤ 10	0.025
AIDS/HIV	0 (0.0)	≤ 10	-0.036	0 (0.0)	0 (0.0)	0.000	0 (0.0)	≤ 10	-0.062	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	17 (1.1)	≤ 10	0.075	≤ 10	≤ 10	0.054	≤ 10	≤ 10	0.014	≤ 10	0 (0.0)	0.178
Primary Sjogren Syndrome	50 (3.3)	50 (3.3)	0.002	14 (2.0)	32 (4.5)	-0.144	15 (2.5)	16 (3.0)	-0.031	≤ 10	≤ 10	-0.079
Liver or pancreatic disorder[d]	40 (2.7)	41 (2.7)	-0.002	19 (2.7)	23 (3.3)	-0.033	21 (3.5)	11 (2.1)	0.088	≤ 10	≤ 10	0.163
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	-0.050	≤ 10	≤ 10	-0.081	≤ 10	≤ 10	-0.135	0 (0.0)	0 (0.0)	0.000
RA Severity (CIRAS Index)			0.036			-0.059			0.017			0.213
Mean (± SD)	6.5 (1.4)	6.4 (1.4)		6.4 (1.3)	6.4 (1.4)		6.5 (1.3)	6.5 (1.4)		6.7 (1.4)	6.4 (1.3)	
Smoking (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
DMARDs, n (%)												
cDMARDs, during baseline period												

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1505	TNFi[a] n = 1521	Std. Diff.	Baricitinib n = 703	TNFi[a] n = 705	Std. Diff.	Baricitinib n = 592	TNFi[a] n = 527	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 111	Std. Diff.
n, total (%)	991 (65.8)	982 (64.6)	0.027	483 (68.7)	486 (68.9)	-0.005	414 (69.9)	369 (70.0)	-0.002	49 (76.6)	84 (75.7)	0.021
Mean (SD)	0.7 (0.6)	0.7 (0.6)	0.027	0.8 (0.6)	0.7 (0.6)	0.030	0.8 (0.6)	0.8 (0.6)	0.031	0.9 (0.7)	0.8 (0.5)	0.165
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	76 (5.0)	68 (4.5)	0.027	42 (6.0)	26 (3.7)	0.107	36 (6.1)	25 (4.7)	0.059	≤ 10	≤ 10	0.114
Hydroxychloroquine	73 (4.9)	78 (5.1)	-0.013	46 (6.5)	31 (4.4)	0.095	33 (5.6)	24 (4.6)	0.047	≤ 10	≤ 10	0.243
Chloroquine	0 (0.0)	≤ 10	-0.036	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0	≤ 10	0 (0.0)	0.178
Azathioprin	≤ 10	≤ 10	-0.010	≤ 10	≤ 10	0.000	≤ 10	≤ 10	-0.007	≤ 10	0 (0.0)	0.178
Leflunomide	198 (13.2)	175 (11.5)	0.050	76 (10.8)	86 (12.2)	-0.044	66 (11.1)	67 (12.7)	-0.048	11 (17.2)	14 (12.6)	0.129
Methotrexate	763 (50.7)	769 (50.6)	0.003	392 (55.8)	382 (54.2)	0.032	335 (56.6)	288 (54.6)	0.039	33 (51.6)	70 (63.1)	-0.234
Mycophenolate mofetil	0 (0.0)	≤ 10	-0.036	0 (0.0)	≤ 10	-0.053	≤ 10	0 (0.0)	0.058	0 (0.0)	0 (0.0)	0.000
Sulfasalazin	51 (3.4)	47 (3.1)	0.017	21 (3.0)	24 (3.4)	-0.024	22 (3.7)	19 (3.6)	0.006	≤ 10	≤ 10	0.334
Cyclosporin	≤ 10	≤ 10	0.000	0 (0.0)	0 (0.0)	0.000	≤ 10	0 (0.0)	0.058	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	0.000	0 (0.0)	0 (0.0)	0.000
bDMARDs, during baseline period												
n, total (%)	807 (53.6)	839 (55.2)	-0.031	401 (57.0)	417 (59.1)	-0.043	356 (60.1)	298 (56.5)	0.073	41 (64.1)	66 (59.5)	0.095
Mean (SD)	0.6 (0.6)	0.6 (0.6)	-0.053	0.6 (0.6)	0.6 (0.6)	-0.038	0.6 (0.6)	0.6 (0.6)	0.072	0.8 (0.6)	0.6 (0.6)	0.165
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;3.0]		[0.0;3.0]	[0.0;2.0]		[0.0;3.0]	[0.0;2.0]		[0.0;2.0]	[0.0;2.0]	
cDMARDs, concomitant	428 (28.4)	430 (28.3)	0.004	241 (34.3)	236 (33.5)	0.017	203 (34.3)	170 (32.3)	0.043	26 (40.6)	42 (37.8)	0.057

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1505	TNFi[a] n = 1521	Std. Diff.	Baricitinib n = 703	TNFi[a] n = 705	Std. Diff.	Baricitinib n = 592	TNFi[a] n = 527	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 111	Std. Diff.
Adalimumab[c]	104 (6.9)	119 (7.8)	-0.035	48 (6.8)	54 (7.7)	-0.032	55 (9.3)	41 (7.8)	0.054	≤ 10	20 (18.0)	-0.253
Certolizumab pegol[c]	53 (3.5)	58 (3.8)	-0.016	36 (5.1)	36 (5.1)	0.001	21 (3.5)	21 (4.0)	-0.023	≤ 10	≤ 10	0.166
Etanercept[c]	177 (11.8)	193 (12.7)	-0.028	83 (11.8)	91 (12.9)	-0.034	57 (9.6)	65 (12.3)	-0.087	≤ 10	13 (11.7)	-0.192
Golimumab[c]	51 (3.4)	62 (4.1)	-0.036	21 (3.0)	22 (3.1)	-0.008	25 (4.2)	20 (3.8)	0.022	≤ 10	≤ 10	-0.033
Infliximab[c]	41 (2.7)	49 (3.2)	-0.029	23 (3.3)	17 (2.4)	0.052	11 (1.9)	11 (2.1)	-0.017	≤ 10	≤ 10	0.159
Rituximab	28 (1.9)	18 (1.2)	0.055	17 (2.4)	14 (2.0)	0.030	14 (2.4)	≤ 10	0.195	≤ 10	≤ 10	0.172
Sarilumab	18 (1.2)	17 (1.1)	0.007	12 (1.7)	≤ 10	0.048	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Abatacept	197 (13.1)	206 (13.5)	-0.013	113 (16.1)	114 (16.2)	-0.003	105 (17.7)	86 (16.3)	0.038	12 (18.8)	≤ 10	0.285
Tocilizumab	180 (12.0)	183 (12.0)	-0.002	83 (11.8)	95 (13.5)	-0.050	91 (15.4)	70 (13.3)	0.060	≤ 10	12 (10.8)	0.143
Anakinra	≤ 10	≤ 10	0.012	≤ 10	≤ 10	-0.031	≤ 10	≤ 10	-0.040	0 (0.0)	0 (0.0)	0.000
TNFi naïve at baseline	1091 (72.5)	1051 (69.1)	0.075	504 (71.7)	487 (69.1)	0.057	430 (72.6)	373 (70.8)	0.041	45 (70.3)	67 (60.4)	0.210
Other prescription medications during baseline period, n (%)												
Antibiotics	616 (40.9)	604 (39.7)	0.025	290 (41.3)	305 (43.3)	-0.041	257 (43.4)	216 (41.0)	0.049	30 (46.9)	36 (32.4)	0.299
Antidiabetic agents	142 (9.4)	134 (8.8)	0.022	63 (9.0)	73 (10.4)	-0.047	60 (10.1)	55 (10.4)	-0.01	≤ 10	13 (11.7)	0.114
Insulins	62 (4.1)	49 (3.2)	0.048	26 (3.7)	20 (2.8)	0.049	16 (2.7)	18 (3.4)	-0.041	≤ 10	≤ 10	0.054
Non-insulins	108 (7.2)	112 (7.4)	-0.007	51 (7.3)	60 (8.5)	-0.047	52 (8.8)	46 (8.7)	0.002	≤ 10	12 (10.8)	0.099
Cardiovascular Antithrombotic agents	222 (14.8)	246 (16.2)	-0.039	119 (16.9)	106 (15.0)	0.052	87 (14.7)	81 (15.4)	-0.019	16 (25.0)	23 (20.7)	0.102

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1505	TNFi[a] n = 1521	Std. Diff.	Baricitinib n = 703	TNFi[a] n = 705	Std. Diff.	Baricitinib n = 592	TNFi[a] n = 527	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 111	Std. Diff.
Anticoagulant	66 (4.4)	63 (4.1)	0.012	41 (5.8)	23 (3.3)	0.124	18 (3.0)	18 (3.4)	-0.021	≤ 10	≤ 10	0.009
Antiplatelet	171 (11.4)	198 (13.0)	-0.051	89 (12.7)	85 (12.1)	0.018	71 (12.0)	65 (12.3)	-0.010	14 (21.9)	19 (17.1)	0.120
Antihypertensives	476 (31.6)	511 (33.6)	-0.042	245 (34.9)	257 (36.5)	-0.034	218 (36.8)	212 (40.2)	-0.070	26 (40.6)	42 (37.8)	0.057
Angiotensin converting enzyme inhibitors (ACE)	115 (7.6)	139 (9.1)	-0.054	59 (8.4)	66 (9.4)	-0.034	65 (11.0)	51 (9.7)	0.043	≤ 10	≤ 10	0.267
Angiotensin receptor blockers (ARB)	201 (13.4)	203 (13.3)	0.000	94 (13.4)	124 (17.6)	-0.117	73 (12.3)	102 (19.4)	-0.193	≤ 10	19 (17.1)	-0.179
Beta blocker	213 (14.2)	213 (14.0)	0.004	98 (13.9)	102 (14.5)	-0.015	98 (16.6)	88 (16.7)	-0.004	11 (17.2)	17 (15.3)	0.051
Calcium channel blocker	122 (8.1)	153 (10.1)	-0.068	78 (11.1)	77 (10.9)	0.006	76 (12.8)	50 (9.5)	0.107	≤ 10	17 (15.3)	-0.13
Nitrates	12 (0.8)	16 (1.1)	-0.027	≤ 10	12 (1.7)	-0.164	≤ 10	≤ 10	0.016	≤ 10	≤ 10	0.060
Acyclovir	≤ 10	14 (0.9)	-0.037	≤ 10	≤ 10	-0.068	≤ 10	≤ 10	-0.005	0 (0.0)	≤ 10	-0.236
Valacyclovir	50 (3.3)	58 (3.8)	-0.027	25 (3.6)	29 (4.1)	-0.029	29 (4.9)	20 (3.8)	0.054	≤ 10	≤ 10	-0.019
Hormonal	172 (11.4)	217 (14.3)	-0.085	97 (13.8)	104 (14.8)	-0.027	69 (11.7)	62 (11.8)	-0.003	11 (17.2)	16 (14.4)	0.076
HRT	102 (6.8)	127 (8.3)	-0.060	51 (7.3)	58 (8.2)	-0.036	44 (7.4)	36 (6.8)	0.023	≤ 10	≤ 10	0.013
Oral Contraceptives	69 (4.6)	86 (5.7)	-0.049	45 (6.4)	38 (5.4)	0.043	23 (3.9)	26 (4.9)	-0.051	≤ 10	≤ 10	0.059
SERMs	≤ 10	≤ 10	0.001	≤ 10	≤ 10	-0.060	≤ 10	≤ 10	0.019	≤ 10	0 (0.0)	0.178
Topic with progestogens and/or estrogens	≤ 10	≤ 10	-0.059	≤ 10	≤ 10	-0.024	≤ 10	0 (0.0)	0.101	0 (0.0)	0 (0.0)	0.000

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1505	TNFi[a] n = 1521	Std. Diff.	Baricitinib n = 703	TNFi[a] n = 705	Std. Diff.	Baricitinib n = 592	TNFi[a] n = 527	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 111	Std. Diff.
Lipid-lowering agents	236 (15.7)	260 (17.1)	-0.038	119 (16.9)	121 (17.2)	-0.006	112 (18.9)	86 (16.3)	0.068	11 (17.2)	31 (27.9)	-0.259
HMG CoA reductase inhibitors	195 (13.0)	213 (14.0)	-0.031	102 (14.5)	102 (14.5)	0.001	87 (14.7)	67 (12.7)	0.058	≤ 10	28 (25.2)	-0.24
Fibrates	14 (0.9)	25 (1.6)	-0.063	≤ 10	≤ 10	0.016	12 (2.0)	11 (2.1)	-0.004	0 (0.0)	0 (0.0)	0.000
Bile acid sequestrants	≤ 10	≤ 10	0.012	≤ 10	≤ 10	-0.043	≤ 10	≤ 10	0.029	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	11 (0.7)	24 (1.6)	-0.079	≤ 10	≤ 10	-0.018	≤ 10	≤ 10	0.043	0 (0.0)	0 (0.0)	0.000
Lipid modifying agents, combinations	20 (1.3)	16 (1.1)	0.026	≤ 10	≤ 10	0.026	≤ 10	≤ 10	-0.016	≤ 10	≤ 10	-0.079
Rheumatoid arthritis-related												
Aspirin	15 (1.0)	20 (1.3)	-0.030	≤ 10	13 (1.8)	-0.072	≤ 10	≤ 10	0.085	≤ 10	0 (0.0)	0.254
Cox-2 Inhibitor	81 (5.4)	89 (5.9)	-0.02	36 (5.1)	40 (5.7)	-0.025	36 (6.1)	27 (5.1)	0.042	≤ 10	12 (10.8)	-0.231
NSAIDs	553 (36.7)	570 (37.5)	-0.015	264 (37.6)	270 (38.3)	-0.015	206 (34.8)	212 (40.2)	-0.112	24 (37.5)	44 (39.6)	-0.044
Glucocorticosteroid	1078 (71.6)	1056 (69.4)	0.048	511 (72.7)	521 (73.9)	-0.027	404 (68.2)	379 (71.9)	-0.08	41 (64.1)	77 (69.4)	-0.113
Vaccines	426 (28.3)	429 (28.2)	0.002	244 (34.7)	229 (32.5)	0.047	177 (29.9)	171 (32.4)	-0.055	17 (26.6)	28 (25.2)	0.031
Antineoplastic agents	≤ 10	≤ 10	-0.026	≤ 10	≤ 10	0.054	≤ 10	≤ 10	0.029	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] 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 6.28. (continued) Baseline characteristics by exposure duration and dose of baricitinib - MACE cohort, Matched [SNDS]

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1192	Bari. 2 mg n = 313	Bari. 4 mg n = 573	Bari. 2 mg n = 128	Bari. 4 mg n = 495	Bari. 2 mg n = 97	Bari. 4 mg n = 54	Bari. 2 mg n = 10
Age [in years]								
N (missing)	1192 (0)	313 (0)	573 (0)	128 (0)	495 (0)	97 (0)	54 (0)	≤ 10
Mean (SD)	55.2 (12.3)	69.1 (13.1)	56.8 (12.0)	69.6 (13.2)	57.2 (11.6)	68.5 (12.2)	55.1 (12.0)	64.1 (6.7)
Median	56.0	72.0	58.0	72.5	58.0	70.0	56.0	65.0
Min; Max	[18.0;90.0]	[25.0;89.0]	[19.0;86.0]	[20.0;88.0]	[20.0;82.0]	[30.0;86.0]	[30.0;76.0]	[55.0;77.0]
Sex, n (%)								
Male	236 (19.8)	52 (16.6)	118 (20.6)	23 (18.0)	121 (24.4)	22 (22.7)	12 (22.2)	≤ 10
Female	956 (80.2)	261 (83.4)	455 (79.4)	105 (82.0)	374 (75.6)	75 (77.3)	42 (77.8)	≤ 10
Clinical conditions during baseline period, n (%)								
Cancer, excluding NMSC	34 (2.9)	17 (5.4)	13 (2.3)	≤ 10	14 (2.8)	≤ 10	≤ 10	0 (0.0)
NMSC	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chronic lung disease, excluding cystic fibrosis[c]	158 (13.3)	55 (17.6)	70 (12.2)	22 (17.2)	54 (10.9)	26 (26.8)	≤ 10	≤ 10
Cardiovascular conditions								
Atrial arrhythmia/fibrillation	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Cardiovascular revascularization	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	≤ 10	0 (0.0)	0 (0.0)

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1192	Bari. 2 mg n = 313	Bari. 4 mg n = 573	Bari. 2 mg n = 128	Bari. 4 mg n = 495	Bari. 2 mg n = 97	Bari. 4 mg n = 54	Bari. 2 mg n = 10
Congestive Heart Failure, hospitalized	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Coronary artery disease	38 (3.2)	21 (6.7)	20 (3.5)	11 (8.6)	16 (3.2)	≤ 10	≤ 10	0 (0.0)
MACE	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Myocardial infarction	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Unstable angina	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ventricular arrhythmia	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Stroke	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Hemorrhagic	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ischemic	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Unknown	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10	0 (0.0)	0 (0.0)
TIA	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Diabetes Mellitus[c]	106 (8.9)	42 (13.4)	50 (8.7)	15 (11.7)	48 (9.7)	15 (15.5)	≤ 10	≤ 10
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)								

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1192	Bari. 2 mg n = 313	Bari. 4 mg n = 573	Bari. 2 mg n = 128	Bari. 4 mg n = 495	Bari. 2 mg n = 97	Bari. 4 mg n = 54	Bari. 2 mg n = 10
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	45 (3.8)	18 (5.8)	≤ 10	≤ 10	14 (2.8)	≤ 10	≤ 10	≤ 10
AIDS/HIV	0 (0.0)	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	15 (1.3)	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)
Primary Sjogren Syndrome	33 (2.8)	17 (5.4)	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10
Liver or pancreatic disorder[c]	32 (2.7)	≤ 10	13 (2.3)	≤ 10	19 (3.8)	≤ 10	≤ 10	≤ 10
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	0 (0.0)	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
RA Severity (CIRAS Index)								
Mean (± SD)	6.7 (1.4)	5.7 (1.4)	6.5 (1.3)	5.8 (1.4)	6.6 (1.3)	6.0 (1.3)	6.8 (1.4)	6.0 (1.1)
Smoking (not available in SNDS)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
DMARDs, n (%)								

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1192	Bari. 2 mg n = 313	Bari. 4 mg n = 573	Bari. 2 mg n = 128	Bari. 4 mg n = 495	Bari. 2 mg n = 97	Bari. 4 mg n = 54	Bari. 2 mg n = 10
cDMARDs, during baseline period								
n, total (%)	797 (66.9)	194 (62.0)	398 (69.5)	83 (64.8)	363 (73.3)	51 (52.6)	42 (77.8)	≤ 10
Mean (SD)	0.7 (0.6)	0.7 (0.6)	0.8 (0.6)	0.8 (0.7)	0.8 (0.6)	0.6 (0.6)	0.9 (0.7)	0.9 (0.9)
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	59 (4.9)	17 (5.4)	31 (5.4)	11 (8.6)	33 (6.7)	≤ 10	≤ 10	≤ 10
Hydroxychloroquine	58 (4.9)	15 (4.8)	31 (5.4)	15 (11.7)	30 (6.1)	≤ 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)	≤ 10
Azathioprin	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)
Leflunomide	163 (13.7)	35 (11.2)	67 (11.7)	≤ 10	58 (11.7)	≤ 10	≤ 10	≤ 10
Methotrexate	616 (51.7)	147 (47.0)	322 (56.2)	68 (53.1)	295 (59.6)	40 (41.2)	29 (53.7)	≤ 10
Mycophenolate mofetil	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Sulfasalazin	38 (3.2)	13 (4.2)	16 (2.8)	≤ 10	17 (3.4)	≤ 10	≤ 10	≤ 10
Cyclosporin	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	≤ 10	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 (%)	677 (56.8)	130 (41.5)	344 (60.0)	55 (43.0)	303 (61.2)	53 (54.6)	36 (66.7)	≤ 10
Mean (SD)	0.6 (0.6)	0.4 (0.5)	0.7 (0.6)	0.5 (0.6)	0.7 (0.6)	0.6 (0.6)	0.8 (0.7)	0.5 (0.5)
Median	1.0	0.0	1.0	0.0	1.0	1.0	1.0	0.5
Min; Max	[0.0;2.0]	[0.0;2.0]	[0.0;3.0]	[0.0;2.0]	[0.0;2.0]	[0.0;3.0]	[0.0;2.0]	[0.0;1.0]

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1192	Bari. 2 mg n = 313	Bari. 4 mg n = 573	Bari. 2 mg n = 128	Bari. 4 mg n = 495	Bari. 2 mg n = 97	Bari. 4 mg n = 54	Bari. 2 mg n = 10
cDMARDs, concomitant	365 (30.6)	63 (20.1)	204 (35.6)	35 (27.3)	183 (37.0)	20 (20.6)	23 (42.6)	≤ 10
Adalimumab[b]	86 (7.2)	18 (5.8)	42 (7.3)	≤ 10	50 (10.1)	≤ 10	≤ 10	0 (0.0)
Certolizumab pegol[b]	49 (4.1)	≤ 10	32 (5.6)	≤ 10	18 (3.6)	≤ 10	≤ 10	≤ 10
Etanercept[b]	147 (12.3)	30 (9.6)	72 (12.6)	11 (8.6)	49 (9.9)	≤ 10	≤ 10	0 (0.0)
Golimumab[b]	49 (4.1)	≤ 10	20 (3.5)	0 (0.0)	22 (4.4)	≤ 10	≤ 10	≤ 10
Infliximab[b]	36 (3.0)	≤ 10	21 (3.7)	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)
Rituximab	23 (1.9)	≤ 10	13 (2.3)	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
Sarilumab	14 (1.2)	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abatacept	158 (13.3)	39 (12.5)	93 (16.2)	19 (14.8)	85 (17.2)	20 (20.6)	11 (20.4)	≤ 10
Tocilizumab	154 (12.9)	26 (8.3)	72 (12.6)	11 (8.6)	81 (16.4)	≤ 10	≤ 10	≤ 10
Anakinra	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
TNFi naïve at baseline	837 (70.2)	254 (81.2)	396 (69.1)	107 (83.6)	352 (71.1)	78 (80.4)	37 (68.5)	≤ 10
Other prescription medications during baseline period, n (%)								
Antibiotics	471 (39.5)	145 (46.3)	226 (39.4)	63 (49.2)	207 (41.8)	50 (51.5)	27 (50.0)	≤ 10
Antidiabetic agents	104 (8.7)	38 (12.1)	48 (8.4)	14 (10.9)	45 (9.1)	15 (15.5)	≤ 10	≤ 10
Insulins	43 (3.6)	19 (6.1)	20 (3.5)	≤ 10	12 (2.4)	≤ 10	≤ 10	0 (0.0)
Non-insulins	83 (7.0)	25 (8.0)	39 (6.8)	11 (8.6)	39 (7.9)	13 (13.4)	≤ 10	≤ 10
Cardiovascular								

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1192	Bari. 2 mg n = 313	Bari. 4 mg n = 573	Bari. 2 mg n = 128	Bari. 4 mg n = 495	Bari. 2 mg n = 97	Bari. 4 mg n = 54	Bari. 2 mg n = 10
Antithrombotic agents	140 (11.7)	82 (26.2)	81 (14.1)	37 (28.9)	65 (13.1)	22 (22.7)	13 (24.1)	≤ 10
Anticoagulant	33 (2.8)	33 (10.5)	26 (4.5)	15 (11.7)	14 (2.8)	≤ 10	≤ 10	≤ 10
Antiplatelet	114 (9.6)	57 (18.2)	60 (10.5)	28 (21.9)	52 (10.5)	19 (19.6)	12 (22.2)	≤ 10
Antihypertensives	310 (26.0)	166 (53.0)	175 (30.5)	69 (53.9)	157 (31.7)	61 (62.9)	18 (33.3)	≤ 10
Angiotensin converting enzyme inhibitors (ACE)	77 (6.5)	38 (12.1)	43 (7.5)	16 (12.5)	44 (8.9)	21 (21.6)	≤ 10	≤ 10
Angiotensin receptor blockers (ARB)	125 (10.5)	76 (24.3)	68 (11.9)	26 (20.3)	57 (11.5)	16 (16.5)	≤ 10	≤ 10
Beta blocker	139 (11.7)	74 (23.6)	64 (11.2)	33 (25.8)	70 (14.1)	28 (28.9)	≤ 10	≤ 10
Calcium channel blocker	63 (5.3)	59 (18.8)	59 (10.3)	18 (14.1)	47 (9.5)	29 (29.9)	≤ 10	≤ 10
Nitrates	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	0 (0.0)
Acyclovir	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Valacyclovir	33 (2.8)	17 (5.4)	22 (3.8)	≤ 10	22 (4.4)	≤ 10	≤ 10	0 (0.0)
Hormonal	149 (12.5)	23 (7.3)	83 (14.5)	14 (10.9)	64 (12.9)	≤ 10	≤ 10	≤ 10
HRT	85 (7.1)	17 (5.4)	42 (7.3)	≤ 10	42 (8.5)	≤ 10	≤ 10	≤ 10
Oral Contraceptives	63 (5.3)	≤ 10	40 (7.0)	≤ 10	21 (4.2)	≤ 10	≤ 10	0 (0.0)
SERMs	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1192	Bari. 2 mg n = 313	Bari. 4 mg n = 573	Bari. 2 mg n = 128	Bari. 4 mg n = 495	Bari. 2 mg n = 97	Bari. 4 mg n = 54	Bari. 2 mg n = 10
Topic with progestogens and/or estrogens	≤ 10	0 (0.0)	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Lipid-lowering agents	153 (12.8)	83 (26.5)	88 (15.4)	30 (23.4)	84 (17.0)	28 (28.9)	11 (20.4)	0 (0.0)
HMG CoA reductase inhibitors	124 (10.4)	71 (22.7)	74 (12.9)	27 (21.1)	67 (13.5)	20 (20.6)	≤ 10	0 (0.0)
Fibrates	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Bile acid sequestrants	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other lipid modifying agents	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Lipid modifying agents, combinations	16 (1.3)	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)
Rheumatoid arthritis-related								
Aspirin	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
Cox-2 Inhibitor	71 (6.0)	≤ 10	31 (5.4)	≤ 10	33 (6.7)	≤ 10	≤ 10	0 (0.0)
NSAIDs	465 (39.0)	88 (28.1)	228 (39.8)	36 (28.1)	179 (36.2)	27 (27.8)	22 (40.7)	≤ 10
Glucocorticosteroid	846 (71.0)	232 (74.1)	406 (70.9)	104 (81.3)	339 (68.5)	65 (67.0)	36 (66.7)	≤ 10
Vaccines	323 (27.1)	103 (32.9)	185 (32.3)	59 (46.1)	136 (27.5)	41 (42.3)	14 (25.9)	≤ 10
Antineoplastic agents	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10	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] 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 6.29. Baseline characteristics by exposure duration - Incident Serious Infection cohort, Matched [SNDS]

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1569	TNFi[a] n = 1544	Std. Diff.	Baricitinib n = 726	TNFi[a] n = 750	Std. Diff.	Baricitinib n = 617	TNFi[a] n = 573	Std. Diff.	Baricitinib n = 67	TNFi[a] n = 112	Std. Diff.
Age [in years]			0.034			0.023			-0.045			-0.265
N (missing)	1569 (0)	1544 (0)		726 (0)	750 (0)		617 (0)	573 (0)		67 (0)	112 (0)	
Mean (SD)	58.6 (13.9)	58.2 (13.9)		59.3 (13.1)	59.0 (13.1)		59.5 (12.5)	60.0 (13.2)		57.0 (11.9)	60.0 (10.9)	
Median	59.0	59.0		60.0	59.0		60.0	61.0		60.0	60.0	
Min; Max	[18.0;91.0]	[18.0;92.0]		[19.0;89.0]	[19.0;91.0]		[20.0;92.0]	[19.0;90.0]		[30.0;79.0]	[33.0;83.0]	
Sex, n (%)			-0.023			-0.024			0.071			0.054
Male	305 (19.4)	314 (20.3)		144 (19.8)	156 (20.8)		144 (23.3)	117 (20.4)		14 (20.9)	21 (18.8)	
Female	1264 (80.6)	1230 (79.7)		582 (80.2)	594 (79.2)		473 (76.7)	456 (79.6)		53 (79.1)	91 (81.3)	
Clinical conditions during baseline period, n (%)												
Cancer, excluding NMSC	53 (3.4)	51 (3.3)	0.004	25 (3.4)	30 (4.0)	-0.029	17 (2.8)	19 (3.3)	-0.033	≤ 10	≤ 10	-0.133
NMSC	≤ 10	≤ 10	-0.001	≤ 10	0 (0.0)	0.091	0 (0.0)	≤ 10	-0.059	0 (0.0)	0 (0.0)	0.000
Chronic lung disease, excluding cystic fibrosis[d]	220 (14.0)	196 (12.7)	0.039	95 (13.1)	100 (13.3)	-0.007	86 (13.9)	63 (11.0)	0.089	≤ 10	12 (10.7)	0.039
Cardiovascular conditions												
Atrial arrhythmia/fibrillation	36 (2.3)	18 (1.2)	0.087	17 (2.3)	≤ 10	0.099	13 (2.1)	13 (2.3)	-0.011	0 (0.0)	≤ 10	-0.134
Cardiovascular revascularization	≤ 10	≤ 10	-0.026	≤ 10	≤ 10	-0.051	≤ 10	≤ 10	-0.004	0 (0.0)	0 (0.0)	0.000

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1569	TNFi[a] n = 1544	Std. Diff.	Baricitinib n = 726	TNFi[a] n = 750	Std. Diff.	Baricitinib n = 617	TNFi[a] n = 573	Std. Diff.	Baricitinib n = 67	TNFi[a] n = 112	Std. Diff.
Congestive Heart Failure, hospitalized	≤ 10	≤ 10	0.029	≤ 10	≤ 10	0.02	≤ 10	≤ 10	0.021	0 (0.0)	0 (0.0)	0
Coronary artery disease	72 (4.6)	62 (4.0)	0.028	36 (5.0)	28 (3.7)	0.060	28 (4.5)	28 (4.9)	-0.016	≤ 10	≤ 10	0.097
Unstable angina	≤ 10	≤ 10	-0.049	0 (0.0)	≤ 10	-0.052	0 (0.0)	≤ 10	-0.084	0 (0.0)	0 (0.0)	0.000
Ventricular arrhythmia	12 (0.8)	17 (1.1)	-0.035	≤ 10	≤ 10	-0.013	≤ 10	≤ 10	-0.060	0 (0.0)	0 (0.0)	0.000
Stroke	15 (1.0)	15 (1.0)	-0.002	≤ 10	≤ 10	0.003	≤ 10	≤ 10	0.037	0 (0.0)	0 (0.0)	0.000
Hemorrhagic	≤ 10	0 (0.0)	0.036	0 (0.0)	≤ 10	-0.052	0 (0.0)	≤ 10	-0.059	0 (0.0)	0 (0.0)	0.000
Ischemic	≤ 10	≤ 10	0.025	≤ 10	≤ 10	-0.022	≤ 10	≤ 10	0.021	0 (0.0)	0 (0.0)	0.000
Unknown	11 (0.7)	12 (0.8)	-0.009	≤ 10	≤ 10	0.055	≤ 10	≤ 10	0.046	0 (0.0)	0 (0.0)	0.000
TIA	≤ 10	≤ 10	-0.021	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[d]	153 (9.8)	154 (10.0)	-0.008	74 (10.2)	82 (10.9)	-0.024	65 (10.5)	50 (8.7)	0.061	≤ 10	≤ 10	0.051
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[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1569	TNFi[a] n = 1544	Std. Diff.	Baricitinib n = 726	TNFi[a] n = 750	Std. Diff.	Baricitinib n = 617	TNFi[a] n = 573	Std. Diff.	Baricitinib n = 67	TNFi[a] n = 112	Std. Diff.
Current hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Immune disorders	71 (4.5)	48 (3.1)	0.074	20 (2.8)	38 (5.1)	-0.120	21 (3.4)	21 (3.7)	-0.014	≤ 10	≤ 10	0.079
AIDS/HIV	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000	0 (0.0)	≤ 10	-0.059	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	23 (1.5)	≤ 10	0.096	≤ 10	≤ 10	0.045	≤ 10	≤ 10	0.043	≤ 10	0 (0.0)	0.174
Primary Sjogren Syndrome	53 (3.4)	43 (2.8)	0.034	17 (2.3)	36 (4.8)	-0.133	17 (2.8)	18 (3.1)	-0.023	≤ 10	≤ 10	-0.023
Liver or pancreatic disorder[d]	46 (2.9)	48 (3.1)	-0.010	22 (3.0)	30 (4.0)	-0.053	21 (3.4)	13 (2.3)	0.068	≤ 10	≤ 10	-0.023
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	-0.059	≤ 10	≤ 10	-0.035	≤ 10	≤ 10	-0.114	0 (0.0)	0 (0.0)	0.000
RA Severity (CIRAS Index)			-0.025			-0.046			0.103			0.105
Mean (± SD)	6.4 (1.4)	6.5 (1.4)		6.3 (1.3)	6.4 (1.4)		6.5 (1.4)	6.4 (1.4)		6.6 (1.4)	6.5 (1.3)	
Smoking (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
DMARDs, n (%)												
cDMARDs, during baseline period												

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1569	TNFi[a] n = 1544	Std. Diff.	Baricitinib n = 726	TNFi[a] n = 750	Std. Diff.	Baricitinib n = 617	TNFi[a] n = 573	Std. Diff.	Baricitinib n = 67	TNFi[a] n = 112	Std. Diff.
n, total (%)	1026 (65.4)	981 (63.5)	0.039	499 (68.7)	520 (69.3)	-0.013	441 (71.5)	415 (72.4)	-0.021	49 (73.1)	89 (79.5)	-0.149
Mean (SD)	0.7 (0.6)	0.7 (0.6)	0.048	0.8 (0.6)	0.8 (0.6)	0.01	0.8 (0.6)	0.8 (0.6)	-0.008	0.9 (0.7)	0.8 (0.5)	0.09
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;2.0]	
>1 cDMARD concomitantly	83 (5.3)	57 (3.7)	0.077	43 (5.9)	34 (4.5)	0.063	34 (5.5)	28 (4.9)	0.028	≤ 10	≤ 10	0.224
Hydroxychloroquine	82 (5.2)	64 (4.1)	0.051	46 (6.3)	29 (3.9)	0.112	35 (5.7)	22 (3.8)	0.086	≤ 10	≤ 10	0.229
Chloroquine	0 (0.0)	≤ 10	-0.036	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0	≤ 10	0 (0.0)	0.174
Azathioprin	≤ 10	≤ 10	0.01	≤ 10	≤ 10	0.002	≤ 10	≤ 10	-0.005	≤ 10	0 (0.0)	0.174
Leflunomide	212 (13.5)	199 (12.9)	0.018	84 (11.6)	84 (11.2)	0.012	65 (10.5)	83 (14.5)	-0.12	≤ 10	15 (13.4)	0.044
Methotrexate	785 (50.0)	761 (49.3)	0.015	398 (54.8)	426 (56.8)	-0.04	356 (57.7)	324 (56.5)	0.023	36 (53.7)	74 (66.1)	-0.254
Mycophenolate mofetil	0 (0.0)	≤ 10	-0.036	0 (0.0)	≤ 10	-0.052	≤ 10	0 (0.0)	0.057	0 (0.0)	0 (0.0)	0.000
Sulfasalazin	51 (3.3)	44 (2.8)	0.023	25 (3.4)	27 (3.6)	-0.009	24 (3.9)	20 (3.5)	0.021	≤ 10	0 (0.0)	0.402
Cyclosporin	≤ 10	0 (0.0)	0.036	0 (0.0)	0 (0.0)	0.000	≤ 10	0 (0.0)	0.057	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	-0.059	0 (0.0)	0 (0.0)	0.000
bDMARDs, during baseline period												
n, total (%)	835 (53.2)	852 (55.2)	-0.039	410 (56.5)	446 (59.5)	-0.061	370 (60.0)	312 (54.5)	0.112	42 (62.7)	60 (53.6)	0.186
Mean (SD)	0.6 (0.6)	0.6 (0.6)	-0.051	0.6 (0.6)	0.7 (0.6)	-0.054	0.6 (0.6)	0.6 (0.6)	0.101	0.7 (0.6)	0.6 (0.6)	0.205
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;2.0]	[0.0;2.0]		[0.0;2.0]	[0.0;2.0]	
cDMARDs, concomitant	449 (28.6)	441 (28.6)	0.001	249 (34.3)	254 (33.9)	0.009	221 (35.8)	184 (32.1)	0.078	27 (40.3)	42 (37.5)	0.057

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1569	TNFi[a] n = 1544	Std. Diff.	Baricitinib n = 726	TNFi[a] n = 750	Std. Diff.	Baricitinib n = 617	TNFi[a] n = 573	Std. Diff.	Baricitinib n = 67	TNFi[a] n = 112	Std. Diff.
Adalimumab[c]	118 (7.5)	117 (7.6)	-0.002	47 (6.5)	57 (7.6)	-0.044	51 (8.3)	51 (8.9)	-0.023	≤ 10	16 (14.3)	-0.167
Certolizumab pegol[c]	57 (3.6)	63 (4.1)	-0.023	30 (4.1)	31 (4.1)	0.000	24 (3.9)	22 (3.8)	0.003	≤ 10	≤ 10	-0.114
Etanercept[c]	181 (11.5)	181 (11.7)	-0.006	84 (11.6)	102 (13.6)	-0.061	61 (9.9)	63 (11.0)	-0.036	≤ 10	11 (9.8)	-0.209
Golimumab[c]	52 (3.3)	63 (4.1)	-0.041	26 (3.6)	21 (2.8)	0.045	27 (4.4)	18 (3.1)	0.065	≤ 10	≤ 10	0.001
Infliximab[c]	47 (3.0)	47 (3.0)	-0.003	23 (3.2)	23 (3.1)	0.006	13 (2.1)	15 (2.6)	-0.034	≤ 10	≤ 10	0.055
Rituximab	21 (1.3)	17 (1.1)	0.022	≤ 10	14 (1.9)	-0.051	16 (2.6)	≤ 10	0.187	≤ 10	≤ 10	0.318
Sarilumab	24 (1.5)	19 (1.2)	0.026	11 (1.5)	≤ 10	0.027	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Abatacept	209 (13.3)	229 (14.8)	-0.044	119 (16.4)	123 (16.4)	0.000	108 (17.5)	87 (15.2)	0.063	15 (22.4)	≤ 10	0.408
Tocilizumab	178 (11.3)	182 (11.8)	-0.014	97 (13.4)	103 (13.7)	-0.011	91 (14.7)	71 (12.4)	0.069	≤ 10	12 (10.7)	0.084
Anakinra	≤ 10	≤ 10	-0.001	≤ 10	≤ 10	-0.027	≤ 10	≤ 10	-0.062	0 (0.0)	0 (0.0)	0.000
TNFi naïve at baseline	1133 (72.2)	1083 (70.1)	0.046	526 (72.5)	521 (69.5)	0.066	449 (72.8)	408 (71.2)	0.035	52 (77.6)	73 (65.2)	0.278
Other prescription medications during baseline period, n (%)												
Antibiotics	654 (41.7)	636 (41.2)	0.010	302 (41.6)	337 (44.9)	-0.067	275 (44.6)	216 (37.7)	0.140	29 (43.3)	36 (32.1)	0.231
Antidiabetic agents	148 (9.4)	141 (9.1)	0.010	71 (9.8)	76 (10.1)	-0.012	60 (9.7)	52 (9.1)	0.022	≤ 10	12 (10.7)	0.039
Insulins	59 (3.8)	61 (4.0)	-0.010	31 (4.3)	22 (2.9)	0.072	21 (3.4)	13 (2.3)	0.068	≤ 10	≤ 10	-0.156
Non-insulins	117 (7.5)	112 (7.3)	0.008	61 (8.4)	62 (8.3)	0.005	48 (7.8)	46 (8.0)	-0.009	≤ 10	11 (9.8)	0.021
Cardiovascular												
Antithrombotic agents	293 (18.7)	266 (17.2)	0.038	146 (20.1)	131 (17.5)	0.068	117 (19.0)	97 (16.9)	0.053	19 (28.4)	23 (20.5)	0.183

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1569	TNFi[a] n = 1544	Std. Diff.	Baricitinib n = 726	TNFi[a] n = 750	Std. Diff.	Baricitinib n = 617	TNFi[a] n = 573	Std. Diff.	Baricitinib n = 67	TNFi[a] n = 112	Std. Diff.
Anticoagulant	136 (8.7)	111 (7.2)	0.055	68 (9.4)	56 (7.5)	0.069	47 (7.6)	45 (7.9)	-0.009	≤ 10	11 (9.8)	-0.030
Antiplatelet	187 (11.9)	175 (11.3)	0.018	92 (12.7)	81 (10.8)	0.058	74 (12.0)	58 (10.1)	0.060	14 (20.9)	15 (13.4)	0.200
Antihypertensives	527 (33.6)	509 (33.0)	0.013	265 (36.5)	277 (36.9)	-0.009	244 (39.5)	219 (38.2)	0.027	28 (41.8)	38 (33.9)	0.163
Angiotensin converting enzyme inhibitors (ACE)	134 (8.5)	154 (10.0)	-0.050	67 (9.2)	75 (10.0)	-0.026	72 (11.7)	50 (8.7)	0.097	11 (16.4)	≤ 10	0.258
Angiotensin receptor blockers (ARB)	209 (13.3)	186 (12.0)	0.038	107 (14.7)	129 (17.2)	-0.067	80 (13.0)	98 (17.1)	-0.116	≤ 10	17 (15.2)	-0.142
Beta blocker	247 (15.7)	217 (14.1)	0.047	113 (15.6)	105 (14.0)	0.044	113 (18.3)	103 (18.0)	0.009	≤ 10	15 (13.4)	0.044
Calcium channel blocker	132 (8.4)	141 (9.1)	-0.025	81 (11.2)	82 (10.9)	0.007	78 (12.6)	58 (10.1)	0.079	≤ 10	14 (12.5)	-0.064
Nitrates	15 (1.0)	13 (0.8)	0.012	≤ 10	11 (1.5)	-0.109	≤ 10	≤ 10	0.107	≤ 10	≤ 10	0.055
Acyclovir	≤ 10	11 (0.7)	-0.017	≤ 10	≤ 10	-0.045	≤ 10	≤ 10	-0.004	0 (0.0)	≤ 10	-0.235
Valacyclovir	50 (3.2)	60 (3.9)	-0.038	26 (3.6)	27 (3.6)	-0.001	31 (5.0)	20 (3.5)	0.076	≤ 10	≤ 10	-0.023
Hormonal	182 (11.6)	228 (14.8)	-0.094	102 (14.0)	96 (12.8)	0.037	68 (11.0)	56 (9.8)	0.041	11 (16.4)	14 (12.5)	0.112
HRT	108 (6.9)	125 (8.1)	-0.046	53 (7.3)	54 (7.2)	0.004	43 (7.0)	31 (5.4)	0.065	≤ 10	≤ 10	0.001
Oral Contraceptives	71 (4.5)	102 (6.6)	-0.091	48 (6.6)	31 (4.1)	0.11	21 (3.4)	23 (4.0)	-0.032	≤ 10	≤ 10	0.171
SERMs	≤ 10	≤ 10	-0.014	≤ 10	≤ 10	-0.072	≤ 10	≤ 10	-0.028	≤ 10	0 (0.0)	0.174
Topic with progestogens and/or estrogens	≤ 10	≤ 10	0.015	≤ 10	≤ 10	-0.072	≤ 10	0 (0.0)	0.099	0 (0.0)	0 (0.0)	0

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1569	TNFi[a] n = 1544	Std. Diff.	Baricitinib n = 726	TNFi[a] n = 750	Std. Diff.	Baricitinib n = 617	TNFi[a] n = 573	Std. Diff.	Baricitinib n = 67	TNFi[a] n = 112	Std. Diff.
Lipid-lowering agents	260 (16.6)	240 (15.5)	0.028	131 (18.0)	125 (16.7)	0.036	119 (19.3)	97 (16.9)	0.061	13 (19.4)	22 (19.6)	-0.006
HMG CoA reductase inhibitors	211 (13.4)	193 (12.5)	0.028	112 (15.4)	107 (14.3)	0.033	92 (14.9)	76 (13.3)	0.047	11 (16.4)	20 (17.9)	-0.038
Fibrates	20 (1.3)	26 (1.7)	-0.034	≤ 10	≤ 10	0.003	15 (2.4)	≤ 10	0.076	0 (0.0)	0 (0.0)	0.000
Bile acid sequestrants	≤ 10	≤ 10	0.032	≤ 10	≤ 10	0.002	≤ 10	≤ 10	-0.004	0 (0.0)	≤ 10	-0.134
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	14 (0.9)	17 (1.1)	-0.021	≤ 10	≤ 10	0.036	≤ 10	≤ 10	0.008	0 (0.0)	0 (0.0)	0.000
Lipid modifying agents, combinations	19 (1.2)	15 (1.0)	0.023	11 (1.5)	≤ 10	0.015	≤ 10	≤ 10	0.004	≤ 10	≤ 10	0.152
Rheumatoid arthritis-related												
Aspirin	18 (1.1)	18 (1.2)	-0.002	≤ 10	14 (1.9)	-0.090	≤ 10	≤ 10	0.050	≤ 10	≤ 10	0.079
Cox-2 Inhibitor	79 (5.0)	93 (6.0)	-0.043	39 (5.4)	42 (5.6)	-0.010	34 (5.5)	31 (5.4)	0.004	≤ 10	≤ 10	-0.147
NSAIDs	564 (35.9)	581 (37.6)	-0.035	261 (36.0)	276 (36.8)	-0.018	214 (34.7)	234 (40.8)	-0.127	21 (31.3)	42 (37.5)	-0.130
Glucocorticosteroid	1139 (72.6)	1105 (71.6)	0.023	532 (73.3)	549 (73.2)	0.002	423 (68.6)	411 (71.7)	-0.069	43 (64.2)	83 (74.1)	-0.216
Vaccines	451 (28.7)	419 (27.1)	0.036	253 (34.8)	253 (33.7)	0.024	191 (31.0)	207 (36.1)	-0.110	18 (26.9)	31 (27.7)	-0.018
Antineoplastic agents	≤ 10	≤ 10	-0.019	≤ 10	≤ 10	0.032	≤ 10	≤ 10	-0.037	≤ 10	0 (0.0)	0.174

Abbreviations: DMARD = disease-modifying antirheumatic drugs; MI = myocardial infarction; mos = months; N = number of patients in specified category; Std. Diff = standardized difference; TNFi = tumor necrosis factor inhibitor, 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

Table 6.29. (continued) Baseline characteristics by exposure duration and dose of baricitinib - Incident Serious Infection cohort, Matched [SNDS]

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1228	Bari. 2 mg n = 340	Bari. 4 mg n = 595	Bari. 2 mg n = 129	Bari. 4 mg n = 507	Bari. 2 mg n = 110	Bari. 4 mg n = 55	Bari. 2 mg n = 12
Age [in years]								
N (missing)	1228 (0)	340 (0)	595 (0)	129 (0)	507 (0)	110 (0)	55 (0)	12 (0)
Mean (SD)	55.6 (12.5)	69.7 (13.1)	57.1 (12.1)	69.5 (12.9)	57.3 (11.4)	69.4 (12.6)	55.3 (11.7)	64.8 (9.6)
Median	57.0	73.0	58.0	72.0	58.0	73.0	58.0	65.0
Min; Max	[18.0;90.0]	[25.0;91.0]	[19.0;86.0]	[20.0;89.0]	[20.0;84.0]	[30.0;92.0]	[30.0;74.0]	[48.0;79.0]
Sex, n (%)								
Male	246 (20.0)	59 (17.4)	124 (20.8)	20 (15.5)	117 (23.1)	27 (24.5)	11 (20.0)	≤ 10
Female	982 (80.0)	281 (82.6)	471 (79.2)	109 (84.5)	390 (76.9)	83 (75.5)	44 (80.0)	≤ 10
Clinical conditions during baseline period, n (%)								
Cancer, excluding NMSC	35 (2.9)	18 (5.3)	17 (2.9)	≤ 10	14 (2.8)	≤ 10	≤ 10	0 (0.0)
NMSC	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chronic lung disease, excluding cystic fibrosis[c]	160 (13.0)	60 (17.6)	74 (12.4)	21 (16.3)	55 (10.8)	31 (28.2)	≤ 10	≤ 10
Cardiovascular conditions								
Atrial arrhythmia/fibrillation	17 (1.4)	19 (5.6)	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Cardiovascular revascularization	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1228	Bari. 2 mg n = 340	Bari. 4 mg n = 595	Bari. 2 mg n = 129	Bari. 4 mg n = 507	Bari. 2 mg n = 110	Bari. 4 mg n = 55	Bari. 2 mg n = 12
Congestive Heart Failure, hospitalized	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Coronary artery disease	51 (4.2)	21 (6.2)	24 (4.0)	12 (9.3)	18 (3.6)	≤ 10	≤ 10	≤ 10
Unstable angina	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ventricular arrhythmia	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Stroke	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Hemorrhagic	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ischemic	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Unknown	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
TIA	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Diabetes Mellitus[c]	103 (8.4)	50 (14.7)	57 (9.6)	16 (12.4)	48 (9.5)	17 (15.5)	≤ 10	≤ 10
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	
	Bari. 4 mg n = 1228	Bari. 2 mg n = 340	Bari. 4 mg n = 595	Bari. 2 mg n = 129	Bari. 4 mg n = 507	Bari. 2 mg n = 110	Bari. 4 mg n = 55	Bari. 2 mg n = 12
Current hypertension	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Immune disorders	51 (4.2)	20 (5.9)	14 (2.4)	≤ 10	16 (3.2)	≤ 10	≤ 10	≤ 10
AIDS/HIV	0 (0.0)	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	20 (1.6)	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)
Primary Sjogren Syndrome	34 (2.8)	19 (5.6)	12 (2.0)	≤ 10	12 (2.4)	≤ 10	0 (0.0)	≤ 10
Liver or pancreatic disorder[c]	34 (2.8)	11 (3.2)	16 (2.7)	≤ 10	18 (3.6)	≤ 10	0 (0.0)	≤ 10
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	0 (0.0)	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
RA Severity (CIRAS Index)								
Mean (± SD)	6.7 (1.4)	5.7 (1.4)	6.5 (1.3)	5.8 (1.4)	6.6 (1.3)	5.8 (1.4)	6.8 (1.4)	5.7 (0.6)
Smoking (not available in SNDS)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
DMARDs, n (%)								
cDMARDs, during baseline period								

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1228	Bari. 2 mg n = 340	Bari. 4 mg n = 595	Bari. 2 mg n = 129	Bari. 4 mg n = 507	Bari. 2 mg n = 110	Bari. 4 mg n = 55	Bari. 2 mg n = 12
n, total (%)	820 (66.8)	205 (60.3)	417 (70.1)	80 (62.0)	380 (75.0)	61 (55.5)	41 (74.5)	≤ 10
Mean (SD)	0.7 (0.6)	0.7 (0.6)	0.8 (0.6)	0.7 (0.7)	0.8 (0.6)	0.6 (0.6)	0.9 (0.7)	1.0 (1.0)
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	65 (5.3)	18 (5.3)	34 (5.7)	≤ 10	30 (5.9)	≤ 10	≤ 10	≤ 10
Hydroxychloroquine	62 (5.0)	20 (5.9)	33 (5.5)	13 (10.1)	31 (6.1)	≤ 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)	≤ 10
Azathioprin	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)
Leflunomide	173 (14.1)	39 (11.5)	75 (12.6)	≤ 10	56 (11.0)	≤ 10	≤ 10	≤ 10
Methotrexate	633 (51.5)	152 (44.7)	330 (55.5)	66 (51.2)	307 (60.6)	49 (44.5)	31 (56.4)	≤ 10
Mycophenolate mofetil	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Sulfasalazin	39 (3.2)	12 (3.5)	20 (3.4)	≤ 10	18 (3.6)	≤ 10	≤ 10	≤ 10
Cyclosporin	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	≤ 10	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 (%)	697 (56.8)	137 (40.3)	355 (59.7)	53 (41.1)	309 (60.9)	61 (55.5)	36 (65.5)	≤ 10
Mean (SD)	0.6 (0.6)	0.4 (0.5)	0.7 (0.6)	0.4 (0.5)	0.7 (0.6)	0.6 (0.5)	0.7 (0.6)	0.5 (0.5)
Median	1.0	0.0	1.0	0.0	1.0	1.0	1.0	0.5
Min; Max	[0.0;3.0]	[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;1.0]
cDMARDs, concomitant	385 (31.4)	63 (18.5)	215 (36.1)	32 (24.8)	193 (38.1)	28 (25.5)	22 (40.0)	≤ 10

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1228	Bari. 2 mg n = 340	Bari. 4 mg n = 595	Bari. 2 mg n = 129	Bari. 4 mg n = 507	Bari. 2 mg n = 110	Bari. 4 mg n = 55	Bari. 2 mg n = 12
Adalimumab[b]	98 (8.0)	20 (5.9)	44 (7.4)	≤ 10	47 (9.3)	≤ 10	≤ 10	0 (0.0)
Certolizumab pegol[b]	51 (4.2)	≤ 10	26 (4.4)	≤ 10	22 (4.3)	≤ 10	≤ 10	≤ 10
Etanercept[b]	153 (12.5)	28 (8.2)	74 (12.4)	≤ 10	51 (10.1)	≤ 10	≤ 10	0 (0.0)
Golimumab[b]	49 (4.0)	≤ 10	25 (4.2)	0 (0.0)	24 (4.7)	≤ 10	≤ 10	≤ 10
Infliximab[b]	41 (3.3)	≤ 10	23 (3.9)	0 (0.0)	12 (2.4)	≤ 10	≤ 10	0 (0.0)
Rituximab	16 (1.3)	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	≤ 10
Sarilumab	19 (1.5)	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abatacept	167 (13.6)	41 (12.1)	96 (16.1)	22 (17.1)	85 (16.8)	23 (20.9)	12 (21.8)	≤ 10
Tocilizumab	149 (12.1)	29 (8.5)	84 (14.1)	13 (10.1)	79 (15.6)	12 (10.9)	≤ 10	0 (0.0)
Anakinra	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
TNFi naïve at baseline	855 (69.6)	278 (81.8)	412 (69.2)	113 (87.6)	359 (70.8)	90 (81.8)	42 (76.4)	≤ 10
Other prescription medications during baseline period, n (%)								
Antibiotics	491 (40.0)	162 (47.6)	241 (40.5)	60 (46.5)	216 (42.6)	59 (53.6)	25 (45.5)	≤ 10
Antidiabetic agents	103 (8.4)	45 (13.2)	55 (9.2)	15 (11.6)	43 (8.5)	17 (15.5)	≤ 10	≤ 10
Insulins	40 (3.3)	19 (5.6)	24 (4.0)	≤ 10	15 (3.0)	≤ 10	≤ 10	0 (0.0)
Non-insulins	85 (6.9)	32 (9.4)	47 (7.9)	13 (10.1)	34 (6.7)	14 (12.7)	≤ 10	≤ 10
Cardiovascular								
Antithrombotic agents	180 (14.7)	113 (33.2)	98 (16.5)	47 (36.4)	87 (17.2)	30 (27.3)	12 (21.8)	≤ 10

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1228	Bari. 2 mg n = 340	Bari. 4 mg n = 595	Bari. 2 mg n = 129	Bari. 4 mg n = 507	Bari. 2 mg n = 110	Bari. 4 mg n = 55	Bari. 2 mg n = 12
Anticoagulant	71 (5.8)	65 (19.1)	45 (7.6)	23 (17.8)	36 (7.1)	11 (10.0)	≤ 10	≤ 10
Antiplatelet	125 (10.2)	62 (18.2)	61 (10.3)	30 (23.3)	53 (10.5)	21 (19.1)	≤ 10	≤ 10
Antihypertensives	341 (27.8)	186 (54.7)	194 (32.6)	70 (54.3)	170 (33.5)	74 (67.3)	19 (34.5)	≤ 10
Angiotensin converting enzyme inhibitors (ACE)	91 (7.4)	43 (12.6)	49 (8.2)	18 (14.0)	47 (9.3)	25 (22.7)	≤ 10	≤ 10
Angiotensin receptor blockers (ARB)	131 (10.7)	78 (22.9)	80 (13.4)	27 (20.9)	58 (11.4)	22 (20.0)	≤ 10	≤ 10
Beta blocker	155 (12.6)	92 (27.1)	75 (12.6)	37 (28.7)	78 (15.4)	35 (31.8)	≤ 10	≤ 10
Calcium channel blocker	70 (5.7)	62 (18.2)	64 (10.8)	16 (12.4)	48 (9.5)	30 (27.3)	≤ 10	≤ 10
Nitrates	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)
Acyclovir	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Valacyclovir	35 (2.9)	15 (4.4)	22 (3.7)	≤ 10	24 (4.7)	≤ 10	≤ 10	0 (0.0)
Hormonal	159 (12.9)	23 (6.8)	88 (14.8)	14 (10.9)	61 (12.0)	≤ 10	≤ 10	≤ 10
HRT	91 (7.4)	17 (5.0)	44 (7.4)	≤ 10	40 (7.9)	≤ 10	≤ 10	≤ 10
Oral Contraceptives	65 (5.3)	≤ 10	43 (7.2)	≤ 10	19 (3.7)	≤ 10	≤ 10	0 (0.0)
SERMs	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)
Topic with progestogens and/or estrogens	≤ 10	0 (0.0)	≤ 10	0 (0.0)	≤ 10	≤ 10	0 (0.0)	0 (0.0)

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1228	Bari. 2 mg n = 340	Bari. 4 mg n = 595	Bari. 2 mg n = 129	Bari. 4 mg n = 507	Bari. 2 mg n = 110	Bari. 4 mg n = 55	Bari. 2 mg n = 12
Lipid-lowering agents	171 (13.9)	89 (26.2)	99 (16.6)	31 (24.0)	87 (17.2)	32 (29.1)	11 (20.0)	≤ 10
HMG CoA reductase inhibitors	135 (11.0)	76 (22.4)	82 (13.8)	29 (22.5)	68 (13.4)	24 (21.8)	≤ 10	≤ 10
Fibrates	15 (1.2)	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Bile acid sequestrants	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other lipid modifying agents	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Lipid modifying agents, combinations	15 (1.2)	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)
Rheumatoid arthritis-related								
Aspirin	12 (1.0)	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
Cox-2 Inhibitor	66 (5.4)	13 (3.8)	35 (5.9)	≤ 10	31 (6.1)	≤ 10	≤ 10	0 (0.0)
NSAIDs	475 (38.7)	89 (26.2)	227 (38.2)	34 (26.4)	186 (36.7)	28 (25.5)	20 (36.4)	≤ 10
Glucocorticosteroid	880 (71.7)	258 (75.9)	423 (71.1)	108 (83.7)	349 (68.8)	74 (67.3)	35 (63.6)	≤ 10
Vaccines	328 (26.7)	123 (36.2)	197 (33.1)	56 (43.4)	143 (28.2)	48 (43.6)	15 (27.3)	≤ 10
Antineoplastic agents	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	≤ 10

Abbreviations: DMARD = disease-modifying antirheumatic drugs; MI = myocardial infarction; mos = months; N = number of patients in specified category; Std. Diff = standardized difference; TNFi = tumor necrosis factor inhibitor, HRT = hormone replacement therapy.

[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 6.30. Baseline characteristics by exposure duration - Hospitalized Tuberculosis Cohort, Matched [SNDS]

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1571	TNFi[a] n = 1536	Std. Diff.	Baricitinib n = 733	TNFi[a] n = 777	Std. Diff.	Baricitinib n = 632	TNFi[a] n = 570	Std. Diff.	Baricitinib n = 69	TNFi[a] n = 122	Std. Diff.
Age [in years]			0.026			-0.018			-0.079			-0.149
N (missing)	1571 (0)	1536 (0)		733 (0)	777 (0)		632 (0)	570 (0)		69 (0)	122 (0)	
Mean (SD)	58.7 (13.9)	58.4 (13.8)		59.7 (13.2)	59.9 (13.1)		59.2 (12.4)	60.2 (12.4)		57.6 (12.1)	59.4 (12.2)	
Median	59.0	59.0		60.0	60.0		60.0	61.0		60.0	59.5	
Min; Max	[18.0;98.0]	[18.0;94.0]		[19.0;88.0]	[19.0;91.0]		[20.0;92.0]	[24.0;90.0]		[30.0;79.0]	[22.0;83.0]	
Sex, n (%)			0.013			0.002			0.062			0.079
Male	308 (19.6)	293 (19.1)		142 (19.4)	150 (19.3)		154 (24.4)	124 (21.8)		17 (24.6)	26 (21.3)	
Female	1263 (80.4)	1243 (80.9)		591 (80.6)	627 (80.7)		478 (75.6)	446 (78.2)		52 (75.4)	96 (78.7)	
Clinical conditions during baseline period, n (%)												
Cancer, excluding NMSC	56 (3.6)	44 (2.9)	0.04	25 (3.4)	29 (3.7)	-0.017	17 (2.7)	25 (4.4)	-0.092	≤ 10	≤ 10	-0.073
NMSC	≤ 10	≤ 10	0.02	≤ 10	≤ 10	0.054	≤ 10	≤ 10	-0.083	0 (0.0)	≤ 10	-0.129
Chronic lung disease, excluding cystic fibrosis[d]	221 (14.1)	188 (12.2)	0.054	108 (14.7)	97 (12.5)	0.066	90 (14.2)	66 (11.6)	0.079	≤ 10	11 (9.0)	0.038
Cardiovascular conditions												
Atrial arrhythmia/fibrillation	38 (2.4)	24 (1.6)	0.061	20 (2.7)	15 (1.9)	0.053	15 (2.4)	11 (1.9)	0.031	0 (0.0)	0 (0.0)	0.000
Cardiovascular revascularization	≤ 10	≤ 10	-0.047	≤ 10	≤ 10	-0.039	≤ 10	0 (0.0)	0.098	0 (0.0)	0 (0.0)	0.000

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1571	TNFi[a] n = 1536	Std. Diff.	Baricitinib n = 733	TNFi[a] n = 777	Std. Diff.	Baricitinib n = 632	TNFi[a] n = 570	Std. Diff.	Baricitinib n = 69	TNFi[a] n = 122	Std. Diff.
Congestive Heart Failure, hospitalized	≤ 10	11 (0.7)	-0.027	≤ 10	≤ 10	-0.009	≤ 10	≤ 10	-0.03	0 (0.0)	0 (0.0)	0.000
Coronary artery disease	70 (4.5)	75 (4.9)	-0.02	34 (4.6)	38 (4.9)	-0.012	31 (4.9)	26 (4.6)	0.016	≤ 10	≤ 10	0.078
Unstable angina	≤ 10	≤ 10	-0.049	0 (0.0)	≤ 10	-0.072	0 (0.0)	≤ 10	-0.084	0 (0.0)	0 (0.0)	0.000
Ventricular arrhythmia	13 (0.8)	17 (1.1)	-0.029	≤ 10	≤ 10	-0.034	≤ 10	≤ 10	-0.01	0 (0.0)	≤ 10	-0.225
Stroke	14 (0.9)	17 (1.1)	-0.022	≤ 10	≤ 10	0.019	≤ 10	≤ 10	0.071	0 (0.0)	0 (0.0)	0.000
Hemorrhagic	0 (0.0)	0 (0.0)	0.000	≤ 10	≤ 10	0.002	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Ischemic	≤ 10	≤ 10	-0.022	≤ 10	≤ 10	0.054	≤ 10	≤ 10	0.053	0 (0.0)	0 (0.0)	0.000
Unknown	11 (0.7)	11 (0.7)	-0.002	≤ 10	≤ 10	0.035	≤ 10	≤ 10	0.065	0 (0.0)	0 (0.0)	0.000
TIA	≤ 10	≤ 10	-0.027	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[d]	155 (9.9)	148 (9.6)	0.008	74 (10.1)	85 (10.9)	-0.028	67 (10.6)	58 (10.2)	0.014	11 (15.9)	14 (11.5)	0.13
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[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1571	TNFi[a] n = 1536	Std. Diff.	Baricitinib n = 733	TNFi[a] n = 777	Std. Diff.	Baricitinib n = 632	TNFi[a] n = 570	Std. Diff.	Baricitinib n = 69	TNFi[a] n = 122	Std. Diff.
Current hypertension	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
Immune disorders	64 (4.1)	58 (3.8)	0.015	20 (2.7)	31 (4.0)	-0.07	23 (3.6)	22 (3.9)	-0.012	≤ 10	≤ 10	-0.022
AIDS/HIV	0 (0.0)	≤ 10	-0.036	0 (0.0)	0 (0.0)	0	0 (0.0)	≤ 10	-0.084	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	18 (1.1)	≤ 10	0.078	≤ 10	≤ 10	0.054	≤ 10	≤ 10	-0.007	≤ 10	≤ 10	0.06
Primary Sjogren Syndrome	50 (3.2)	52 (3.4)	-0.011	18 (2.5)	30 (3.9)	-0.08	20 (3.2)	17 (3.0)	0.011	≤ 10	≤ 10	-0.073
Liver or pancreatic disorder[d]	46 (2.9)	44 (2.9)	0.004	23 (3.1)	21 (2.7)	0.026	25 (4.0)	15 (2.6)	0.074	≤ 10	≤ 10	0.159
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	-0.059	≤ 10	≤ 10	0.004	≤ 10	≤ 10	-0.038	0 (0.0)	0 (0.0)	0.000
RA Severity (CIRAS Index)			0.018			-0.008			0.068			-0.021
Mean (± SD)	6.5 (1.4)	6.4 (1.4)		6.3 (1.3)	6.3 (1.4)		6.5 (1.3)	6.4 (1.3)		6.5 (1.3)	6.5 (1.3)	
Smoking (not available in SNDS)	N/A	N/A		N/A	N/A		N/A	N/A		N/A	N/A	
DMARDs, n (%)												

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1571	TNFi[a] n = 1536	Std. Diff.	Baricitinib n = 733	TNFi[a] n = 777	Std. Diff.	Baricitinib n = 632	TNFi[a] n = 570	Std. Diff.	Baricitinib n = 69	TNFi[a] n = 122	Std. Diff.
cDMARDs, during baseline period												
n, total (%)	1036 (65.9)	982 (63.9)	0.042	502 (68.5)	538 (69.2)	-0.016	444 (70.3)	404 (70.9)	-0.014	51 (73.9)	95 (77.9)	-0.093
Mean (SD)	0.7 (0.6)	0.7 (0.6)	0.047	0.8 (0.6)	0.7 (0.6)	0.03	0.8 (0.6)	0.8 (0.6)	-0.025	0.9 (0.7)	0.8 (0.5)	0.07
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	81 (5.2)	53 (3.5)		46 (6.3)	30 (3.9)	0.11	37 (5.9)	38 (6.7)	-0.034	≤ 10	≤ 10	0.098
Hydroxychloroquine	75 (4.8)	63 (4.1)	0.084	52 (7.1)	30 (3.9)	0.142	36 (5.7)	29 (5.1)	0.027	≤ 10	≤ 10	0.15
Chloroquine	0 (0.0)	≤ 10	0.033	0 (0.0)	0 (0.0)	0	0 (0.0)	0 (0.0)	0.000	≤ 10	0 (0.0)	0.172
Azathioprin	≤ 10	≤ 10	-0.036	≤ 10	≤ 10	0.003	≤ 10	≤ 10	-0.032	≤ 10	0 (0.0)	0.172
Leflunomide	214 (13.6)	192 (12.5)	-0.043	78 (10.6)	93 (12.0)	-0.042	73 (11.6)	72 (12.6)	-0.033	11 (15.9)	11 (9.0)	0.211
Methotrexate	791 (50.4)	763 (49.7)	0.033	404 (55.1)	436 (56.1)	-0.02	355 (56.2)	327 (57.4)	-0.024	36 (52.2)	83 (68.0)	-0.328
Mycophenolate mofetil	0 (0.0)	≤ 10	0.014	0 (0.0)	≤ 10	-0.051	≤ 10	0 (0.0)	0.056	0 (0.0)	0 (0.0)	0.000
Sulfasalazin	51 (3.2)	41 (2.7)	-0.036	24 (3.3)	18 (2.3)	0.058	26 (4.1)	22 (3.9)	0.013	≤ 10	≤ 10	0.331
Cyclosporin	≤ 10	0 (0.0)	0.034	0 (0.0)	0 (0.0)	0	≤ 10	0 (0.0)	0.056	0 (0.0)	0 (0.0)	0.000
Penicillamin	0 (0.0)	0 (0.0)	0.036	0 (0.0)	0 (0.0)	0	0 (0.0)	≤ 10	-0.059	0 (0.0)	0 (0.0)	0.000
bDMARDs, during baseline period			0									
n, total (%)	835 (53.2)	841 (54.8)	-0.032	414 (56.5)	441 (56.8)	-0.006	382 (60.4)	325 (57.0)	0.07	43 (62.3)	73 (59.8)	0.051
Mean (SD)	0.6 (0.6)	0.6 (0.6)	-0.045	0.6 (0.6)	0.6 (0.6)	-0.008	0.6 (0.6)	0.6 (0.6)	0.072	0.7 (0.6)	0.6 (0.6)	0.082
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	1.0	

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1571	TNFi[a] n = 1536	Std. Diff.	Baricitinib n = 733	TNFi[a] n = 777	Std. Diff.	Baricitinib n = 632	TNFi[a] n = 570	Std. Diff.	Baricitinib n = 69	TNFi[a] n = 122	Std. Diff.
Min; Max	[0.0;3.0]	[0.0;3.0]		[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	458 (29.2)	433 (28.2)	0.021	250 (34.1)	250 (32.2)	0.041	221 (35.0)	182 (31.9)	0.064	27 (39.1)	49 (40.2)	-0.021
Adalimumab[c]	116 (7.4)	116 (7.6)	-0.006	51 (7.0)	60 (7.7)	-0.029	54 (8.5)	49 (8.6)	-0.002	≤ 10	19 (15.6)	-0.264
Certolizumab pegol[c]	57 (3.6)	61 (4.0)	-0.018	27 (3.7)	31 (4.0)	-0.016	26 (4.1)	22 (3.9)	0.013	≤ 10	≤ 10	0.061
Etanercept[c]	188 (12.0)	190 (12.4)	-0.012	81 (11.1)	96 (12.4)	-0.041	60 (9.5)	71 (12.5)	-0.095	≤ 10	15 (12.3)	-0.291
Golimumab[c]	53 (3.4)	56 (3.6)	-0.015	28 (3.8)	21 (2.7)	0.063	29 (4.6)	24 (4.2)	0.018	≤ 10	≤ 10	-0.097
Infliximab[c]	45 (2.9)	41 (2.7)	0.012	24 (3.3)	21 (2.7)	0.034	15 (2.4)	15 (2.6)	-0.017	≤ 10	≤ 10	-0.073
Rituximab	22 (1.4)	17 (1.1)	0.026	16 (2.2)	15 (1.9)	0.018	17 (2.7)	≤ 10	0.192	≤ 10	≤ 10	0.274
Sarilumab	18 (1.1)	18 (1.2)	-0.002	≤ 10	≤ 10	0.006	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Abatacept	206 (13.1)	225 (14.6)	-0.044	116 (15.8)	123 (15.8)	0.000	114 (18.0)	85 (14.9)	0.084	13 (18.8)	12 (9.8)	0.259
Tocilizumab	179 (11.4)	184 (12.0)	-0.018	97 (13.2)	102 (13.1)	0.003	93 (14.7)	74 (13.0)	0.05	12 (17.4)	12 (9.8)	0.222
Anakinra	≤ 10	≤ 10	0.04	≤ 10	≤ 10	-0.022	≤ 10	≤ 10	-0.083	0 (0.0)	0 (0.0)	0.000
TNFi naïve at baseline	1132 (72.1)	1082 (70.4)	0.036	533 (72.7)	551 (70.9)	0.04	455 (72.0)	394 (69.1)	0.063	53 (76.8)	73 (59.8)	0.371
Other prescription medications during baseline period, n (%)												
Antibiotics	656 (41.8)	650 (42.3)	-0.011	307 (41.9)	335 (43.1)	-0.025	282 (44.6)	230 (40.4)	0.086	32 (46.4)	39 (32.0)	0.299
Antidiabetic agents	149 (9.5)	136 (8.9)	0.022	70 (9.5)	76 (9.8)	-0.008	67 (10.6)	55 (9.6)	0.032	12 (17.4)	16 (13.1)	0.119
Insulins	61 (3.9)	56 (3.6)	0.013	29 (4.0)	15 (1.9)	0.12	21 (3.3)	17 (3.0)	0.02	≤ 10	≤ 10	0.121
Non-insulins	115 (7.3)	111 (7.2)	0.004	62 (8.5)	68 (8.8)	-0.011	54 (8.5)	47 (8.2)	0.011	≤ 10	15 (12.3)	0.065

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1571	TNFi[a] n = 1536	Std. Diff.	Baricitinib n = 733	TNFi[a] n = 777	Std. Diff.	Baricitinib n = 632	TNFi[a] n = 570	Std. Diff.	Baricitinib n = 69	TNFi[a] n = 122	Std. Diff.
Cardiovascular												
Antithrombotic agents	293 (18.7)	280 (18.2)	0.011	154 (21.0)	134 (17.2)	0.096	112 (17.7)	95 (16.7)	0.028	23 (33.3)	25 (20.5)	0.293
Anticoagulant	136 (8.7)	115 (7.5)	0.043	74 (10.1)	54 (6.9)	0.113	46 (7.3)	50 (8.8)	-0.055	≤ 10	≤ 10	0.068
Antiplatelet	185 (11.8)	189 (12.3)	-0.016	94 (12.8)	86 (11.1)	0.054	71 (11.2)	52 (9.1)	0.07	17 (24.6)	18 (14.8)	0.251
Antihypertensives	524 (33.4)	542 (35.3)	-0.041	270 (36.8)	291 (37.5)	-0.013	248 (39.2)	219 (38.4)	0.017	33 (47.8)	44 (36.1)	0.24
Angiotensin converting enzyme inhibitors (ACE)	131 (8.3)	159 (10.4)	-0.069	67 (9.1)	83 (10.7)	-0.052	73 (11.6)	53 (9.3)	0.074	13 (18.8)	≤ 10	0.375
Angiotensin receptor blockers (ARB)	203 (12.9)	207 (13.5)	-0.016	106 (14.5)	133 (17.1)	-0.073	80 (12.7)	91 (16.0)	-0.095	≤ 10	20 (16.4)	-0.139
Beta blocker	246 (15.7)	241 (15.7)	-0.001	116 (15.8)	121 (15.6)	0.007	116 (18.4)	98 (17.2)	0.03	14 (20.3)	18 (14.8)	0.146
Calcium channel blocker	132 (8.4)	161 (10.5)	-0.071	90 (12.3)	80 (10.3)	0.063	86 (13.6)	62 (10.9)	0.083	≤ 10	17 (13.9)	0.016
Nitrates	16 (1.0)	16 (1.0)	-0.002	≤ 10	11 (1.4)	-0.146	13 (2.1)	≤ 10	0.081	≤ 10	0 (0.0)	0.172
Acyclovir	≤ 10	16 (1.0)	-0.052	≤ 10	≤ 10	-0.055	≤ 10	≤ 10	-0.032	0 (0.0)	≤ 10	-0.183
Valacyclovir	51 (3.2)	58 (3.8)	-0.029	24 (3.3)	27 (3.5)	-0.011	32 (5.1)	22 (3.9)	0.058	0 (0.0)	≤ 10	-0.183
Hormonal	173 (11.0)	222 (14.5)	-0.103	107 (14.6)	95 (12.2)	0.07	72 (11.4)	61 (10.7)	0.022	≤ 10	17 (13.9)	0.016
HRT	104 (6.6)	128 (8.3)	-0.065	58 (7.9)	54 (6.9)	0.037	44 (7.0)	36 (6.3)	0.026	≤ 10	≤ 10	-0.005
Oral Contraceptives	66 (4.2)	89 (5.8)	-0.073	48 (6.5)	36 (4.6)	0.083	25 (4.0)	23 (4.0)	-0.004	≤ 10	≤ 10	-0.005

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1571	TNFi[a] n = 1536	Std. Diff.	Baricitinib n = 733	TNFi[a] n = 777	Std. Diff.	Baricitinib n = 632	TNFi[a] n = 570	Std. Diff.	Baricitinib n = 69	TNFi[a] n = 122	Std. Diff.
SERMs	≤ 10	≤ 10	-0.015	≤ 10	≤ 10	-0.039	≤ 10	≤ 10	-0.03	0 (0.0)	0 (0.0)	0.000
Topic with progestogens and/or estrogens	≤ 10	≤ 10	-0.055	≤ 10	≤ 10	0.003	≤ 10	0 (0.0)	0.113	0 (0.0)	0 (0.0)	0.000
Lipid-lowering agents	261 (16.6)	277 (18.0)	-0.038	133 (18.1)	136 (17.5)	0.017	123 (19.5)	86 (15.1)	0.116	14 (20.3)	28 (23.0)	-0.065
HMG CoA reductase inhibitors	212 (13.5)	220 (14.3)	-0.024	115 (15.7)	117 (15.1)	0.018	95 (15.0)	66 (11.6)	0.102	12 (17.4)	25 (20.5)	-0.079
Fibrates	19 (1.2)	23 (1.5)	-0.025	≤ 10	≤ 10	0.006	14 (2.2)	≤ 10	0.076	0 (0.0)	≤ 10	-0.129
Bile acid sequestrants	≤ 10	≤ 10	-0.01	≤ 10	≤ 10	0.003	≤ 10	≤ 10	-0.007	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	14 (0.9)	27 (1.8)	-0.076	≤ 10	≤ 10	-0.042	≤ 10	≤ 10	-0.01	0 (0.0)	0 (0.0)	0.000
Lipid modifying agents, combinations	19 (1.2)	22 (1.4)	-0.02	≤ 10	≤ 10	0.044	12 (1.9)	≤ 10	0.054	≤ 10	≤ 10	0.085
Rheumatoid arthritis-related												
Aspirin	17 (1.1)	23 (1.5)	-0.037	≤ 10	12 (1.5)	-0.067	11 (1.7)	≤ 10	0.076	≤ 10	0 (0.0)	0.244
Cox-2 Inhibitor	82 (5.2)	82 (5.3)	-0.005	40 (5.5)	46 (5.9)	-0.02	37 (5.9)	33 (5.8)	0.003	≤ 10	≤ 10	-0.064
NSAIDs	572 (36.4)	561 (36.5)	-0.002	255 (34.8)	296 (38.1)	-0.069	216 (34.2)	228 (40.0)	-0.121	23 (33.3)	47 (38.5)	-0.108
Glucocorticosteroid	1142 (72.7)	1075 (70.0)	0.06	530 (72.3)	563 (72.5)	-0.003	432 (68.4)	414 (72.6)	-0.094	44 (63.8)	83 (68.0)	-0.09

Characteristics[b]	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1571	TNFi[a] n = 1536	Std. Diff.	Baricitinib n = 733	TNFi[a] n = 777	Std. Diff.	Baricitinib n = 632	TNFi[a] n = 570	Std. Diff.	Baricitinib n = 69	TNFi[a] n = 122	Std. Diff.
Vaccines	458 (29.2)	427 (27.8)	0.03	264 (36.0)	274 (35.3)	0.016	191 (30.2)	195 (34.2)	-0.085	20 (29.0)	29 (23.8)	0.119
Antineoplastic agents	≤ 10	≤ 10	-0.02	≤ 10	0 (0.0)	0.074	≤ 10	≤ 10	-0.038	≤ 10	0 (0.0)	0.172

Abbreviations: DMARD = disease-modifying antirheumatic drugs; MI = myocardial infarction; mos = months; N = number of patients in the specified category; Std. Diff = standardized difference; TNFi = tumor necrosis factor inhibitor, 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

Table 6.30. (continued) Baseline characteristics by exposure duration and dose of baricitinib - Hospitalized Tuberculosis Cohort, Matched [SNDS]

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1225	Bari. 2 mg n = 346	Bari. 4 mg n = 595	Bari. 2 mg n = 136	Bari. 4 mg n = 520	Bari. 2 mg n = 111	Bari. 4 mg n = 56	Bari. 2 mg n = 13
Age [in years]								
N (missing)	1225 (0)	346 (0)	595 (0)	136 (0)	520 (0)	111 (0)	56 (0)	13 (0)
Mean (SD)	55.6 (12.4)	69.8 (13.0)	57.4 (12.2)	70.0 (12.7)	57.2 (11.4)	68.7 (12.6)	55.9 (12.2)	64.9 (9.2)
Median	57.0	73.0	58.0	73.0	58.0	71.0	57.5	65.0
Min; Max	[18.0;90.0]	[25.0;98.0]	[19.0;86.0]	[20.0;88.0]	[20.0;84.0]	[30.0;92.0]	[30.0;76.0]	[48.0;79.0]
Sex, n (%)								
Male	246 (20.1)	62 (17.9)	120 (20.2)	22 (16.2)	125 (24.0)	29 (26.1)	15 (26.8)	≤ 10
Female	979 (79.9)	284 (82.1)	475 (79.8)	114 (83.8)	395 (76.0)	82 (73.9)	41 (73.2)	11 (84.6)
Clinical conditions during baseline period, n (%)								
Cancer, excluding NMSC	37 (3.0)	19 (5.5)	17 (2.9)	≤ 10	14 (2.7)	≤ 10	≤ 10	0 (0.0)
NMSC	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)
Chronic lung disease, excluding cystic fibrosis[c]	162 (13.2)	59 (17.1)	81 (13.6)	27 (19.9)	58 (11.2)	31 (27.9)	≤ 10	≤ 10
Cardiovascular conditions								
Atrial arrhythmia/fibrillation	16 (1.3)	22 (6.4)	≤ 10	12 (8.8)	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Cardiovascular revascularization	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1225	Bari. 2 mg n = 346	Bari. 4 mg n = 595	Bari. 2 mg n = 136	Bari. 4 mg n = 520	Bari. 2 mg n = 111	Bari. 4 mg n = 56	Bari. 2 mg n = 13
Congestive Heart Failure, hospitalized	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Coronary artery disease	46 (3.8)	24 (6.9)	22 (3.7)	12 (8.8)	20 (3.8)	11 (9.9)	≤ 10	≤ 10
Unstable angina	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ventricular arrhythmia	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Stroke	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Hemorrhagic	0 (0.0)	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ischemic	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Unknown	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
TIA	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Diabetes Mellitus[c]	106 (8.7)	49 (14.2)	55 (9.2)	18 (13.2)	50 (9.6)	17 (15.3)	≤ 10	≤ 10
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	
	Bari. 4 mg n = 1225	Bari. 2 mg n = 346	Bari. 4 mg n = 595	Bari. 2 mg n = 136	Bari. 4 mg n = 520	Bari. 2 mg n = 111	Bari. 4 mg n = 56	Bari. 2 mg n = 13
Current hypertension	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Immune disorders	41 (3.3)	23 (6.6)	14 (2.4)	≤ 10	17 (3.3)	≤ 10	≤ 10	≤ 10
AIDS/HIV	0 (0.0)	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	15 (1.2)	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)
Primary Sjogren Syndrome	29 (2.4)	21 (6.1)	13 (2.2)	≤ 10	14 (2.7)	≤ 10	0 (0.0)	≤ 10
Liver or pancreatic disorder[c]	34 (2.8)	12 (3.5)	16 (2.7)	≤ 10	20 (3.8)	≤ 10	≤ 10	≤ 10
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	0 (0.0)	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
RA Severity (CIRAS Index)								
Mean (± SD)	6.7 (1.4)	5.7 (1.4)	6.5 (1.3)	5.8 (1.4)	6.6 (1.3)	5.8 (1.3)	6.6 (1.4)	5.9 (1.1)
Smoking (not available in SNDS)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
DMARDs, n (%)								
cDMARDs, during baseline period								

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1225	Bari. 2 mg n = 346	Bari. 4 mg n = 595	Bari. 2 mg n = 136	Bari. 4 mg n = 520	Bari. 2 mg n = 111	Bari. 4 mg n = 56	Bari. 2 mg n = 13
n, total (%)	823 (67.2)	213 (61.6)	418 (70.3)	82 (60.3)	382 (73.5)	62 (55.9)	43 (76.8)	≤ 10
Mean (SD)	0.7 (0.6)	0.7 (0.6)	0.8 (0.6)	0.7 (0.7)	0.8 (0.6)	0.6 (0.6)	0.9 (0.7)	0.8 (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;4.0]	[0.0;3.0]	[0.0;3.0]	[0.0;3.0]
>1 cDMARD concomitantly	61 (5.0)	20 (5.8)	36 (6.1)	≤ 10	32 (6.2)	≤ 10	≤ 10	≤ 10
Hydroxychloroquine	57 (4.7)	18 (5.2)	36 (6.1)	16 (11.8)	32 (6.2)	≤ 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)	≤ 10
Azathioprin	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)
Leflunomide	172 (14.0)	42 (12.1)	70 (11.8)	≤ 10	63 (12.1)	≤ 10	≤ 10	≤ 10
Methotrexate	634 (51.8)	157 (45.4)	335 (56.3)	67 (49.3)	306 (58.8)	49 (44.1)	31 (55.4)	≤ 10
Mycophenolate mofetil	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Sulfasalazin	38 (3.1)	13 (3.8)	19 (3.2)	≤ 10	20 (3.8)	≤ 10	≤ 10	≤ 10
Cyclosporin	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	≤ 10	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 (%)	694 (56.7)	141 (40.8)	354 (59.5)	58 (42.6)	321 (61.7)	60 (54.1)	37 (66.1)	≤ 10
Mean (SD)	0.6 (0.6)	0.4 (0.5)	0.7 (0.6)	0.5 (0.6)	0.7 (0.6)	0.6 (0.5)	0.8 (0.6)	0.5 (0.5)
Median	1.0	0.0	1.0	0.0	1.0	1.0	1.0	0.0
Min; Max	[0.0;3.0]	[0.0;2.0]	[0.0;3.0]	[0.0;2.0]	[0.0;2.0]	[0.0;2.0]	[0.0;2.0]	[0.0;1.0]
cDMARDs, concomitant	390 (31.8)	68 (19.7)	214 (36.0)	34 (25.0)	194 (37.3)	27 (24.3)	23 (41.1)	≤ 10

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1225	Bari. 2 mg n = 346	Bari. 4 mg n = 595	Bari. 2 mg n = 136	Bari. 4 mg n = 520	Bari. 2 mg n = 111	Bari. 4 mg n = 56	Bari. 2 mg n = 13
Adalimumab[b]	95 (7.8)	21 (6.1)	45 (7.6)	≤ 10	49 (9.4)	≤ 10	≤ 10	0 (0.0)
Certolizumab pegol[b]	50 (4.1)	≤ 10	24 (4.0)	≤ 10	24 (4.6)	≤ 10	≤ 10	≤ 10
Etanercept[b]	157 (12.8)	31 (9.0)	70 (11.8)	11 (8.1)	49 (9.4)	≤ 10	≤ 10	0 (0.0)
Golimumab[b]	50 (4.1)	≤ 10	27 (4.5)	0 (0.0)	26 (5.0)	≤ 10	≤ 10	≤ 10
Infliximab[b]	40 (3.3)	≤ 10	22 (3.7)	≤ 10	13 (2.5)	≤ 10	≤ 10	0 (0.0)
Rituximab	17 (1.4)	≤ 10	14 (2.4)	≤ 10	11 (2.1)	≤ 10	≤ 10	≤ 10
Sarilumab	15 (1.2)	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abatacept	165 (13.5)	41 (11.8)	93 (15.6)	22 (16.2)	92 (17.7)	21 (18.9)	11 (19.6)	≤ 10
Tocilizumab	151 (12.3)	28 (8.1)	84 (14.1)	13 (9.6)	80 (15.4)	13 (11.7)	11 (19.6)	≤ 10
Anakinra	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
TNFi naïve at baseline	853 (69.6)	279 (80.6)	416 (69.9)	116 (85.3)	365 (70.2)	90 (81.1)	42 (75.0)	11 (84.6)
Other prescription medications during baseline period, n (%)								
Antibiotics	491 (40.1)	165 (47.7)	241 (40.5)	65 (47.8)	220 (42.3)	62 (55.9)	28 (50.0)	≤ 10
Antidiabetic agents	106 (8.7)	43 (12.4)	52 (8.7)	17 (12.5)	50 (9.6)	17 (15.3)	≤ 10	≤ 10
Insulins	41 (3.3)	20 (5.8)	21 (3.5)	≤ 10	16 (3.1)	≤ 10	≤ 10	0 (0.0)
Non-insulins	86 (7.0)	29 (8.4)	46 (7.7)	15 (11.0)	40 (7.7)	14 (12.6)	≤ 10	≤ 10
Cardiovascular								
Antithrombotic agents	177 (14.4)	116 (33.5)	104 (17.5)	49 (36.0)	80 (15.4)	32 (28.8)	17 (30.4)	≤ 10

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1225	Bari. 2 mg n = 346	Bari. 4 mg n = 595	Bari. 2 mg n = 136	Bari. 4 mg n = 520	Bari. 2 mg n = 111	Bari. 4 mg n = 56	Bari. 2 mg n = 13
Anticoagulant	69 (5.6)	67 (19.4)	48 (8.1)	26 (19.1)	32 (6.2)	14 (12.6)	≤ 10	≤ 10
Antiplatelet	121 (9.9)	64 (18.5)	64 (10.8)	29 (21.3)	51 (9.8)	20 (18.0)	14 (25.0)	≤ 10
Antihypertensives	334 (27.3)	190 (54.9)	195 (32.8)	74 (54.4)	177 (34.0)	70 (63.1)	23 (41.1)	≤ 10
Angiotensin converting enzyme inhibitors (ACE)	87 (7.1)	44 (12.7)	49 (8.2)	18 (13.2)	50 (9.6)	23 (20.7)	≤ 10	≤ 10
Angiotensin receptor blockers (ARB)	126 (10.3)	77 (22.3)	77 (12.9)	29 (21.3)	62 (11.9)	18 (16.2)	≤ 10	≤ 10
Beta blocker	148 (12.1)	98 (28.3)	75 (12.6)	40 (29.4)	84 (16.2)	32 (28.8)	≤ 10	≤ 10
Calcium channel blocker	67 (5.5)	65 (18.8)	67 (11.3)	22 (16.2)	53 (10.2)	32 (28.8)	≤ 10	≤ 10
Nitrates	≤ 10	11 (3.2)	0 (0.0)	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)
Acyclovir	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Valacyclovir	33 (2.7)	18 (5.2)	21 (3.5)	≤ 10	26 (5.0)	≤ 10	0 (0.0)	0 (0.0)
Hormonal	151 (12.3)	22 (6.4)	90 (15.1)	17 (12.5)	66 (12.7)	≤ 10	≤ 10	≤ 10
HRT	88 (7.2)	16 (4.6)	46 (7.7)	12 (8.8)	42 (8.1)	≤ 10	≤ 10	≤ 10
Oral Contraceptives	60 (4.9)	≤ 10	43 (7.2)	≤ 10	23 (4.4)	≤ 10	≤ 10	0 (0.0)
SERMs	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Topic with progestogens and/or estrogens	≤ 10	0 (0.0)	≤ 10	0 (0.0)	≤ 10	≤ 10	0 (0.0)	0 (0.0)

Characteristics[a]	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1225	Bari. 2 mg n = 346	Bari. 4 mg n = 595	Bari. 2 mg n = 136	Bari. 4 mg n = 520	Bari. 2 mg n = 111	Bari. 4 mg n = 56	Bari. 2 mg n = 13
Lipid-lowering agents	168 (13.7)	93 (26.9)	99 (16.6)	33 (24.3)	90 (17.3)	33 (29.7)	13 (23.2)	≤ 10
HMG CoA reductase inhibitors	134 (10.9)	78 (22.5)	83 (13.9)	31 (22.8)	71 (13.7)	24 (21.6)	11 (19.6)	≤ 10
Fibrates	13 (1.1)	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Bile acid sequestrants	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other lipid modifying agents	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	0 (0.0)
Lipid modifying agents, combinations	15 (1.2)	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)
Rheumatoid arthritis-related								
Aspirin	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
Cox-2 Inhibitor	70 (5.7)	12 (3.5)	34 (5.7)	≤ 10	34 (6.5)	≤ 10	≤ 10	0 (0.0)
NSAIDs	480 (39.2)	92 (26.6)	223 (37.5)	32 (23.5)	188 (36.2)	27 (24.3)	21 (37.5)	≤ 10
Glucocorticosteroid	877 (71.6)	265 (76.6)	415 (69.7)	114 (83.8)	356 (68.5)	75 (67.6)	37 (66.1)	≤ 10
Vaccines	335 (27.3)	123 (35.5)	202 (33.9)	62 (45.6)	139 (26.7)	52 (46.8)	17 (30.4)	≤ 10
Antineoplastic agents	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	≤ 10

Abbreviations: DMARD = disease-modifying antirheumatic drugs; MI = myocardial infarction; mos = months; N = number of patients in the specified category; Std. Diff = standardized difference; TNFi = tumor necrosis factor inhibitor, HRT = hormone replacement therapy.

[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

1.4.2 BASELINE HEALTHCARE RESOURCE UTILIZATION BY EXPOSURE DURATION

Table 6.31. 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 = 1686	TNFi n = 5372	Std. Diff.	Baricitinib n = 801	TNFi n = 2543	Std. Diff.	Baricitinib n = 676	TNFi n = 1910	Std. Diff.	Baricitinib n = 79	TNFi n = 377	Std. Diff.
Physician Office Visits (rheumatologist visits excluded)												
n, patients (%)	991 (58.8)	3335 (62.1)	-0.068	507 (63.3)	1621 (63.7)	-0.009	428 (63.3)	1198 (62.7)	0.012	57 (72.2)	271 (71.9)	0.006
n, events	2713	10580		1400	5163		1344	3566		159	999	
Mean (SD)	1.6 (2.4)	2.0 (3.2)	-0.127	1.7 (2.6)	2.0 (3.2)	-0.098	2.0 (2.9)	1.9 (2.7)	0.043	2.0 (2.4)	2.6 (3.3)	-0.223
Median	1.0	1.0		1.0	1.0		1.0	1.0		2.0	2.0	
Min; Max	[0.0;41.0]	[0.0;85.0]		[0.0;25.0]	[0.0;49.0]		[0.0;31.0]	[0.0;25.0]		[0.0;16.0]	[0.0;22.0]	
Rheumatologist Visits												
n, patients (%)	1045 (62.0)	3270 (60.9)	0.023	511 (63.8)	1661 (65.3)	-0.032	438 (64.8)	1302 (68.2)	-0.072	58 (73.4)	286 (75.9)	-0.056
n, events	2321	7231		1125	3839		1000	3010		139	677	
Mean (SD)	1.4 (1.5)	1.3 (1.5)	0.020	1.4 (1.5)	1.5 (1.5)	-0.068	1.5 (1.6)	1.6 (1.6)	-0.062	1.8 (1.5)	1.8 (1.6)	-0.024
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 (%)	1570 (93.1)	4860 (90.5)	0.097	751 (93.8)	2335 (91.8)	0.075	632 (93.5)	1772 (92.8)	0.028	71 (89.9)	344 (91.2)	-0.047
n, events	32958	82647		16216	38975		14040	29687		1274	5652	
Mean (SD)	19.5 (33.5)	15.4 (27.4)	0.136	20.2 (32.4)	15.3 (25.0)	0.170	20.8 (34.6)	15.5 (25.2)	0.173	16.1 (26.0)	15.0 (25.5)	0.044

Type of resource use during baseline period	<6 mos			6 mos to <12 mos			12 mos to <24 mos			≥24 mos		
	Baricitinib n = 1686	TNFi n = 5372	Std. Diff.	Baricitinib n = 801	TNFi n = 2543	Std. Diff.	Baricitinib n = 676	TNFi n = 1910	Std. Diff.	Baricitinib n = 79	TNFi n = 377	Std. Diff.
Median	8.0	6.0		9.0	7.0		8.0	7.0		6.0	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 (%)	816 (48.4)	2441 (45.4)	0.059	395 (49.3)	1266 (49.8)	-0.009	341 (50.4)	923 (48.3)	0.042	41 (51.9)	172 (45.6)	0.126
n, events	2025	4203		958	2200		906	1589		95	282	
Mean (SD)	1.2 (1.8)	0.8 (1.5)	0.251	1.2 (1.8)	0.9 (1.9)	0.176	1.3 (2.0)	0.8 (1.7)	0.273	1.2 (1.7)	0.7 (1.2)	0.311
Median	0.0	0.0		0.0	0.0		1.0	0.0		1.0	0.0	
Min; Max	[0.0;14.0]	[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: 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 6.31 (continued). Baseline healthcare resource utilization by exposure duration and dose of baricitinib - Unmatched cohort [SNDS]

Type of resource use during baseline period	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1336	Bari. 2 mg n = 349	Bari. 4 mg n = 652	Bari. 2 mg n = 147	Bari. 4 mg n = 562	Bari. 2 mg n = 113	Bari. 4 mg n = 66	Bari. 2 mg n = 13
Physician Office Visits (rheumatologist visits excluded)								
n, patients (%)	759 (56.8)	232 (66.5)	403 (61.8)	104 (70.7)	345 (61.4)	83 (73.5)	46 (69.7)	11 (84.6)
n, events	2073	640	1076	324	1013	331	129	30
Mean (SD)	1.6 (2.5)	1.8 (2.2)	1.7 (2.5)	2.2 (2.7)	1.8 (2.8)	2.9 (3.5)	2.0 (2.5)	2.3 (1.8)
Median	1.0	1.0	1.0	1.0	1.0	2.0	1.0	2.0
Min; Max	[0.0;41.0]	[0.0;12.0]	[0.0;25.0]	[0.0;17.0]	[0.0;31.0]	[0.0;19.0]	[0.0;16.0]	[0.0;6.0]
Rheumatologist Visits								
n, patients (%)	838 (62.7)	207 (59.3)	420 (64.4)	90 (61.2)	368 (65.5)	69 (61.1)	47 (71.2)	11 (84.6)
n, events	1825	496	930	189	821	173	116	23
Mean (SD)	1.4 (1.5)	1.4 (1.7)	1.4 (1.5)	1.3 (1.6)	1.5 (1.5)	1.5 (1.8)	1.8 (1.5)	1.8 (1.2)
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;11.0]	[0.0;8.0]	[0.0;8.0]	[0.0;9.0]	[0.0;9.0]	[0.0;6.0]	[0.0;4.0]
Other Outpatient Visits								
n, patients (%)	1232 (92.2)	337 (96.6)	608 (93.3)	142 (96.6)	520 (92.5)	111 (98.2)	58 (87.9)	13 (100.0)
n, events	22736	10146	10908	5269	9583	4455	969	305
Mean (SD)	17.0 (30.3)	29.1 (42.3)	16.7 (24.9)	35.8 (51.7)	17.1 (27.8)	39.4 (53.9)	14.7 (22.4)	23.5 (40.1)
Median	7.0	14.0	8.0	15.0	7.0	17.0	6.0	8.0

Type of resource use during baseline period	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1336	Bari. 2 mg n = 349	Bari. 4 mg n = 652	Bari. 2 mg n = 147	Bari. 4 mg n = 562	Bari. 2 mg n = 113	Bari. 4 mg n = 66	Bari. 2 mg n = 13
Min; Max	[0.0;322.0]	[0.0;226.0]	[0.0;236.0]	[0.0;266.0]	[0.0;254.0]	[0.0;257.0]	[0.0;125.0]	[3.0;152.0]
Inpatient Visits[a]								
n, patients (%)	624 (46.7)	191 (54.7)	307 (47.1)	87 (59.2)	269 (47.9)	72 (63.7)	33 (50.0)	≤ 10
n, events	1576	442	750	205	695	211	78	17
Mean (SD)	1.2 (1.8)	1.3 (1.8)	1.2 (1.8)	1.4 (1.8)	1.2 (1.9)	1.9 (2.3)	1.2 (1.7)	1.3 (1.7)
Median	0.0	1.0	0.0	1.0	0.0	1.0	0.5	1.0
Min; Max	[0.0;14.0]	[0.0;12.0]	[0.0;12.0]	[0.0;7.0]	[0.0;10.0]	[0.0;8.0]	[0.0;7.0]	[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 6.32. 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 = 1496	TNFi[a] n = 1472	Std. Diff.	Baricitinib n = 701	TNFi[a] n = 734	Std. Diff.	Baricitinib n = 598	TNFi[a] n = 534	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 119	Std. Diff.
Physician Office Visits (rheumatologist visits excluded)												
n, patients (%)	878 (58.7)	905 (61.5)	-0.057	449 (64.1)	467 (63.6)	0.009	390 (65.2)	305 (57.1)	0.167	48 (75.0)	79 (66.4)	0.190
n, events	2431	2764		1255	1400		1225	852		130	251	
Mean (SD)	1.6 (2.5)	1.9 (3.5)	-0.084	1.8 (2.6)	1.9 (3.1)	-0.041	2.0 (2.9)	1.6 (2.3)	0.172	2.0 (2.4)	2.1 (2.7)	-0.031
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.5	1.0	
Min; Max	[0.0;41.0]	[0.0;85.0]		[0.0;25.0]	[0.0;43.0]		[0.0;31.0]	[0.0;18.0]		[0.0;16.0]	[0.0;17.0]	
Rheumatologist Visits												
n, patients (%)	926 (61.9)	889 (60.4)	0.031	449 (64.1)	460 (62.7)	0.029	395 (66.1)	349 (65.4)	0.015	45 (70.3)	88 (73.9)	-0.081
n, events	2064	2018		982	1017		895	808		106	190	
Mean (SD)	1.4 (1.5)	1.4 (1.5)	0.006	1.4 (1.5)	1.4 (1.5)	0.010	1.5 (1.6)	1.5 (1.6)	-0.011	1.7 (1.4)	1.6 (1.5)	0.041
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;10.0]		[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 (%)	1388 (92.8)	1359 (92.3)	0.017	655 (93.4)	691 (94.1)	-0.029	557 (93.1)	497 (93.1)	0.003	57 (89.1)	105 (88.2)	0.026
n, events	28266	25313		13779	12599		12269	10036		1017	1741	
Mean (SD)	18.9 (32.5)	17.2 (29.6)	0.055	19.7 (31.7)	17.2 (28.2)	0.083	20.5 (32.8)	18.8 (31.6)	0.054	15.9 (27.1)	14.6 (28.8)	0.045
Median	7.0	7.0		8.0	7.0		8.0	8.0		6.0	6.0	
Min; Max	[0.0;322.0]	[0.0;259.0]		[0.0;266.0]	[0.0;238.0]		[0.0;201.0]	[0.0;242.0]		[0.0;152.0]	[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 = 1496	TNFi[a] n = 1472	Std. Diff.	Baricitinib n = 701	TNFi[a] n = 734	Std. Diff.	Baricitinib n = 598	TNFi[a] n = 534	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 119	Std. Diff.
Inpatient Visits[b]												
n, patients (%)	697 (46.6)	631 (42.9)	0.075	335 (47.8)	364 (49.6)	-0.036	286 (47.8)	247 (46.3)	0.032	29 (45.3)	45 (37.8)	0.153
n, events	1590	1473		757	879		703	616		60	83	
Mean (SD)	1.1 (1.7)	1.0 (1.7)	0.037	1.1 (1.7)	1.2 (3.2)	-0.046	1.2 (1.9)	1.2 (2.9)	0.009	0.9 (1.5)	0.7 (1.3)	0.174
Median	0.0	0.0		0.0	0.0		0.0	0.0		0.0	0.0	
Min; Max	[0.0;14.0]	[0.0;11.0]		[0.0;12.0]	[0.0;76.0]		[0.0;10.0]	[0.0;56.0]		[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: 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 6.32 (continued). Baseline healthcare resource utilization by exposure duration and dose of baricitinib - Matched VTE cohort, [SNDS]

Type of resource use during baseline period	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1183	Bari. 2 mg n = 312	Bari. 4 mg n = 574	Bari. 2 mg n = 126	Bari. 4 mg n = 497	Bari. 2 mg n = 101	Bari. 4 mg n = 52	Bari. 2 mg n = 12
Physician Office Visits (rheumatologist visits excluded)								
n, patients (%)	671 (56.7)	207 (66.3)	359 (62.5)	90 (71.4)	314 (63.2)	76 (75.2)	38 (73.1)	≤ 10
n, events	1837	594	976	279	910	315	104	26
Mean (SD)	1.6 (2.5)	1.9 (2.3)	1.7 (2.6)	2.2 (2.6)	1.8 (2.7)	3.1 (3.6)	2.0 (2.5)	2.2 (1.8)
Median	1.0	1.0	1.0	1.0	1.0	2.0	1.0	2.0
Min; Max	[0.0;41.0]	[0.0;12.0]	[0.0;25.0]	[0.0;15.0]	[0.0;31.0]	[0.0;19.0]	[0.0;16.0]	[0.0;6.0]
Rheumatologist Visits								
n, patients (%)	743 (62.8)	183 (58.7)	369 (64.3)	79 (62.7)	331 (66.6)	64 (63.4)	35 (67.3)	≤ 10
n, events	1636	428	814	162	739	156	84	22
Mean (SD)	1.4 (1.5)	1.4 (1.6)	1.4 (1.5)	1.3 (1.5)	1.5 (1.5)	1.5 (1.8)	1.6 (1.5)	1.8 (1.3)
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;11.0]	[0.0;8.0]	[0.0;8.0]	[0.0;9.0]	[0.0;9.0]	[0.0;5.0]	[0.0;4.0]
Other Outpatient Visits								
n, patients (%)	1086 (91.8)	301 (96.5)	533 (92.9)	121 (96.0)	458 (92.2)	99 (98.0)	45 (86.5)	12 (100.0)
n, events	19275	8915	9290	4450	8251	4018	718	299
Mean (SD)	16.3 (28.6)	28.6 (42.8)	16.2 (23.6)	35.3 (52.7)	16.6 (25.7)	39.8 (51.8)	13.8 (22.6)	24.9 (41.5)
Median	7.0	13.0	8.0	14.0	7.0	20.0	5.5	10.5

Type of resource use during baseline period	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1183	Bari. 2 mg n = 312	Bari. 4 mg n = 574	Bari. 2 mg n = 126	Bari. 4 mg n = 497	Bari. 2 mg n = 101	Bari. 4 mg n = 52	Bari. 2 mg n = 12
Min; Max	[0.0;322.0]	[0.0;226.0]	[0.0;236.0]	[0.0;266.0]	[0.0;198.0]	[0.0;201.0]	[0.0;125.0]	[3.0;152.0]
Inpatient Visits[a]								
n, patients (%)	523 (44.2)	173 (55.4)	263 (45.8)	72 (57.1)	222 (44.7)	64 (63.4)	22 (42.3)	≤ 10
n, events	1216	367	606	151	526	177	45	15
Mean (SD)	1.0 (1.7)	1.2 (1.6)	1.1 (1.7)	1.2 (1.6)	1.1 (1.7)	1.8 (2.3)	0.9 (1.4)	1.3 (1.8)
Median	0.0	1.0	0.0	1.0	0.0	1.0	0.0	1.0
Min; Max	[0.0;14.0]	[0.0;12.0]	[0.0;12.0]	[0.0;7.0]	[0.0;10.0]	[0.0;8.0]	[0.0;6.0]	[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 6.33. Baseline healthcare resource utilization by exposure duration, Alternate VTE Cohort (Case Definition I), Matched [SNDS]

Not applicable for SNDS data

Table 6.34. Baseline healthcare resource utilization by exposure duration, Alternate VTE Cohort (Case Definition II), Matched [SNDS]

Not applicable for SNDS data

Table 6.35. 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 = 1505	TNFi[a] n = 1521	Std. Diff.	Baricitinib n = 703	TNFi[a] n = 705	Std. Diff.	Baricitinib n = 592	TNFi[a] n = 527	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 111	Std. Diff.
Physician Office Visits (rheumatologist visits excluded)												
n, patients (%)	889 (59.1)	925 (60.8)	-0.036	449 (63.9)	449 (63.7)	0.004	379 (64.0)	320 (60.7)	0.068	46 (71.9)	78 (70.3)	0.035
n, events	2448	2689		1275	1320		1207	928		120	254	
Mean (SD)	1.6 (2.5)	1.8 (2.7)	-0.055	1.8 (2.7)	1.9 (3.2)	-0.02	2.0 (3.0)	1.8 (2.5)	0.102	1.9 (2.4)	2.3 (2.8)	-0.159
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;25.0]	[0.0;49.0]		[0.0;31.0]	[0.0;18.0]		[0.0;16.0]	[0.0;17.0]	
Rheumatologist Visits												
n, patients (%)	936 (62.2)	917 (60.3)	0.039	447 (63.6)	442 (62.7)	0.018	391 (66.0)	349 (66.2)	-0.004	45 (70.3)	87 (78.4)	-0.186
n, events	2050	2068		979	1048		893	767		105	199	
Mean (SD)	1.4 (1.5)	1.4 (1.5)	0.002	1.4 (1.5)	1.5 (1.6)	-0.060	1.5 (1.6)	1.5 (1.5)	0.035	1.6 (1.4)	1.8 (1.7)	-0.099
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;8.0]		[0.0;9.0]	[0.0;13.0]		[0.0;5.0]	[0.0;10.0]	
Other Outpatient Visits												
n, patients (%)	1397 (92.8)	1405 (92.4)	0.017	659 (93.7)	647 (91.8)	0.076	549 (92.7)	487 (92.4)	0.013	57 (89.1)	97 (87.4)	0.052
n, events	28926	26879		14290	11704		12218	9637		977	1811	
Mean (SD)	19.2 (32.7)	17.7 (31.1)	0.049	20.3 (31.7)	16.6 (26.7)	0.127	20.6 (34.2)	18.3 (29.3)	0.074	15.3 (27.0)	16.3 (31.9)	-0.036
Median	7.0	7.0		9.0	8.0		8.0	9.0		6.0	6.0	
Min; Max	[0.0;283.0]	[0.0;283.0]		[0.0;266.0]	[0.0;238.0]		[0.0;242.0]	[0.0;242.0]		[0.0;152.0]	[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 = 1505	TNFi[a] n = 1521	Std. Diff.	Baricitinib n = 703	TNFi[a] n = 705	Std. Diff.	Baricitinib n = 592	TNFi[a] n = 527	Std. Diff.	Baricitinib n = 64	TNFi[a] n = 111	Std. Diff.
Inpatient Visits[b]												
n, patients (%)	709 (47.1)	705 (46.4)	0.015	326 (46.4)	347 (49.2)	-0.057	283 (47.8)	253 (48.0)	-0.004	28 (43.8)	38 (34.2)	0.196
n, events	1703	1555		717	771		701	596		65	71	
Mean (SD)	1.1 (1.8)	1.0 (1.8)	0.061	1.0 (1.6)	1.1 (1.7)	-0.045	1.2 (1.8)	1.1 (2.9)	0.022	1.0 (1.7)	0.6 (1.2)	0.253
Median	0.0	0.0		0.0	0.0		0.0	0.0		0.0	0.0	
Min; Max	[0.0;14.0]	[0.0;25.0]		[0.0;12.0]	[0.0;9.0]		[0.0;8.0]	[0.0;56.0]		[0.0;7.0]	[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 6.35 (continued). Baseline healthcare resource utilization by exposure duration and dose of baricitinib - 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	
	Bari. 4 mg n = 1192	Bari. 2 mg n = 313	Bari. 4 mg n = 573	Bari. 2 mg n = 128	Bari. 4 mg n = 495	Bari. 2 mg n = 97	Bari. 4 mg n = 54	Bari. 2 mg n = 10
Physician Office Visits (rheumatologist visits excluded)								
n, patients (%)	683 (57.3)	206 (65.8)	357 (62.3)	92 (71.9)	308 (62.2)	71 (73.2)	37 (68.5)	≤ 10
n, events	1864	584	973	302	912	295	95	25
Mean (SD)	1.6 (2.5)	1.9 (2.2)	1.7 (2.6)	2.4 (2.9)	1.8 (2.8)	3.0 (3.7)	1.8 (2.5)	2.5 (1.8)
Median	1.0	1.0	1.0	1.0	1.0	2.0	1.0	2.0
Min; Max	[0.0;41.0]	[0.0;12.0]	[0.0;25.0]	[0.0;17.0]	[0.0;31.0]	[0.0;19.0]	[0.0;16.0]	[0.0;6.0]
Rheumatologist Visits								
n, patients (%)	750 (62.9)	186 (59.4)	365 (63.7)	81 (63.3)	327 (66.1)	64 (66.0)	37 (68.5)	≤ 10
n, events	1625	425	804	169	733	160	91	14
Mean (SD)	1.4 (1.5)	1.4 (1.6)	1.4 (1.5)	1.3 (1.6)	1.5 (1.5)	1.6 (1.8)	1.7 (1.5)	1.4 (1.1)
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;9.0]	[0.0;5.0]	[0.0;3.0]
Other Outpatient Visits								
n, patients (%)	1095 (91.9)	302 (96.5)	534 (93.2)	124 (96.9)	455 (91.9)	94 (96.9)	47 (87.0)	≤ 10
n, events	19767	9159	9634	4617	8375	3843	711	266
Mean (SD)	16.6 (29.0)	29.3 (42.8)	16.8 (23.6)	36.1 (52.4)	16.9 (27.7)	39.6 (52.9)	13.2 (22.0)	26.6 (45.6)
Median	6.5	14.0	8.0	15.0	7.0	17.0	4.5	7.5

Type of resource use during baseline period	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1192	Bari. 2 mg n = 313	Bari. 4 mg n = 573	Bari. 2 mg n = 128	Bari. 4 mg n = 495	Bari. 2 mg n = 97	Bari. 4 mg n = 54	Bari. 2 mg n = 10
Min; Max	[0.0;283.0]	[0.0;226.0]	[0.0;236.0]	[0.0;266.0]	[0.0;242.0]	[0.0;201.0]	[0.0;125.0]	[3.0;152.0]
Inpatient Visits[a]								
n, patients (%)	540 (45.3)	169 (54.0)	252 (44.0)	73 (57.0)	223 (45.1)	60 (61.9)	22 (40.7)	≤ 10
n, events	1329	374	558	156	536	165	50	15
Mean (SD)	1.1 (1.8)	1.2 (1.8)	1.0 (1.6)	1.2 (1.7)	1.1 (1.7)	1.7 (2.2)	0.9 (1.7)	1.5 (1.9)
Median	0.0	1.0	0.0	1.0	0.0	1.0	0.0	1.0
Min; Max	[0.0;14.0]	[0.0;12.0]	[0.0;12.0]	[0.0;7.0]	[0.0;8.0]	[0.0;8.0]	[0.0;7.0]	[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 6.36. 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 = 1569	TNFi[a] n = 1544	Std. Diff.	Baricitinib n = 726	TNFi[a] n = 750	Std. Diff.	Baricitinib n = 617	TNFi[a] n = 573	Std. Diff.	Baricitinib n = 67	TNFi[a] n = 112	Std. Diff.
Physician Office Visits (rheumatologist visits excluded)												
n, patients (%)	934 (59.5)	939 (60.8)	-0.026	468 (64.5)	476 (63.5)	0.021	395 (64.0)	352 (61.4)	0.054	48 (71.6)	78 (69.6)	0.044
n, events	2618	2783		1334	1420		1264	1017		132	236	
Mean (SD)	1.7 (2.5)	1.8 (2.9)	-0.049	1.8 (2.7)	1.9 (2.8)	-0.021	2.0 (3.0)	1.8 (2.5)	0.100	2.0 (2.5)	2.1 (2.3)	-0.057
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;25.0]	[0.0;26.0]		[0.0;31.0]	[0.0;17.0]		[0.0;16.0]	[0.0;11.0]	
Rheumatologist Visits												
n, patients (%)	960 (61.2)	956 (61.9)	-0.015	451 (62.1)	467 (62.3)	-0.003	402 (65.2)	380 (66.3)	-0.025	46 (68.7)	88 (78.6)	-0.226
n, events	2120	2102		995	1068		912	829		108	191	
Mean (SD)	1.4 (1.5)	1.4 (1.5)	-0.007	1.4 (1.5)	1.4 (1.5)	-0.035	1.5 (1.6)	1.4 (1.5)	0.020	1.6 (1.4)	1.7 (1.6)	-0.062
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;5.0]	[0.0;10.0]	
Other Outpatient Visits												
n, patients (%)	1457 (92.9)	1418 (91.8)	0.039	681 (93.8)	693 (92.4)	0.055	576 (93.4)	533 (93.0)	0.013	59 (88.1)	101 (90.2)	-0.068
n, events	31579	28978		15257	12875		13631	9853		784	1960	
Mean (SD)	20.1 (34.5)	18.8 (32.3)	0.041	21.0 (34.6)	17.2 (26.5)	0.125	22.1 (36.8)	17.2 (28.2)	0.149	11.7 (15.4)	17.5 (35.2)	-0.213
Median	8.0	8.0		9.0	8.0		8.0	7.0		6.0	6.0	
Min; Max	[0.0;322.0]	[0.0;255.0]		[0.0;266.0]	[0.0;222.0]		[0.0;257.0]	[0.0;242.0]		[0.0;62.0]	[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 = 1569	TNFi[a] n = 1544	Std. Diff.	Baricitinib n = 726	TNFi[a] n = 750	Std. Diff.	Baricitinib n = 617	TNFi[a] n = 573	Std. Diff.	Baricitinib n = 67	TNFi[a] n = 112	Std. Diff.
Inpatient Visits[b]												
n, patients (%)	741 (47.2)	727 (47.1)	0.003	357 (49.2)	380 (50.7)	-0.030	300 (48.6)	276 (48.2)	0.009	31 (46.3)	45 (40.2)	0.123
n, events	1754	1680		832	822		722	569		75	85	
Mean (SD)	1.1 (1.8)	1.1 (2.2)	0.015	1.1 (1.8)	1.1 (1.6)	0.029	1.2 (1.8)	1.0 (1.5)	0.106	1.1 (1.8)	0.8 (1.3)	0.229
Median	0.0	0.0		0.0	1.0		0.0	0.0		0.0	0.0	
Min; Max	[0.0;14.0]	[0.0;51.0]		[0.0;12.0]	[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: mos = months; N = number of patients in the specified category; 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 6.36 (continued). Baseline healthcare resource utilization by exposure duration and dose of baricitinib - 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	
	Bari. 4 mg n = 1228	Bari. 2 mg n = 340	Bari. 4 mg n = 595	Bari. 2 mg n = 129	Bari. 4 mg n = 507	Bari. 2 mg n = 110	Bari. 4 mg n = 55	Bari. 2 mg n = 12
Physician Office Visits (rheumatologist visits excluded)								
n, patients (%)	708 (57.7)	226 (66.5)	377 (63.4)	91 (70.5)	316 (62.3)	79 (71.8)	37 (67.3)	11 (91.7)
n, events	1936	682	1046	288	940	324	99	33
Mean (SD)	1.6 (2.5)	2.0 (2.5)	1.8 (2.6)	2.2 (2.8)	1.9 (2.8)	2.9 (3.6)	1.8 (2.4)	2.8 (2.6)
Median	1.0	1.0	1.0	1.0	1.0	2.0	1.0	2.0
Min; Max	[0.0;41.0]	[0.0;20.0]	[0.0;25.0]	[0.0;17.0]	[0.0;31.0]	[0.0;19.0]	[0.0;16.0]	[0.0;9.0]
Rheumatologist Visits								
n, patients (%)	765 (62.3)	195 (57.4)	373 (62.7)	77 (59.7)	339 (66.9)	63 (57.3)	36 (65.5)	≤ 10
n, events	1670	450	833	156	762	150	89	19
Mean (SD)	1.4 (1.5)	1.3 (1.6)	1.4 (1.5)	1.2 (1.5)	1.5 (1.5)	1.4 (1.7)	1.6 (1.5)	1.6 (1.1)
Median	1.0	1.0	1.0	1.0	1.0	1.0	2.0	1.5
Min; Max	[0.0;8.0]	[0.0;11.0]	[0.0;8.0]	[0.0;8.0]	[0.0;9.0]	[0.0;9.0]	[0.0;5.0]	[0.0;3.0]
Other Outpatient Visits								
n, patients (%)	1129 (91.9)	327 (96.2)	555 (93.3)	125 (96.9)	469 (92.5)	107 (97.3)	47 (85.5)	12 (100.0)
n, events	20387	11116	10224	4994	8954	4677	674	110
Mean (SD)	16.6 (28.9)	32.7 (47.5)	17.2 (26.5)	38.7 (55.9)	17.7 (29.6)	42.5 (55.5)	12.3 (16.6)	9.2 (7.5)
Median	7.0	15.0	8.0	16.0	7.0	21.0	5.0	6.5

Type of resource use during baseline period	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1228	Bari. 2 mg n = 340	Bari. 4 mg n = 595	Bari. 2 mg n = 129	Bari. 4 mg n = 507	Bari. 2 mg n = 110	Bari. 4 mg n = 55	Bari. 2 mg n = 12
Min; Max	[0.0;322.0]	[0.0;226.0]	[0.0;242.0]	[0.0;266.0]	[0.0;254.0]	[0.0;257.0]	[0.0;62.0]	[3.0;28.0]
Inpatient Visits[a]								
n, patients (%)	552 (45.0)	188 (55.3)	281 (47.2)	75 (58.1)	228 (45.0)	72 (65.5)	24 (43.6)	≤ 10
n, events	1341	406	665	164	525	197	59	16
Mean (SD)	1.1 (1.8)	1.2 (1.7)	1.1 (1.8)	1.3 (1.7)	1.0 (1.7)	1.8 (2.2)	1.1 (1.8)	1.3 (1.8)
Median	0.0	1.0	0.0	1.0	0.0	1.0	0.0	1.0
Min; Max	[0.0;14.0]	[0.0;12.0]	[0.0;12.0]	[0.0;7.0]	[0.0;8.0]	[0.0;8.0]	[0.0;7.0]	[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 6.37. Baseline healthcare resource utilization by exposure duration - Hospitalized Tuberculosis 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 = 1571	TNFi[a] n = 1536	Std. Diff.	Baricitinib n = 733	TNFi[a] n = 777	Std. Diff.	Baricitinib n = 632	TNFi[a] n = 570	Std. Diff.	Baricitinib n = 69	TNFi[a] n = 122	Std. Diff.
Physician Office Visits (rheumatologist visits excluded)												
n, patients (%)	930 (59.2)	957 (62.3)	-0.064	476 (64.9)	491 (63.2)	0.036	410 (64.9)	334 (58.6)	0.129	51 (73.9)	84 (68.9)	0.112
n, events	2594	2760		1369	1511		1274	936		141	292	
Mean (SD)	1.7 (2.5)	1.8 (3.0)	-0.053	1.9 (2.7)	1.9 (2.9)	-0.027	2.0 (2.9)	1.6 (2.4)	0.139	2.0 (2.6)	2.4 (2.9)	-0.128
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;25.0]	[0.0;27.0]		[0.0;31.0]	[0.0;18.0]		[0.0;16.0]	[0.0;17.0]	
Rheumatologist Visits												
n, patients (%)	967 (61.6)	945 (61.5)	0.001	463 (63.2)	494 (63.6)	-0.009	409 (64.7)	375 (65.8)	-0.023	46 (66.7)	94 (77.0)	-0.232
n, events	2146	2101		1013	1156		927	832		101	209	
Mean (SD)	1.4 (1.5)	1.4 (1.5)	-0.001	1.4 (1.5)	1.5 (1.6)	-0.068	1.5 (1.5)	1.5 (1.5)	0.005	1.5 (1.4)	1.7 (1.5)	-0.170
Median	1.0	1.0		1.0	1.0		1.0	1.0		1.0	2.0	
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;6.0]	[0.0;7.0]	
Other Outpatient Visits												
n, patients (%)	1461 (93.0)	1415 (92.1)	0.033	688 (93.9)	723 (93.1)	0.033	590 (93.4)	531 (93.2)	0.008	61 (88.4)	108 (88.5)	-0.004
n, events	32101	27779		15644	13693		13116	11299		1080	2351	
Mean (SD)	20.4 (35.4)	18.1 (30.9)	0.071	21.3 (35.0)	17.6 (29.1)	0.116	20.8 (34.4)	19.8 (33.0)	0.028	15.7 (26.9)	19.3 (40.1)	-0.106
Median	8.0	8.0		9.0	8.0		8.0	9.0		6.0	6.0	
Min; Max	[0.0;322.0]	[0.0;264.0]		[0.0;247.0]	[0.0;275.0]		[0.0;254.0]	[0.0;242.0]		[0.0;152.0]	[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 = 1571	TNFi[a] n = 1536	Std. Diff.	Baricitinib n = 733	TNFi[a] n = 777	Std. Diff.	Baricitinib n = 632	TNFi[a] n = 570	Std. Diff.	Baricitinib n = 69	TNFi[a] n = 122	Std. Diff.
Inpatient Visits[b]												
n, patients (%)	750 (47.7)	706 (46.0)	0.036	361 (49.2)	396 (51.0)	-0.034	309 (48.9)	276 (48.4)	0.009	35 (50.7)	52 (42.6)	0.163
n, events	1782	1606		817	877		785	588		90	100	
Mean (SD)	1.1 (1.8)	1.0 (2.2)	0.044	1.1 (1.7)	1.1 (1.6)	-0.008	1.2 (1.9)	1.0 (1.6)	0.121	1.3 (1.9)	0.8 (1.4)	0.287
Median	0.0	0.0		0.0	1.0		0.0	0.0		1.0	0.0	
Min; Max	[0.0;14.0]	[0.0;51.0]		[0.0;12.0]	[0.0;10.0]		[0.0;10.0]	[0.0;8.0]		[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: mos = months; N = number of patients in the specified category; 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 6.37 (continued). Baseline healthcare resource utilization by exposure duration and dose of baricitinib - Hospitalized Tuberculosis cohort, Matched [SNDS]

Type of resource use during baseline period	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1225	Bari. 2 mg n = 346	Bari. 4 mg n = 595	Bari. 2 mg n = 136	Bari. 4 mg n = 520	Bari. 2 mg n = 111	Bari. 4 mg n = 56	Bari. 2 mg n = 13
Physician Office Visits (rheumatologist visits excluded)								
n, patients (%)	699 (57.1)	231 (66.8)	378 (63.5)	98 (72.1)	329 (63.3)	81 (73.0)	39 (69.6)	12 (92.3)
n, events	1906	688	1059	310	946	328	105	36
Mean (SD)	1.6 (2.5)	2.0 (2.4)	1.8 (2.6)	2.3 (2.8)	1.8 (2.7)	3.0 (3.5)	1.9 (2.6)	2.8 (2.5)
Median	1.0	1.0	1.0	1.0	1.0	2.0	1.0	2.0
Min; Max	[0.0;41.0]	[0.0;13.0]	[0.0;25.0]	[0.0;17.0]	[0.0;31.0]	[0.0;19.0]	[0.0;16.0]	[0.0;9.0]
Rheumatologist Visits								
n, patients (%)	765 (62.4)	202 (58.4)	379 (63.7)	83 (61.0)	345 (66.3)	63 (56.8)	36 (64.3)	≤ 10
n, events	1672	474	834	173	775	146	82	19
Mean (SD)	1.4 (1.5)	1.4 (1.6)	1.4 (1.5)	1.3 (1.6)	1.5 (1.5)	1.3 (1.5)	1.5 (1.5)	1.5 (1.1)
Median	1.0	1.0	1.0	1.0	1.0	1.0	1.0	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;6.0]	[0.0;6.0]	[0.0;3.0]
Other Outpatient Visits								
n, patients (%)	1128 (92.1)	333 (96.2)	555 (93.3)	132 (97.1)	481 (92.5)	108 (97.3)	48 (85.7)	13 (100.0)
n, events	20637	11464	10303	5302	9268	3846	798	282
Mean (SD)	16.8 (29.9)	33.1 (48.0)	17.3 (27.1)	39.0 (54.9)	17.8 (30.8)	34.6 (45.5)	14.3 (22.9)	21.7 (40.6)
Median	7.0	15.5	8.0	16.5	7.0	17.0	5.5	7.0

Type of resource use during baseline period	<6 mos		6 mos to <12 mos		12 mos to <24 mos		≥24 mos	
	Bari. 4 mg n = 1225	Bari. 2 mg n = 346	Bari. 4 mg n = 595	Bari. 2 mg n = 136	Bari. 4 mg n = 520	Bari. 2 mg n = 111	Bari. 4 mg n = 56	Bari. 2 mg n = 13
Min; Max	[0.0;322.0]	[0.0;226.0]	[0.0;242.0]	[0.0;247.0]	[0.0;254.0]	[0.0;201.0]	[0.0;125.0]	[3.0;152.0]
Inpatient Visits[a]								
n, patients (%)	556 (45.4)	194 (56.1)	282 (47.4)	78 (57.4)	236 (45.4)	73 (65.8)	27 (48.2)	≤ 10
n, events	1361	421	646	168	585	200	72	18
Mean (SD)	1.1 (1.8)	1.2 (1.7)	1.1 (1.7)	1.2 (1.7)	1.1 (1.8)	1.8 (2.2)	1.3 (2.0)	1.4 (1.7)
Median	0.0	1.0	0.0	1.0	0.0	1.0	0.0	1.0
Min; Max	[0.0;14.0]	[0.0;12.0]	[0.0;12.0]	[0.0;7.0]	[0.0;10.0]	[0.0;8.0]	[0.0;7.0]	[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

2 OUTCOMES

2.1 VENOUS THROMBOEMBOLISM (VTE)

Table 6.38. Primary (Main) case definition for VTE and alternate case definitions for sensitivity analyses

Not applicable for SNDS data

Table 6.39. Pattern of VTE and related diagnostic codes in patients with RA - VTE cohort, Unmatched [SNDS]

Code	Unmatched Total Patients n = 13444	
Deep vein thrombosis (main hospitalized diagnosis), n (%)	**≤ 10**	
I801-Phlebitis and thrombophlebitis of femoral vein	0	(0.0)
I802-Phlebitis and thrombophlebitis of other and unspecified deep vesseis of lower extremities	≤ 10	
I803-Phlebitis and thrombophlebitis of lower extremities, unspecified	0	(0.0)
I808-Phlebitis and thrombophlebitis of other sites	≤ 10	
I809-Phlebitis and thrombophlebitis of unspecified site	0	(0.0)
I81-Portal vein thrombosis	≤ 10	
I82-Other venous embolism and thrombosis	0	(0.0)
Pulmonary embolism (main hospitalized diagnosis), n (%)	**21**	**(0.2)**
I260-Pulmonary embolism with acute cor pulmonale	≤ 10	
I269-Pulmonary embolism without acute cor pulmonale	18	(0.1)
Deep vein thrombosis (all hospitalized diagnosis), n (%)	**22**	**(0.2)**
I801-Phlebitis and thrombophlebitis of femoral vein	≤ 10	

I802-Phlebitis and thrombophlebitis of other and unspecified deep vesseis of lower extremities	14	(0.1)
I803-Phlebitis and thrombophlebitis of lower extremities, unspecified	0	(0.0)
I808-Phlebitis and thrombophlebitis of other sites	≤ 10	
I809-Phlebitis and thrombophlebitis of unspecified site	≤ 10	
I81-Portal vein thrombosis	≤ 10	
I82-Other venous embolism and thrombosis	0	(0.0)
Pulmonary embolism (all hospitalized diagnosis), n (%)	**24**	**(0.2)**
I260-Pulmonary embolism with acute cor pulmonale	≤ 10	
I269-Pulmonary embolism without acute cor pulmonale	21	(0.2)
Medical imaging for pulmonary embolism or deep vein thrombosis (in- and outpatient), n (%)	**29**	**(0.2)**
Lung scintigraphy	≤ 10	
Lower limb compression ultrasound	19	(0.1)
Phlebography	0	(0.0)
Thorax scanner	≤ 10	

Abbreviations: ICD-10 = International Classification of Disease, 10th Revision; RA = rheumatoid arthritis; VTE = venous thromboembolism.

Table 6.40. Clinical characteristics during baseline period in patients with VTE, VTE matched cohort [SNDS]

Characteristics[b]	Baricitinib Any n = 20	Baricitinib 4 mg n = 14	Baricitinib 2 mg n = ≤ 10	TNFi[a] n = 13	Total n = 33
Age [in years]					
N	20 (0)	14 (0)		13 (0)	33 (0)
Mean (SD)	68.6 (9.8)	65.8 (9.2)		66.2 (12.3)	67.6 (10.8)
Median	70.0	68.5		66.0	69.0
Min; Max	[49.0;87.0]	[49.0;83.0]		[51.0;88.0]	[49.0;88.0]
Sex, n (%)					
Female	≤ 10	≤ 10		≤ 10	≤ 10
Male	19 (95.0)	13 (92.9)		≤ 10	25 (75.8)
Clinical conditions during baseline period, n (%)					
Cancer, excluding NMSC	≤ 10	≤ 10		0 (0.0)	≤ 10
NMSC	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Chronic lung disease, excluding cystic fibrosis[d]	≤ 10	≤ 10		≤ 10	≤ 10
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Cardiovascular revascularization	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Congestive Heart Failure, hospitalized	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Coronary artery disease	≤ 10	0 (0.0)		≤ 10	≤ 10
Unstable angina	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Ventricular arrhythmia	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Stroke	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Hemorrhagic	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)

Characteristics[b]	Baricitinib Any n = 20	Baricitinib 4 mg n = 14	Baricitinib 2 mg n = ≤ 10	TNFi[a] n = 13	Total n = 33
Ischemic	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Unknown	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
TIA	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Diabetes Mellitus[d]	≤ 10	≤ 10		≤ 10	≤ 10
Treated insulin dependent	N/A	N/A		N/A	N/A
Treated non insulin dependent	N/A	N/A		N/A	N/A
Dyslipidemia (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	≤ 10	≤ 10		0 (0.0)	≤ 10
AIDS/HIV	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Antiphospholipid syndrome	N/A	N/A		N/A	N/A
SLE	≤ 10	≤ 10		0 (0.0)	≤ 10
Primary Sjogren Syndrome	≤ 10	≤ 10		0 (0.0)	≤ 10
Liver or pancreatic disorder[d]	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Obesity (not available in SNDS)	N/A	N/A		N/A	N/A
Recent pregnancy	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
RA Severity (CIRAS Index)					
Mean (± SD)	5.6 (0.6)	5.7 (0.6)		6.6 (1.6)	6.0 (1.2)
Smoking (not available in SNDS)	N/A	N/A		N/A	N/A
Surgery or trauma	≤ 10	≤ 10		≤ 10	≤ 10

Characteristics[b]	Baricitinib Any n = 20	Baricitinib 4 mg n = 14	Baricitinib 2 mg n = ≤ 10	TNFi[a] n = 13	Total n = 33
Other prescription medications during baseline period, n (%)	≤ 10	≤ 10		≤ 10	≤ 10
Antibiotics	14 (70.0)	≤ 10		≤ 10	21 (63.6)
Antidiabetic agents	≤ 10	≤ 10		≤ 10	≤ 10
Insulins	≤ 10	≤ 10		0 (0.0)	≤ 10
Non-insulins	≤ 10	≤ 10		≤ 10	≤ 10
Cardiovascular					
Antithrombotic agents	≤ 10	≤ 10		≤ 10	≤ 10
Anticoagulant	≤ 10	≤ 10		≤ 10	≤ 10
Antiplatelet	≤ 10	≤ 10		≤ 10	≤ 10
Antihypertensives	≤ 10	≤ 10		≤ 10	13 (39.4)
Angiotensin converting enzyme inhibitors (ACE)	≤ 10	≤ 10		≤ 10	≤ 10
Angiotensin receptor blockers (ARB)	≤ 10	≤ 10		≤ 10	≤ 10
Beta blocker	≤ 10	0 (0.0)		≤ 10	≤ 10
Calcium channel blocker	≤ 10	≤ 10		≤ 10	≤ 10
Nitrates	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Acyclovir	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Valacyclovir	≤ 10	≤ 10		≤ 10	≤ 10
Hormonal	≤ 10	≤ 10		≤ 10	≤ 10
HRT	≤ 10	≤ 10		0 (0.0)	≤ 10
Oral Contraceptives	0 (0.0)	0 (0.0)		≤ 10	≤ 10
SERMs	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Topic with progestogens and/or estrogens	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)

Characteristics[b]	Baricitinib Any n = 20	Baricitinib 4 mg n = 14	Baricitinib 2 mg n = ≤ 10	TNFi[a] n = 13	Total n = 33
Lipid-lowering agents	≤ 10	≤ 10		≤ 10	13 (39.4)
HMG CoA reductase inhibitors	≤ 10	≤ 10		≤ 10	≤ 10
Fibrates	≤ 10	≤ 10		≤ 10	≤ 10
Bile acid sequestrants	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Other lipid modifying agents	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Lipid modifying agents, combinations	≤ 10	≤ 10		0 (0.0)	≤ 10
Rheumatoid arthritis-related					
Aspirin	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Cox-2 Inhibitor	0 (0.0)	0 (0.0)		≤ 10	≤ 10
NSAIDs	≤ 10	≤ 10		≤ 10	12 (36.4)
Glucocorticosteroid	18 (90.0)	12 (85.7)		≤ 10	28 (84.8)
Vaccines	14 (70.0)	≤ 10		≤ 10	21 (63.6)
Antineoplastic agents	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Post-index Occurrence[c], n (%)				-	
Cancer	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Hospitalization	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Surgery	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)

Abbreviations: 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 6.41. Pattern of RA medication use in patients with VTE [SNDS]

Characteristics[b]	Unmatched				Matched				
	Baricitinib n = 23	Bari. 4 mg n = 16	Bari. 2 mg n ≤ 10	TNFi n = 29	Baricitinib n = 20	Bari. 4 mg n = 14	Bari. 2 mg n ≤ 10	TNFi n = 13	Total n = 33
Baseline Medication, n (%)			-						
cDMARDs, during baseline period									
n, total (%)	15 (65.2)	12 (75.0)		20 (69.0)	14 (70.0)	11 (78.6)		≤ 10	22 (66.7)
Mean (SD)	0.7 (0.6)	0.8 (0.4)		0.8 (0.6)	0.8 (0.6)	0.8 (0.4)		0.6 (0.5)	0.7 (0.5)
Median	1.0	1.0		1.0	1.0	1.0		1.0	1.0
Min; Max	[0.0;2.0]	[0.0;1.0]		[0.0;2.0]	[0.0;2.0]	[0.0;1.0]		[0.0;1.0]	[0.0;2.0]
>1 cDMARD concomitantly	≤ 10	0 (0.0)		0 (0.0)	≤ 10	0 (0.0)		0 (0.0)	≤ 10
Hydroxychloroquine	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		0 (0.0)	≤ 10
Chloroquine	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Azathioprin	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Leflunomide	0 (0.0)	0 (0.0)		≤ 10	0 (0.0)	0 (0.0)		≤ 10	≤ 10
Methotrexate	13 (56.5)	≤ 10		11 (37.9)	12 (60.0)	≤ 10		≤ 10	17 (51.5)
Mycophenolate mofetil	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Sulfasalazin	≤ 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)
Penicillamin	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
bDMARDs, during baseline period									
n, total (%)	14 (60.9)	11 (68.8)		≤ 10	11 (55.0)	≤ 10		≤ 10	17 (51.5)
Mean (SD)	0.7 (0.6)	0.8 (0.6)		0.3 (0.5)	0.6 (0.6)	0.7 (0.6)		0.5 (0.5)	0.5 (0.6)
Median	1.0	1.0		0.0	1.0	1.0		0.0	1.0

Characteristics[b]	Unmatched				Matched				
	Baricitinib n = 23	Bari. 4 mg n = 16	Bari. 2 mg n ≤ 10	TNFi n = 29	Baricitinib n = 20	Bari. 4 mg n = 14	Bari. 2 mg n ≤ 10	TNFi n = 13	Total n = 33
Min; Max	[0.0;2.0]	[0.0;2.0]		[0.0;1.0]	[0.0;2.0]	[0.0;2.0]		[0.0;1.0]	[0.0;2.0]
cDMARDs, concomitant	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10	≤ 10
Adalimumab[c]	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10	≤ 10
Certolizumab pegol[c]	≤ 10	≤ 10		0 (0.0)	≤ 10	≤ 10		0 (0.0)	≤ 10
Etanercept[c]	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10	≤ 10
Golimumab[c]	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Infliximab[c]	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10	≤ 10
Rituximab	≤ 10	≤ 10		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Sarilumab	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Abatacept	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10	≤ 10
Tocilizumab	≤ 10	≤ 10		0 (0.0)	≤ 10	≤ 10		0 (0.0)	≤ 10
Anakinra	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
TNFi naïve at baseline	16 (69.6)	≤ 10		24 (82.8)	14 (70.0)	≤ 10		≤ 10	24 (72.7)
Post-index Medication, n (%)			-						
Methotrexate, concomitant	≤ 10	≤ 10		12 (41.4)	≤ 10	≤ 10		≤ 10	13 (39.4)
Other Concomitant cDMARD	0 (0.0)	0 (0.0)		≤ 10	0 (0.0)	0 (0.0)		≤ 10	≤ 10
Dose change, baricitinib	≤ 10	≤ 10		N/A	≤ 10	≤ 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] 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 6.42. Time to first VTE (Days) [SNDS]

	Unmatched				Matched				
	Baricitinib n = 23	Bari. 4 mg n = 16	Bari. 2 mg n ≤ 10	TNFi n = 29	Baricitinib n = 20	Bari. 4 mg n = 14	Bari. 2 mg n ≤ 10	TNFi[a] n = 13	Total n = 33
Time to first VTE (in days)									
N (missing)	23 (0)	16 (0)		29 (0)	20 (0)	14 (0)		13 (0)	33 (0)
Mean (SD)	239.9 (179.7)	261.6 (200.9)		197.7 (175.0)	227.0 (165.4)	245.1 (181.1)		181.4 (156.3)	209.0 (161.0)
Median	209.0	183.5		144.0	204.0	183.5		113.0	168.0
Min; Max	[17.0;650.0]	[75.0;650.0]		[26.0;624.0]	[17.0;632.0]	[75.0;632.0]		[28.0;555.0]	[17.0;632.0]

Abbreviations: 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 6.43. Time to first VTE (Days), Alternate Definition I [SNDS]

Not applicable for SNDS data

Table 6.44. Time to first VTE (Days), Alternate Definition II [SNDS]

Not applicable for SNDS data

Table 6.45. Crude rates of incident VTE [SNDS]

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

	Unmatched				Matched				
VTE	**Bari. Any[b] n = 3242**	**Bari. 4 mg n = 2616**	**Bari. 2 mg n = 622**	**TNFi n = 10202**	**Bari. Any[b] n = 2859**	**Bari. 4 mg n = 2306**	**Bari. 2 mg n = 551**	**TNFi[a] n = 2859**	**Total n = 5718**
95% CI	[0.7 ; 2.1]	[0.4 ; 1.8]	[1.0 ; 5.7]	[0.4 ; 1.0]	[0.7 ; 2.2]	[0.4 ; 1.9]	[0.8 ; 5.7]	[0.4 ; 1.8]	[0.7 ; 1.7]
IRD[d] /100 PY	0.6				0.4				
IRD[d] 95% CI	[-0.03 ; 1.3]				[-0.6 ; 1.3]				

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

[a] Matching ratio 1:1 is applied

[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

Table 6.46. Crude rates of incident VTE, Alternate Definition I [SNDS]

Not applicable for SNDS data

Table 6.47. Crude rates of incident VTE, Alternate Definition II [SNDS]

Not applicable for SNDS data

Table 6.48. Comparative risk of incident VTE, matched cohort [SNDS]

VTE	TNFi	Baricitinib, HR [95% CI]	P-value
Base model	Ref	1.57 [0.78 ; 3.18]	0.2055
Adjusted – Model [1]	Ref	1.57 [0.78 ; 3.18]	0.2055
Adjusted – Model [2]	Ref	1.55 [0.77 ; 3.13]	0.2234
Concomitant Glucocorticoid use	*Ref*	*1.49 [0.74 ; 3.00]*	*0.2682*
Concomitant cDMARD use	*Ref*	*0.77 [0.39 ; 1.54]*	*0.4659*
Adjusted – Model [3]	Ref	1.56 [0.77 ; 3.16]	0.2135
Concomitant Glucocorticoid use	*Ref*	*1.47 [0.73 ; 2.97]*	*0.2858*
Adjusted – Model [n]	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 6.49. Comparative risk of incident VTE, Alternate Definition I [SNDS]
Not applicable for SNDS data

Table 6.50. Comparative risk of incident VTE, Alternate Definition II [SNDS]
Not applicable for SNDS data

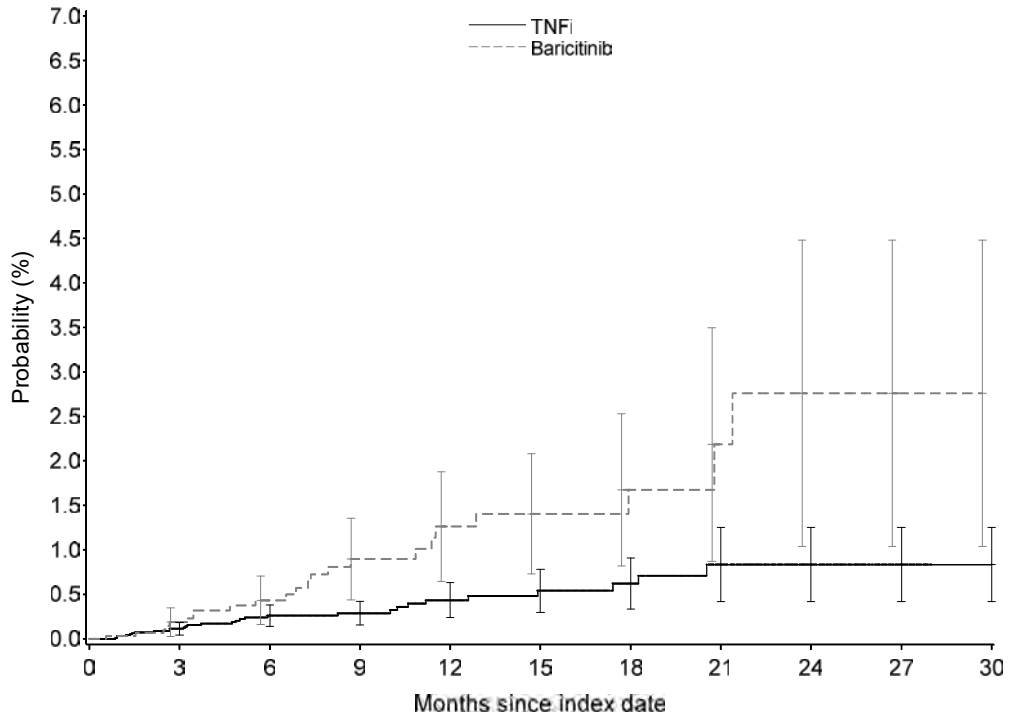

Figure 6.2. Kaplan-Meier survival curve for VTE, pre-matched cohort [SNDS]

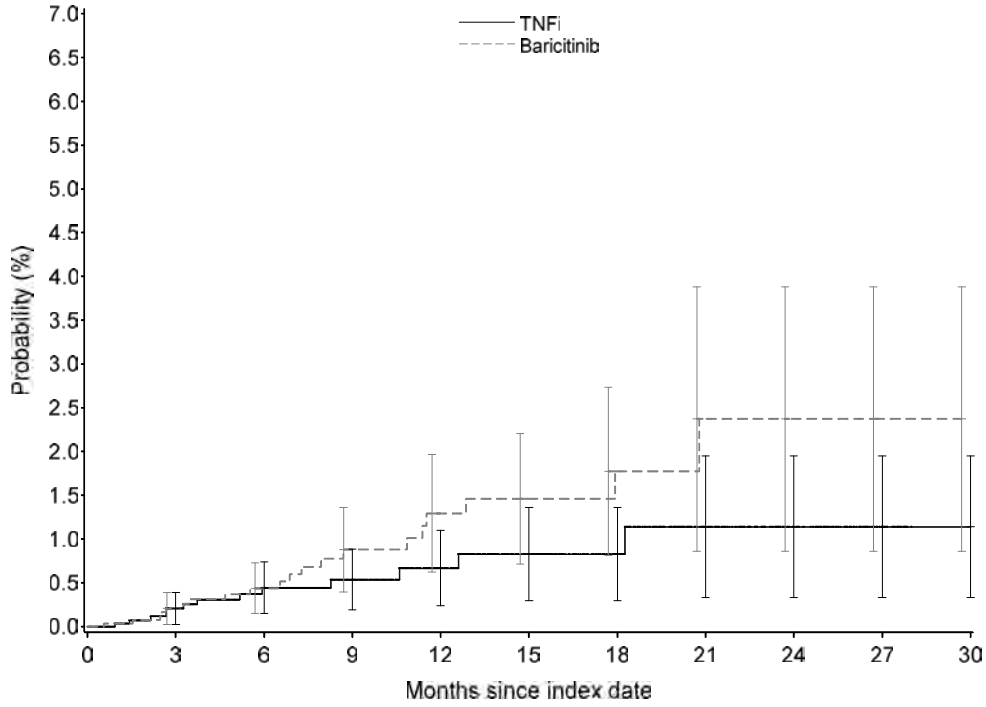

Figure 6.3 . Kaplan-Meier survival curve for VTE, Matched cohort [SNDS]

Figure 6.4. Adjusted survival curve for VTE [SNDS]

Not applicable for SNDS data

2.2 MAJOR ADVERSE CARDIOVASCULAR EVENTS

Table 6.51. Clinical characteristics in patients with MACE, MACE matched cohort [SNDS]

Characteristics[b]	Baricitinib Any n = 25	Baricitinib 4 mg n = 16	Baricitinib 2 mg n ≤ 10	TNFi[a] n = 11	Total n = 36
Age [in years]			-		
N (missing)	25 (0)	16 (0)		11 (0)	36 (0)
Mean (SD)	67.5 (8.6)	64.1 (5.8)		69.2 (11.8)	68.0 (9.5)
Median	65.0	64.0		66.0	65.5
Min; Max	[48.0;80.0]	[55.0;79.0]		[52.0;92.0]	[48.0;92.0]
Sex, n (%)					
Female	≤ 10	≤ 10		≤ 10	14 (38.9)
Male	16 (64.0)	11 (68.8)		≤ 10	22 (61.1)
Clinical conditions during baseline period, n (%)			-		
Cancer, excluding NMSC	≤ 10	≤ 10		0 (0.0)	≤ 10
NMSC	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Chronic lung disease, excluding cystic fibrosis[d]	≤ 10	≤ 10		≤ 10	≤ 10
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	0 (0.0)	0 (0.0)		≤ 10	≤ 10
Cardiovascular revascularization	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Congestive Heart Failure, hospitalized	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Coronary artery disease	≤ 10	≤ 10		≤ 10	≤ 10
Unstable angina	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Ventricular arrhythmia	≤ 10	≤ 10		0 (0.0)	≤ 10
Stroke	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)

Characteristics[b]	Baricitinib Any n = 25	Baricitinib 4 mg n = 16	Baricitinib 2 mg n ≤ 10	TNFi[a] n = 11	Total n = 36
Hemorrhagic	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Ischemic	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Unknown	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
TIA	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Diabetes Mellitus[d]	≤ 10	≤ 10		≤ 10	≤ 10
Treated insulin dependent	N/A	N/A		N/A	N/A
Treated non insulin dependent	N/A	N/A		N/A	N/A
Dyslipidemia (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	≤ 10	0 (0.0)		≤ 10	≤ 10
AIDS/HIV	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Antiphospholipid syndrome	N/A	N/A		N/A	N/A
SLE	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Primary Sjogren Syndrome	≤ 10	0 (0.0)		≤ 10	≤ 10
Liver or pancreatic disorder[d]	≤ 10	≤ 10		0 (0.0)	≤ 10
Obesity (not available in SNDS)	N/A	N/A		N/A	N/A
Recent pregnancy	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
RA Severity (CIRAS Index)					
Mean (SD)	5.7 (0.9)	5.8 (0.8)		6.5 (1.8)	5.9 (1.3)
Smoking (not available in SNDS)	N/A	N/A		N/A	N/A
Surgery or trauma	≤ 10	≤ 10		0 (0.0)	≤ 10

Characteristics[b]	Baricitinib Any n = 25	Baricitinib 4 mg n = 16	Baricitinib 2 mg n ≤ 10	TNFi[a] n = 11	Total n = 36
Other prescription medications during baseline period, n (%)			-		
Antibiotics	11 (44.0)	≤ 10		≤ 10	18 (50.0)
Antidiabetic agents	≤ 10	≤ 10		≤ 10	≤ 10
Insulins	≤ 10	≤ 10		≤ 10	≤ 10
Non-insulins	≤ 10	≤ 10		≤ 10	≤ 10
Cardiovascular					
Antithrombotic agents	≤ 10	≤ 10		≤ 10	12 (33.3)
Anticoagulant	≤ 10	0 (0.0)		≤ 10	≤ 10
Antiplatelet	≤ 10	≤ 10		≤ 10	≤ 10
Antihypertensives	16 (64.0)	≤ 10		≤ 10	22 (61.1)
Angiotensin converting enzyme inhibitors (ACE)	≤ 10	≤ 10		≤ 10	≤ 10
Angiotensin receptor blockers (ARB)	≤ 10	≤ 10		≤ 10	≤ 10
Beta blocker	≤ 10	≤ 10		≤ 10	11 (30.6)
Calcium channel blocker	≤ 10	≤ 10		≤ 10	≤ 10
Nitrates	≤ 10	≤ 10		0 (0.0)	≤ 10
Acyclovir	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Valacyclovir	≤ 10	0 (0.0)		0 (0.0)	≤ 10
Hormonal	≤ 10	≤ 10		≤ 10	≤ 10
HRT	≤ 10	≤ 10		≤ 10	≤ 10
Oral Contraceptives	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
SERMs	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Topic with progestogens and/or estrogens	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)

Characteristics[b]	Baricitinib Any n = 25	Baricitinib 4 mg n = 16	Baricitinib 2 mg n ≤ 10	TNFi[a] n = 11	Total n = 36
Lipid-lowering agents	≤ 10	≤ 10		≤ 10	≤ 10
HMG CoA reductase inhibitors	≤ 10	≤ 10		≤ 10	≤ 10
Fibrates	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Bile acid sequestrants	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Other lipid modifying agents	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Lipid modifying agents, combinations	≤ 10	≤ 10		0 (0.0)	≤ 10
Rheumatoid arthritis-related					
Aspirin	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Cox-2 Inhibitor	≤ 10	≤ 10		≤ 10	≤ 10
NSAIDs	≤ 10	≤ 10		≤ 10	≤ 10
Glucocorticosteroid	18 (72.0)	12 (75.0)		11 (100.0)	29 (80.6)
Vaccines	≤ 10	≤ 10		≤ 10	15 (41.7)
Antineoplastic agents	≤ 10	0 (0.0)		0 (0.0)	≤ 10
Post-index Occurrence[c], n (%)					
Cancer	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Hospitalization	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Surgery	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)

Abbreviations: 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 6.52. Pattern of RA medication use in patients with MACE [SNDS]

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

Characteristics[b]	Unmatched				Matched				
	Baricitinib n = 28	Bari. 4 mg n = 19	Bari. 2 mg n ≤ 10	TNFi n = 34	Baricitinib n = 25	Bari. 4 mg n = 16	Bari. 2 mg n ≤ 10	TNFi n = 11	Total n = 36
Median	1.0	1.0		0.0	1.0	1.0		0.0	1.0
Min; Max	[0.0;2.0]	[0.0;2.0]		[0.0;1.0]	[0.0;1.0]	[0.0;1.0]		[0.0;1.0]	[0.0;1.0]
cDMARDs, concomitant	11 (39.3)	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10	11 (30.6)
Adalimumab[c]	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10	≤ 10
Certolizumab pegol[c]	≤ 10	≤ 10		0 (0.0)	≤ 10	≤ 10		0 (0.0)	≤ 10
Etanercept[c]	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10	≤ 10
Golimumab[c]	≤ 10	0 (0.0)		0 (0.0)	≤ 10	0 (0.0)		0 (0.0)	≤ 10
Infliximab[c]	≤ 10	≤ 10		0 (0.0)	≤ 10	≤ 10		0 (0.0)	≤ 10
Rituximab	≤ 10	≤ 10		0 (0.0)	≤ 10	≤ 10		0 (0.0)	≤ 10
Sarilumab	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Abatacept	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10	≤ 10
Tocilizumab	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		≤ 10	≤ 10
Anakinra	≤ 10	0 (0.0)		0 (0.0)	≤ 10	0 (0.0)		0 (0.0)	≤ 10
TNFi naïve at baseline	17 (60.7)	≤ 10		29 (85.3)	17 (68.0)	≤ 10		≤ 10	25 (69.4)
Post-index Medication, n (%)									
Methotrexate, concomitant	≤ 10	≤ 10		23 (67.6)	≤ 10	≤ 10		≤ 10	11 (30.6)
Other Concomitant cDMARD	≤ 10	≤ 10		≤ 10	≤ 10	≤ 10		0 (0.0)	≤ 10
Dose change, baricitinib	≤ 10	≤ 10		0 (0.0)	≤ 10	≤ 10		0 (0.0)	≤ 10

Abbreviations: 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;
N = number of patients in the specified category
RA = rheumatoid arthritis; SD = standard deviation; 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 6.53. Time to first MACE (Days) [SNDS]

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

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

[a] Matching ratio 1:1 is applied

Table 6.54. Crude rates of first MACE [SNDS]

	Unmatched				Matched				
MACE	Bari. Any[b] n = 3236	Bari. 4 mg n = 2613	Bari. 2 mg n = 619	TNFi n = 10175	Bari. Any[b] n = 2864	Bari. 4 mg n = 2314	Bari. 2 mg n = 548	TNFi[a] n = 2864	Total n = 5728
Overall (MI or stroke)									
Person-Years	2102	1727	372	6681	1848	1521	326	1896	3744
MACE	28	19	9	34	25	16	9	11	36
MACE/100 PY	1.3	1.1	2.4	0.5	1.4	1.1	2.8	0.6	1.0
95% CI	[0.9 ; 1.9]	[0.7 ; 1.7]	[1.1 ; 4.6]	[0.4 ; 0.7]	[0.9 ; 2.0]	[0.6 ; 1.7]	[1.3 ; 5.2]	[0.3 ; 1.0]	[0.7 ; 1.3]
IRD[d] /100 PY	0.8			.	0.8				
IRD[d] 95% CI	[0.4 ; 1.2]				[0.1 ; 1.4]				
Overall (MI)									
Person-Years	2102	1727	372	6681	1848	1521	326	1896	3744
MI	16	12	4	23	13	9	4	6	19
MI/100 PY	0.8	0.7	1.1	0.3	0.7	0.6	1.2	0.3	0.5
95% CI	[0.4 ; 1.2]	[0.1 ; 1.2]	[0.3 ; 2.8]	[0.2 ; 0.5]	[0.4 ; 1.2]	[0.3 ; 1.1]	[0.3 ; 3.1]	[0.1 ; 0.7]	[0.3 ; 0.8]
IRD[d] /100 PY	0.4			.	0.4				
IRD[d] 95% CI	[0.1 ; 0.7]				[-0.1 ; 0.8]				
Overall (stroke)									
Person-Years	2102	1727	372	6681	1848	1521	326	1896	3744
Stroke	12	7	5	11	12	7	5	5	17
Stroke /100 PY	0.6	0.4	1.3	0.2	0.6	0.5	1.5	0.3	0.5
95% CI	[0.3 ; 1.0]	[0.2 ; 0.8]	[0.4 ; 3.1]	[0.1 ; 0.3]	[0.3 ; 1.1]	[0.2 ; 0.9]	[0.5 ; 3.6]	[0.1 ; 0.6]	[0.3 ; 0.7]
IRD[d] /100 PY	0.4			.	0.4				

	Unmatched				Matched				
MACE	**Bari. Any[b] n = 3236**	**Bari. 4 mg n = 2613**	**Bari. 2 mg n = 619**	**TNFi n = 10175**	**Bari. Any[b] n = 2864**	**Bari. 4 mg n = 2314**	**Bari. 2 mg n = 548**	**TNFi[a] n = 2864**	**Total n = 5728**
IRD[d] 95% CI	[0.2 ; 0.7]				[-0.05 ; 0.8]				
Concomitant MTX Use, n (%)	1357 (41.9)	1148 (43.9)	207 (33.4)	5376 (52.8)	1218 (42.5)	1031 (44.6)	185 (33.8)	1370 (47.8)	2588 (45.2)
Person-Years	1004	857	145	4093	895	764	130	1032	1927
MACE	9	6	3	23	7	4	3	4	11
MACE/100 PY	0.9	0.7	2.1	0.6	0.8	0.5	2.3	0.4	0.6
95% CI	[0.4 ; 1.7]	[0.3 ; 1.5]	[0.4 ; 6.0]	[0.4 ; 0.8]	[0.3 ; 1.6]	[0.1 ; 1.3]	[0.5 ; 6.7]	[0.1 ; 1.0]	[0.3 ; 1.0]
IRD[d] /100 PY	0.3			.	0.4				
IRD[d] 95% CI	[-0.2 ; 0.9]				[-0.3 ; 1.1]				
No concomitant MTX Use, n (%)	1879 (58.1)	1465 (56.1)	412 (66.6)	4799 (47.2)	1646 (57.5)	1283 (55.4)	363 (66.2)	1494 (52.2)	3140 (54.8)
Person-Years	1098	869	227	2589	953	757	196	864	1818
MACE	19	13	6	11	18	12	6	7	25
MACE/100 PY	1.7	1.5	2.6	0.4	1.9	1.6	3.1	0.8	1.4
95% CI	[1.0 ; 2.7]	[0.8 ; 2.6]	[1.0 ; 5.8]	[0.2 ; 0.8]	[1.1 ; 3.0]	[0.8 ; 2.8]	[1.1 ; 6.7]	[0.3 ; 1.7]	[0.9 ; 2.0]
IRD[d] /100 PY	1.3			.	1.1				
IRD[d] 95% CI	[0.7 ; 1.9]				[-0.001 ; 2.2]				

Abbreviations: CI = confidence interval; 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; IRD = incidence risk difference; TNFi = tumor necrosis factor inhibitor.

[a] Matching ratio 1:1 is applied

[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

Table 6.55. Comparative risk of incident MACE, matched cohort [SNDS]

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

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

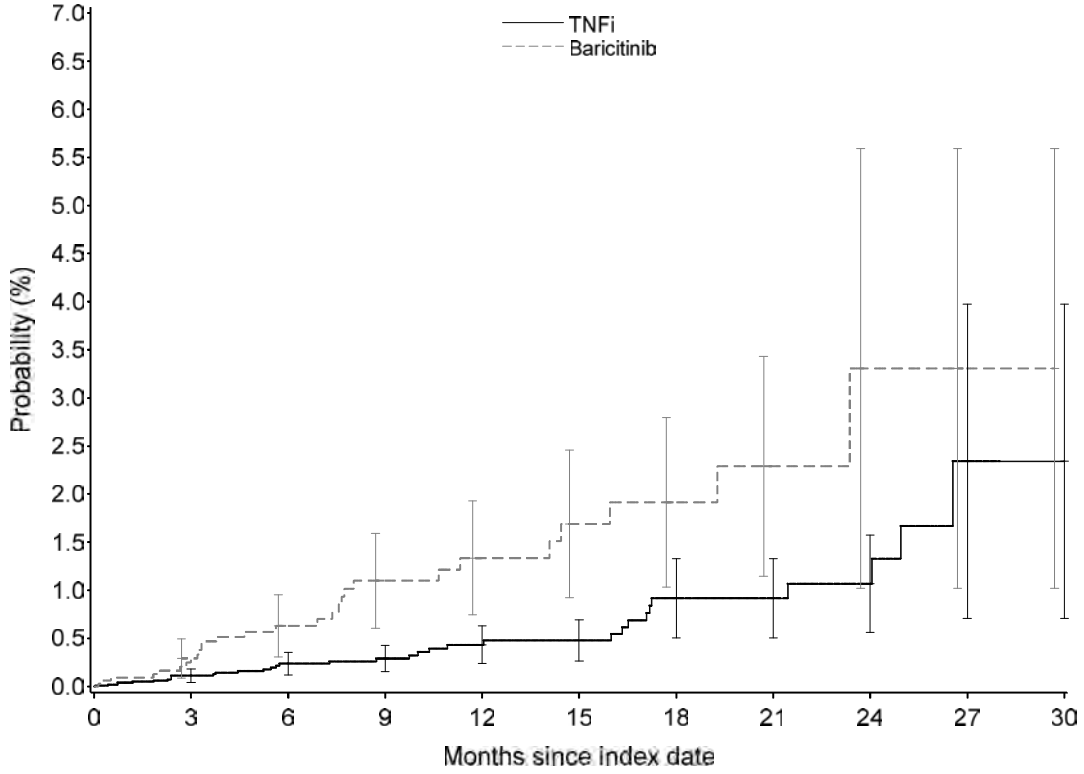

Figure 6.5 . Kaplan-Meier survival curve for MACE, pre-matched cohort [SNDS]

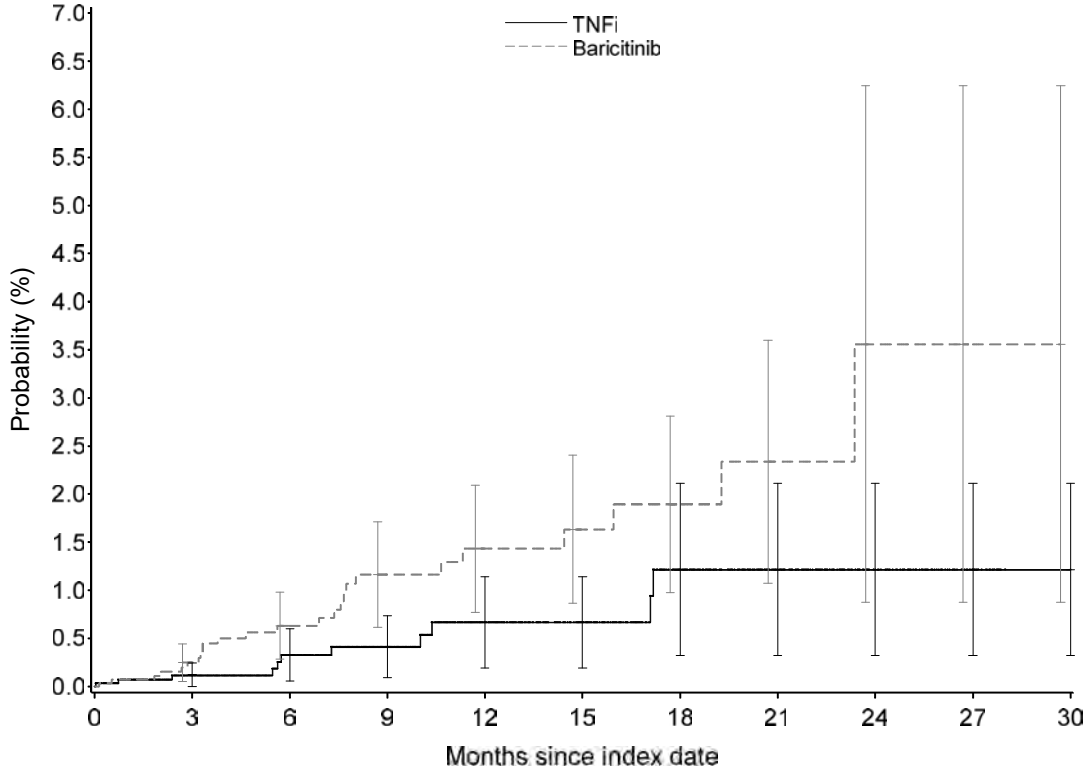

Figure 6.6. Kaplan-Meier survival curve for MACE, matched cohort [SNDS]

Figure 6.7. Adjusted survival curve for MACE [SNDS]

Not applicable for SNDS data.

2.3 SERIOUS INFECTIONS

Table 6.56. Clinical characteristics in patients with serious infections – Serious infection matched cohort [SNDS]

Characteristics[b]	Baricitinib n = 36	Baricitinib 4 mg n = 25	Baricitinib 2 mg n = 11	TNFi[a] n = 36	Total n = 72
Age [in years]					
N (missing)	36 (0)	25 (0)	11 (0)	36 (0)	72 (0)
Mean (SD)	66.3 (11.4)	62.9 (10.8)	74.2 (9.1)	65.7 (11.6)	66.0 (11.5)
Median	67.0	62.0	73.0	66.0	67.0
Min; Max	[34.0;85.0]	[34.0;79.0]	[56.0;85.0]	[33.0;87.0]	[33.0;87.0]
Sex, n (%)					
Female	12 (33.3)	≤ 10	≤ 10	≤ 10	20 (27.8)
Male	24 (66.7)	16 (64.0)	≤ 10	28 (77.8)	52 (72.2)
Clinical conditions during baseline period, n (%)					
Cancer, excluding NMSC	≤ 10	0 (0.0)	≤ 10	0 (0.0)	≤ 10
NMSC	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	14 (19.4)
Cardiovascular conditions					
Atrial arrhythmia/fibrillation	≤ 10	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)
Congestive Heart Failure, hospitalized	≤ 10	0 (0.0)	≤ 10	0 (0.0)	≤ 10
Coronary artery disease	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
Unstable angina	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ventricular arrhythmia	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10
Stroke	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	≤ 10

Characteristics[b]	Baricitinib n = 36	Baricitinib 4 mg n = 25	Baricitinib 2 mg n = 11	TNFi[a] n = 36	Total n = 72
Hemorrhagic	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)
Unknown	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	≤ 10
TIA	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Diabetes Mellitus[c]	≤ 10	≤ 10	≤ 10	≤ 10	18 (25.0)
Treated insulin dependent	N/A	N/A	N/A	N/A	N/A
Treated non insulin dependent	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
Hypertension (not available in SNDS)					
History of hypertension	N/A	N/A	N/A	N/A	N/A
Current hypertension	N/A	N/A	N/A	N/A	N/A
Immune disorders	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	≤ 10
AIDS/HIV	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
SLE	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	≤ 10
Primary Sjogren Syndrome	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	≤ 10
Liver or pancreatic disorder[c]	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 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)
RA Severity (CIRAS Index)					
Mean (± SD)	5.9 (1.2)	6.1 (1.0)	5.4 (1.6)	6.5 (1.3)	6.2 (1.3)
Smoking (not available in SNDS)	N/A	N/A	N/A	N/A	N/A
Surgery or trauma	≤ 10	≤ 10	≤ 10	≤ 10	13 (18.1)

Characteristics[b]	Baricitinib n = 36	Baricitinib 4 mg n = 25	Baricitinib 2 mg n = 11	TNFi[a] n = 36	Total n = 72
Other prescription medications during baseline period, n (%)					
Antibiotics	20 (55.6)	13 (52.0)	≤ 10	16 (44.4)	36 (50.0)
Antidiabetic agents	≤ 10	≤ 10	≤ 10	≤ 10	14 (19.4)
Insulins	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10
Non-insulins	≤ 10	≤ 10	≤ 10	≤ 10	13 (18.1)
Cardiovascular					
Antithrombotic agents	15 (41.7)	≤ 10	≤ 10	13 (36.1)	28 (38.9)
Anticoagulant	≤ 10	≤ 10	≤ 10	≤ 10	11 (15.3)
Antiplatelet	11 (30.6)	≤ 10	≤ 10	11 (30.6)	22 (30.6)
Antihypertensives	23 (63.9)	15 (60.0)	≤ 10	16 (44.4)	39 (54.2)
Angiotensin converting enzyme inhibitors (ACE)	≤ 10	≤ 10	0 (0.0)	≤ 10	13 (18.1)
Angiotensin receptor blockers (ARB)	≤ 10	≤ 10	≤ 10	≤ 10	12 (16.7)
Beta blocker	11 (30.6)	≤ 10	≤ 10	≤ 10	19 (26.4)
Calcium channel blocker	≤ 10	≤ 10	≤ 10	≤ 10	14 (19.4)
Nitrates	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)
Valacyclovir	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10
Hormonal	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10
HRT	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10
Oral Contraceptives	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	≤ 10
SERMs	≤ 10	≤ 10	0 (0.0)	0 (0.0)	≤ 10
Topic with progestogens and/or estrogens	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Characteristics[b]	Baricitinib n = 36	Baricitinib 4 mg n = 25	Baricitinib 2 mg n = 11	TNFi[a] n = 36	Total n = 72
Lipid-lowering agents	≤ 10	≤ 10	≤ 10	≤ 10	18 (25.0)
HMG CoA reductase inhibitors	≤ 10	≤ 10	≤ 10	≤ 10	15 (20.8)
Fibrates	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10
Bile acid sequestrants	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nicotinic acid and derivatives	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other lipid modifying agents	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)
Rheumatoid arthritis-related					
Aspirin	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	≤ 10
Cox-2 Inhibitor	≤ 10	≤ 10	0 (0.0)	0 (0.0)	≤ 10
NSAIDs	12 (33.3)	≤ 10	≤ 10	11 (30.6)	23 (31.9)
Glucocorticosteroid	28 (77.8)	18 (72.0)	≤ 10	33 (91.7)	61 (84.7)
Vaccines	13 (36.1)	≤ 10	≤ 10	19 (52.8)	32 (44.4)
Antineoplastic agents	≤ 10	0 (0.0)	≤ 10	0 (0.0)	≤ 10

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 6.57. Pattern of RA medication use in patients with serious infection event [SNDS]

Characteristics[b]	Unmatched				Matched				
	Baricitinib n = 44	Bari. 4 mg n = 29	Bari. 2 mg n = 15	TNFi n = 68	Baricitinib n = 36	Bari. 4 mg n = 25	Bari. 2 mg n = 11	TNFi n = 36	Total n = 72
Baseline Medication, n (%)									
cDMARDs, during baseline period									
n, total (%)	29 (65.9)	21 (72.4)	≤ 10	53 (77.9)	25 (69.4)	19 (76.0)	≤ 10	29 (80.6)	54 (75.0)
Mean (SD)	0.8 (0.7)	0.9 (0.7)	0.5 (0.5)	0.8 (0.5)	0.8 (0.7)	0.9 (0.7)	0.5 (0.5)	0.9 (0.6)	0.9 (0.6)
Median	1.0	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;1.0]	[0.0;3.0]	[0.0;3.0]	[0.0;3.0]	[0.0;1.0]	[0.0;3.0]	[0.0;3.0]
>1 cDMARD concomitantly	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10
Hydroxychloroquine	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10
Chloroquine									
Azathioprin									
Leflunomide	≤ 10	≤ 10	0 (0.0)	13 (19.1)	≤ 10	≤ 10	0 (0.0)	≤ 10	14 (19.4)
Methotrexate	19 (43.2)	12 (41.4)	≤ 10	39 (57.4)	17 (47.2)	12 (48.0)	≤ 10	21 (58.3)	38 (52.8)
Mycophenolate mofetil									
Sulfasalazin	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
Cyclosporin									
Penicillamin									
bDMARDs, during baseline period									
n, total (%)	27 (61.4)	18 (62.1)	≤ 10	24 (35.3)	19 (52.8)	14 (56.0)	≤ 10	19 (52.8)	38 (52.8)

Characteristics[b]	Unmatched				Matched				
	Baricitinib n = 44	Bari. 4 mg n = 29	Bari. 2 mg n = 15	TNFi n = 68	Baricitinib n = 36	Bari. 4 mg n = 25	Bari. 2 mg n = 11	TNFi n = 36	Total n = 72
Mean (SD)	0.7 (0.6)	0.7 (0.6)	0.7 (0.6)	0.4 (0.6)	0.6 (0.6)	0.6 (0.6)	0.5 (0.5)	0.6 (0.6)	0.6 (0.6)
Median	1.0	1.0	1.0	0.0	1.0	1.0	0.0	1.0	1.0
Min; Max	[0.0;2.0]	[0.0;2.0]	[0.0;2.0]	[0.0;2.0]	[0.0;2.0]	[0.0;2.0]	[0.0;1.0]	[0.0;2.0]	[0.0;2.0]
cDMARDs, concomitant	18 (40.9)	13 (44.8)	≤ 10	15 (22.1)	14 (38.9)	11 (44.0)	≤ 10	13 (36.1)	27 (37.5)
Adalimumab[c]	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10
Certolizumab pegol[c]	≤ 10	≤ 10	0 (0.0)	0 (0.0)	≤ 10	≤ 10	0 (0.0)	0 (0.0)	≤ 10
Etanercept[c]	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10
Golimumab[c]	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	≤ 10
Infliximab[c]	≤ 10	≤ 10	0 (0.0)	0 (0.0)	≤ 10	≤ 10	0 (0.0)	0 (0.0)	≤ 10
Rituximab	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10
Sarilumab	≤ 10	≤ 10	0 (0.0)	0 (0.0)	≤ 10	≤ 10	0 (0.0)	0 (0.0)	≤ 10
Abatacept	11 (25.0)	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	14 (19.4)
Tocilizumab	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
Anakinra	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	≤ 10	≤ 10
TNFi naïve at baseline	36 (81.8)	22 (75.9)	14 (93.3)	57 (83.8)	30 (83.3)	19 (76.0)	11 (100.0)	27 (75.0)	57 (79.2)
Post-index Medication, n (%)									
Methotrexate, concomitant	16 (36.4)	11 (37.9)	≤ 10	32 (47.1)	14 (38.9)	11 (44.0)	≤ 10	17 (47.2)	31 (43.1)
Other Concomitant cDMARD	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10	0 (0.0)	≤ 10	12 (16.7)
Dose change, baricitinib	≤ 10	≤ 10	0 (0.0)	0 (0.0)	≤ 10	≤ 10	0 (0.0)	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] 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 6.58. Time to first serious infection event (Days) [SNDS]

	Unmatched				Matched				
	Baricitinib n = 44	**Bari. 4 mg n = 29**	**Bari. 2 mg n = 15**	**TNFi n = 68**	**Baricitinib n = 36**	**Bari. 4 mg n = 25**	**Bari. 2 mg n = 11**	**TNFi[a] n = 36**	**Total n = 72**
Time to first serious infection event (in days)									
N (missing)	44 (0)	29 (0)	15 (0)	68 (0)	36 (0)	25 (0)	11 (0)	36 (0)	72 (0)
Mean (SD)	211.5 (191.3)	250.8 (202.4)	135.5 (144.9)	161.4 (162.9)	206.4 (188.4)	241.5 (193.1)	126.6 (157.0)	155.2 (169.8)	180.8 (179.9)
Median	134.5	175.0	102.0	119.5	127.0	175.0	83.0	100.0	114.5
Min; Max	[6.0;629.0]	[10.0;629.0]	[6.0;577.0]	[1.0;743.0]	[6.0;629.0]	[10.0;629.0]	[6.0;577.0]	[1.0;743.0]	[1.0;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 6.59. Crude rates of first serious infection event [SNDS]

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

	Unmatched				Matched				
	Bari. Any[b]	**Bari. 4 mg**	**Bari. 2 mg**	**TNFi**	**Bari. Any[b]**	**Bari. 4 mg**	**Bari. 2 mg**	**TNFi[a]**	**Total**
SI	**n = 3366**	**n = 2696**	**n = 666**	**n = 10451**	**n = 2979**	**n = 2385**	**n = 591**	**n = 2979**	**n = 5958**
95% CI	[1.6 ; 3.5]	[1.2 ; 3.1]	[2.0 ; 7.5]	[0.9 ; 1.9]	[1.4 ; 3.4]	[1.0 ; 3.1]	[1.6 ; 7.4]	[1.3 ; 3.3]	[1.6 ; 2.9]
IRD[d] /100 PY	1.1			.	0.2				
IRD[d] 95% CI	[0.2 ; 2.0]				[-1.2 ; 1.5]				

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

[a] Matching ratio 1:1 is applied

[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

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

Table 6.60. 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 = 3366	TNFi n = 10451	Baricitinib n = 2979	TNFi[a] n = 2979	Total n = 5958
0	3322 (98.7)	10383 (99.3)	2943 (98.8)	2943 (98.8)	5886 (98.8)
1	39 (1.2)	63 (0.6)	31 (1.0)	32 (1.1)	63 (1.1)
2	≤ 10	≤ 10	≤ 10	≤ 10	≤ 10
3	≤ 10	0 (0.0)	≤ 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 6.61. Comparative risk of first serious infection event, matched cohort [SNDS]

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

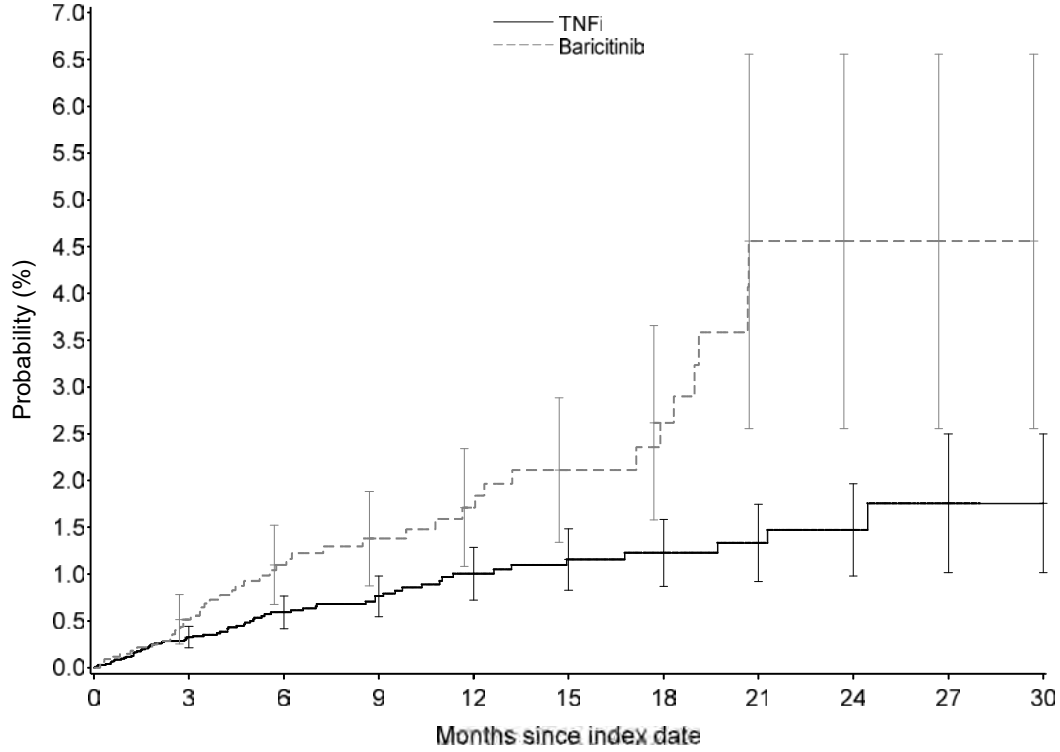

Figure 6.8. Kaplan-Meier survival curve for serious infection, pre-matched cohort

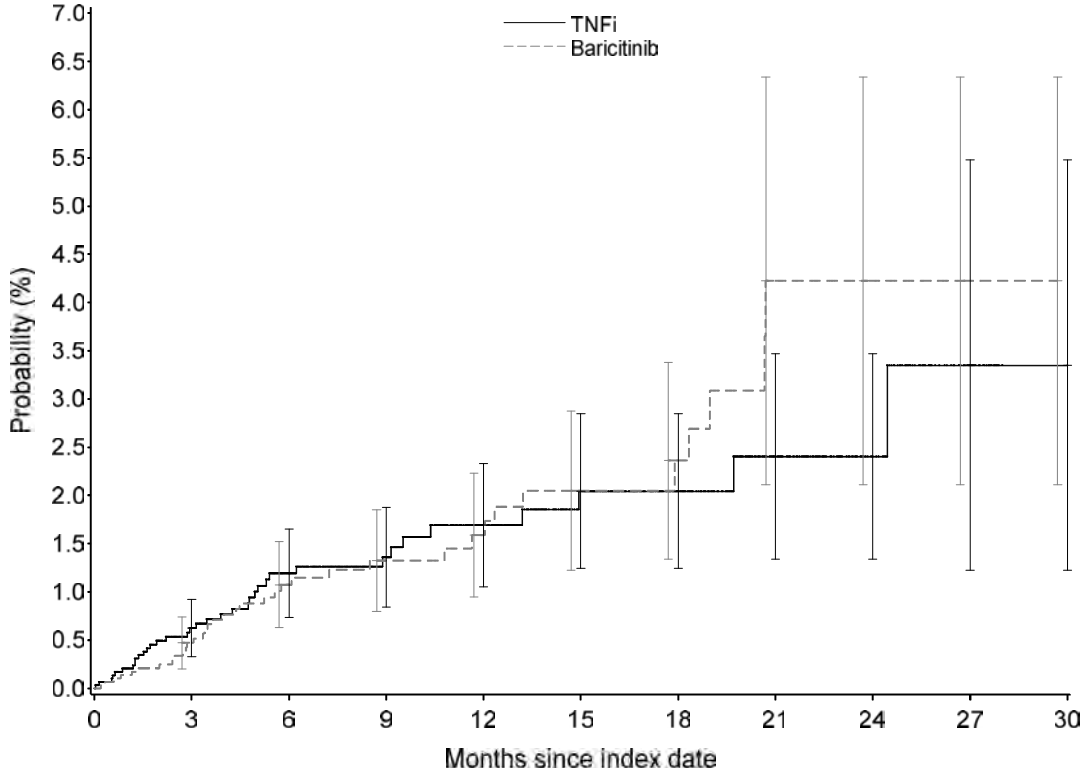

Figure 6.9. Kaplan-Meier survival curve for serious infection, matched cohort [SNDS]

Figure 6.10. Adjusted survival curve for serious infection [SNDS]
Not applicable for SNDS data.

2.4 TUBERCULOSIS (TB)

Table 6.62. Pattern of RA medication use in patients with hospitalized TB [SNDS]

	Unmatched				Matched				
Characteristics[b]	**Baricitinib n = 0**	**Bari. 4 mg n = 0**	**Bari. 2 mg n = 0**	**TNFi n ≤ 10**	**Baricitinib n = 0**	**Bari. 4 mg n = 0**	**Bari. 2 mg n = 0**	**TNFi n ≤ 10**	**Total n = 0**
Baseline Medication, n (%)	-	-	-	-	-	-	-	-	-
cDMARDs									
n, total (%)									
>1 concomitant cDMARD									
bDMARDs									
n, total (%)									
Concomitant cDMARD									

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] 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.

Table 6.63. Time to first hospitalized TB (Days) [SNDS]

	Unmatched				Matched				
	Baricitinib n = 0	Bari. 4 mg n = 0	Bari. 2 mg n = 0	TNFi n ≤ 10	Baricitinib n = 0	Bari. 4 mg n = 0	Bari. 2 mg n = 0	TNFi n ≤ 10	Total n = 0
Time to first TB (in days)	-	-	-	-	-	-	-	-	-
N (missing)									
Mean (SD)									
Median									
Min; Max									

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

[a] Matching ratio 1:1 is applied

Table 6.64. Crude rates of first hospitalized TB [SNDS]

	Unmatched				Matched				
	Bari. Any[b]	Bari. 4 mg	Bari. 2 mg	TNFi	Bari. Any[b]	Bari. 4 mg	Bari. 2 mg	TNFi[a]	Total
Tuberculosis	**n = 3398**	**n = 2708**	**n = 686**	**n = 10512**	**n = 3005**	**n = 2396**	**n = 606**	**n = 3005**	**n = 6010**
Overall									
Person-Years	2223	1804	416	6926	1955	1584	368	2027	3982
TB	0	0	0	3	0	0	0	1	1
TB/100 PY	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
95% CI	[0.0 ; 0.2]	[0.0 ; 0.2]	[0.0 ; 0.9]	[0.0 ; 0.1]	[0.0 ; 0.2]	[0.0 ; 0.2]	[0.0 ; 1]	[0.0 ; 0.3]	[0.0 ; 0.1]
IRD[c] /100 PY	0.0			.	0.0				
IRD[c] 95% CI	[-0.1 ; 0.0]				[-0.1 ; 0.0]				
Concomitant MTX Use, n (%)	1408 (41.4)	1182 (43.6)	224 (32.7)	5532 (52.6)	1283 (42.7)	1077 (44.9)	204 (33.7)	1439 (47.9)	2722 (45.3)
Person-Years	1046	886	159	4223	944	799	143	1129	2073
TB	0	0	0	2	0	0	0	1	1
SI/100 PY	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
95% CI	[0.0 ; 0.4]	[0.0 ; 0.4]	[0.0 ; 2.3]	[0.0 ; 0.2]	[0.0 ; 0.4]	[0.0 ; 0.5]	[0.0 ; 2.6]	[0.0 ; 0.5]	[0.0 ; 0.3]
IRD[c] /100 PY	0.0			.	-0.1				
IRD[c] 95% CI	[-0.2 ; 0.1]				[-0.3 ; 0.1]				
No concomitant MTX Use, n (%)	1990 (58.6)	1526 (56.4)	462 (67.3)	4980 (47.4)	1722 (57.3)	1319 (55.1)	402 (66.3)	1566 (52.1)	3288 (54.7)
Person-Years	1177	918	257	2703	1010	784	225	898	1909
TB	0	0	0	1	0	0	0	0	0
TB/100 PY	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

	Unmatched				Matched				
	Bari. Any[b]	**Bari. 4 mg**	**Bari. 2 mg**	**TNFi**	**Bari. Any[b]**	**Bari. 4 mg**	**Bari. 2 mg**	**TNFi[a]**	**Total**
Tuberculosis	**n = 3398**	**n = 2708**	**n = 686**	**n = 10512**	**n = 3005**	**n = 2396**	**n = 606**	**n = 3005**	**n = 6010**
95% CI	[0.0 ; 0.3]	[0.0 ; 0.4]	[0.0 ; 1.4]	[0.0 ; 0.2]	[0.0 ; 0.4]	[0.0 ; 0.5]	[0.0 ; 1.6]	[0.0 ; 0.4]	[0.0 ; 0.2]
IRD[c] /100 PY	0.0			.	-				
IRD[c] 95% CI	[-0.1 ; 0.1]				-				

Abbreviations: CI = confidence interval; N = number of patients in the specified category; PY = person-years; IRD = incidence risk difference; TB = tuberculosis; TNFi = tumor necrosis factor inhibitor.

[a] Matching ratio 1:1 is applied

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

Table 6.65. Hospitalized TB per patient during all available follow-up [SNDS]

Number of Events per person during the follow-up, n (%)	Unmatched		Matched		
	Baricitinib[b] n = 3398	TNFi n = 10512	Baricitinib n = 3005	TNFi[a] n = 3005	Total n = 6010
0	3398 (100.0)	10509 (100.0)	3005 (100.0)	3004 (100.0)	6009 (100.0)
1	0 (0.0)	≤ 10	0 (0.0)	≤ 10	≤ 10

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

[a] Matching ratio 1:1 is applied

Figure 6.11. Kaplan-Meier survival curve for hospitalized TB, pre-matched cohort [SNDS]

Not applicable for SNDS data.

Figure 6.12. Kaplan-Meier survival curve for hospitalized TB, matched cohort [SNDS]

Not applicable for SNDS data.

Figure 6.13. Adjusted survival curve for hospitalized TB [SNDS]

Not applicable for SNDS data.

3 SENSITIVITY ANALYSES - INCLUDING PATIENTS WITH PRIOR EVENT OF INTEREST

Table 6.67. Incidence rate of VTE *prior to* cohort entry, by PS-matched treatment cohort [SNDS]

Not applicable for SNDS data. The sensitivity analyses « Including patients with prior event of interest » have not been conducted due to the small number of total patients added (< 10%), cf figure 6.1 in section 1.1.

4 SENSITIVITY ANALYSES - VTE: DESCRIPTIVE ANALYSIS BY DOSE

Table 6.68. Incidence rate of VTE, by dose, Unmatched cohort [SNDS]

	Bari. 2 mg n = 622	Bari. 4 mg n = 2616	TNFi n = 10202
Person-Years	377	1734	6706
VTE	7	16	29
VTE/100 PY	1.9	0.9	0.4
95% CI	[0.7 ; 3.8]	[0.5 ; 1.5]	[0.3 ; 0.6]

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

Table 6.69. bDMARD Experienced and Naïve Patients: Incidence rate of VTE by dose, Matched cohort [SNDS]

	Bari. 2 mg[a] n = 553	Bari. 4 mg[a] n = 2305	TNFi n = 2860
bDMARD-experienced patients			
Person-Years	160	914	1095
VTE	2	9	8
VTE/100 PY	1.3	1	0.7
95% CI	[0.2 ; 4.5]	[0.5 ; 1.9]	[0.3 ; 1.4]
bDMARD-naïve patients			
Person-Years	172	597	781
VTE	4	5	2
VTE/100 PY	2.3	0.8	0.3
95% CI	[0.6 ; 6]	[0.3 ; 2]	[0 ; 0.9]

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

[a] 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

5 SENSITIVITY ANALYSES (FDA REQUEST) - ANALYSIS BY BDMARD STATUS

Note1: Baricitinib subjects have been matched to TNFi subjects on the propensity score ± 0.01 and the bDMARD naïve status at index date. Naïve status will be assessed during the 6-month before index date.

Note2: 4 subjects who 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.

5.1 BASELINE CHARACTERISTICS

Table 6.70. bDMARD-Experienced and bDMARD naïve: Baseline demographics - Unmatched cohort [SNDS]

	bDMARD-Experienced					bDMARD naïve				
Characteristics	**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)**
Age at index date [in years]					0.223					0.344
N (missing)	1982 (0)	1661 (0)	317 (0)	2374 (0)		1260 (0)	955 (0)	305 (0)	7828 (0)	
Mean (SD)	58.4 (13.1)	56.4 (12.1)	69.3 (13.0)	55.4 (14.0)		59.5 (13.2)	56.4 (11.9)	69.1 (12.5)	54.8 (14.2)	
Median	59.0	58.0	72.0	56.0		60.0	57.0	71.0	56.0	
Min; Max	[18.0;92.0]	[18.0;90.0]	[21.0;92.0]	[18.0;91.0]		[19.0;89.0]	[19.0;85.0]	[20.0;89.0]	[18.0;94.0]	
Age (in years), in categories, n (%)										
[18-30[	46 (2.3)	42 (2.5)	≤ 10	100 (4.2)		24 (1.9)	21 (2.2)	≤ 10	335 (4.3)	
[30-40[	131 (6.6)	126 (7.6)	≤ 10	243 (10.2)		77 (6.1)	69 (7.2)	≤ 10	988 (12.6)	
[40-50[	298 (15.0)	275 (16.6)	23 (7.3)	414 (17.4)		164 (13.0)	149 (15.6)	15 (4.9)	1329 (17.0)	
[50-60[	548 (27.6)	515 (31.0)	31 (9.8)	661 (27.8)		351 (27.9)	320 (33.5)	31 (10.2)	2115 (27.0)	
[60-65[	289 (14.6)	261 (15.7)	27 (8.5)	290 (12.2)		172 (13.7)	142 (14.9)	30 (9.8)	961 (12.3)	
≥65	670 (33.8)	442 (26.6)	227 (71.6)	666 (28.1)		472 (37.5)	254 (26.6)	218 (71.5)	2100 (26.8)	
Sex, n (%)					-0.064					-0.177
Male	396 (20.0)	342 (20.6)	54 (17.0)	536 (22.6)		249 (19.8)	194 (20.3)	55 (18.0)	2132 (27.2)	
Female	1586 (80.0)	1319 (79.4)	263 (83.0)	1838 (77.4)		1011 (80.2)	761 (79.7)	250 (82.0)	5696 (72.8)	

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 6.71. bDMARD-Experienced and bDMARD naïve: Baseline demographics - Unmatched cohort [SNDS]

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

Table 6.72. bDMARD-Experienced and bDMARD naïve: Baseline demographics - VTE cohort, Matched [SNDS]

	bDMARD-Experienced					bDMARD naïve				
Characteristics	**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)**
Age at index date [in years]					-0.002					0.021
N (missing)	1600 (0)	1350 (0)	248 (0)	1600 (0)		1260 (0)	955 (0)	305 (0)	1260 (0)	
Mean (SD)	57.6 (13.1)	55.6 (12.1)	68.1 (13.4)	57.6 (13.4)		59.5 (13.2)	56.4 (11.9)	69.1 (12.5)	59.2 (13.1)	
Median	58.0	57.0	71.0	58.0		60.0	57.0	71.0	60.0	
Min; Max	[18.0;92.0]	[18.0;90.0]	[21.0;92.0]	[18.0;91.0]		[19.0;89.0]	[19.0;85.0]	[20.0;89.0]	[18.0;92.0]	
Age (in years), in categories, n (%)										
[18-30[	41 (2.6)	37 (2.7)	≤ 10	41 (2.6)		24 (1.9)	21 (2.2)	≤ 10	20 (1.6)	
[30-40[	117 (7.3)	113 (8.4)	≤ 10	111 (6.9)		77 (6.1)	69 (7.2)	≤ 10	84 (6.7)	
[40-50[	263 (16.4)	241 (17.9)	22 (8.9)	254 (15.9)		164 (13.0)	149 (15.6)	15 (4.9)	149 (11.8)	
[50-60[	458 (28.6)	430 (31.9)	28 (11.3)	465 (29.1)		351 (27.9)	320 (33.5)	31 (10.2)	370 (29.4)	
[60-65[	219 (13.7)	197 (14.6)	21 (8.5)	213 (13.3)		172 (13.7)	142 (14.9)	30 (9.8)	173 (13.7)	
≥65	502 (31.4)	332 (24.6)	169 (68.1)	516 (32.3)		472 (37.5)	254 (26.6)	218 (71.5)	464 (36.8)	
Sex, n (%)					0.070					-0.057
Male	346 (21.6)	296 (21.9)	50 (20.2)	301 (18.8)		249 (19.8)	194 (20.3)	55 (18.0)	278 (22.1)	
Female	1254 (78.4)	1054 (78.1)	198 (79.8)	1299 (81.2)		1011 (80.2)	761 (79.7)	250 (82.0)	982 (77.9)	

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

[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 6.73. bDMARD-Experienced and bDMARD naïve: Baseline demographics - VTE cohort, Matched [SNDS]

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

Table 6.74. bDMARD-Experienced and bDMARD naïve: Baseline demographics - MACE cohort, Matched [SNDS]

Characteristics[b]	bDMARD-Experienced					bDMARD naïve				
	Bari. Any[f] 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)
Age at index date [in years]					0.013					0.020
N (missing)	1606 (0)	1360 (0)	244 (0)	1606 (0)		1257 (0)	954 (0)	303 (0)	1257 (0)	
Mean (SD)	57.8 (13.2)	55.9 (12.2)	68.6 (13.1)	57.6 (13.4)		59.5 (13.2)	56.4 (11.9)	69.1 (12.5)	59.2 (13.2)	
Median	58.0	57.0	71.5	58.0		60.0	57.0	71.0	60.0	
Min; Max	[18.0;90.0]	[18.0;90.0]	[21.0;88.0]	[18.0;91.0]		[19.0;89.0]	[19.0;85.0]	[20.0;89.0]	[19.0;93.0]	
Age (in years), in categories, n (%)										
[18-30[	42 (2.6)	38 (2.8)	≤ 10	47 (2.9)		24 (1.9)	21 (2.2)	≤ 10	21 (1.7)	
[30-40[	119 (7.4)	115 (8.5)	≤ 10	114 (7.1)		77 (6.1)	69 (7.2)	≤ 10	91 (7.2)	
[40-50[	249 (15.5)	233 (17.1)	16 (6.6)	236 (14.7)		164 (13.0)	149 (15.6)	15 (5.0)	153 (12.2)	
[50-60[	451 (28.1)	420 (30.9)	30 (12.3)	462 (28.8)		351 (27.9)	320 (33.5)	31 (10.2)	347 (27.6)	
[60-65[	229 (14.3)	209 (15.4)	20 (8.2)	221 (13.8)		170 (13.5)	141 (14.8)	29 (9.6)	165 (13.1)	
≥65	516 (32.1)	345 (25.4)	170 (69.7)	526 (32.8)		471 (37.5)	254 (26.6)	217 (71.6)	480 (38.2)	
Sex, n (%)					0.071					0.004
Male	338 (21.0)	294 (21.6)	44 (18.0)	293 (18.2)		249 (19.8)	193 (20.2)	56 (18.5)	247 (19.6)	
Female	1268 (79.0)	1066 (78.4)	200 (82.0)	1313 (81.8)		1008 (80.2)	761 (79.8)	247 (81.5)	1010 (80.4)	

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

[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 6.75. bDMARD-Experienced and bDMARD naïve: Baseline demographics - MACE cohort, Matched [SNDS]

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

Table 6.76. bDMARD-Experienced and bDMARD naïve: Baseline demographics - Incident serious infection cohort, Matched [SNDS]

Characteristics	bDMARD-Experienced					bDMARD naïve				
	Bari. Any[b] 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)
Age at index date [in years]					-0.009					0.024
N (missing)	1643 (0)	1376 (0)	264 (0)	1643 (0)		1319 (0)	985 (0)	334 (0)	1319 (0)	
Mean (SD)	57.9 (13.3)	55.8 (12.3)	68.6 (13.2)	58.0 (13.5)		60.1 (13.4)	56.7 (12.0)	70.1 (12.5)	59.8 (13.2)	
Median	58.0	57.0	71.0	59.0		60.0	58.0	73.0	61.0	
Min; Max	[18.0;98.0]	[18.0;87.0]	[21.0;98.0]	[18.0;91.0]		[19.0;91.0]	[19.0;85.0]	[20.0;91.0]	[18.0;94.0]	
Age (in years), in categories, n (%)										
[18-30[	41 (2.5)	37 (2.7)	≤ 10	43 (2.6)		24 (1.8)	21 (2.1)	≤ 10	26 (2.0)	
[30-40[	119 (7.2)	115 (8.4)	≤ 10	116 (7.1)		77 (5.8)	69 (7.0)	≤ 10	75 (5.7)	
[40-50[	264 (16.1)	244 (17.7)	20 (7.6)	251 (15.3)		167 (12.7)	152 (15.4)	15 (4.5)	169 (12.8)	
[50-60[	461 (28.1)	428 (31.1)	31 (11.7)	455 (27.7)		354 (26.8)	324 (32.9)	30 (9.0)	333 (25.2)	
[60-65[	225 (13.7)	204 (14.8)	21 (8.0)	233 (14.2)		176 (13.3)	145 (14.7)	31 (9.3)	200 (15.2)	
≥65	533 (32.4)	348 (25.3)	184 (69.7)	545 (33.2)		521 (39.5)	274 (27.8)	247 (74.0)	516 (39.1)	
Sex, n (%)					0.060					0.015
Male	340 (20.7)	294 (21.4)	46 (17.4)	301 (18.3)		265 (20.1)	202 (20.5)	63 (18.9)	257 (19.5)	
Female	1303 (79.3)	1082 (78.6)	218 (82.6)	1342 (81.7)		1054 (79.9)	783 (79.5)	271 (81.1)	1062 (80.5)	

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

[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 6.77. bDMARD-Experienced and bDMARD naïve: Baseline demographics - Incident serious infection cohort, Matched [SNDS]

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

Table 6.78. bDMARD-Experienced: Baseline demographics - Hospitalized tuberculosis, Matched [SNDS]

Not applicable for SNDS data: no event

Table 6.79. bDMARD naïve: Baseline demographics - Hospitalized tuberculosis, Matched [SNDS]

Not applicable for SNDS data: no event

Table 6.80. bDMARD-Experienced and bDMARD naïve: Clinical history at baseline - Unmatched cohort [SNDS]

	bDMARD-Experienced					bDMARD naïve				
Characteristics[a]	**Bari. Any[d] 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)**
Clinical conditions during baseline period, n (%)										
Cancer, excluding NMSC	45 (2.3)	35 (2.1)	≤ 10	62 (2.6)	-0.022	50 (4.0)	34 (3.6)	16 (5.2)	239 (3.1)	0.050
NMSC	≤ 10	≤ 10	≤ 10	≤ 10	0.031	≤ 10	≤ 10	≤ 10	19 (0.2)	-0.019
Chronic lung disease, excluding cystic fibrosis[d]	267 (13.5)	204 (12.3)	62 (19.6)	251 (10.6)	0.089	173 (13.7)	116 (12.1)	57 (18.7)	798 (10.2)	0.109
Cardiovascular conditions										
Atrial arrhythmia/fibrillation	20 (1.0)	14 (0.8)	≤ 10	11 (0.5)	0.064	14 (1.1)	≤ 10	≤ 10	42 (0.5)	0.064
Cardiovascular revascularization procedure	≤ 10	≤ 10	≤ 10	≤ 10	-0.006	≤ 10	≤ 10	≤ 10	18 (0.2)	0.002
Congestive heart failure, hospitalized	≤ 10	≤ 10	≤ 10	≤ 10	0.019	≤ 10	≤ 10	≤ 10	21 (0.3)	0.022
Coronary artery disease	73 (3.7)	48 (2.9)	25 (7.9)	92 (3.9)	-0.01	65 (5.2)	42 (4.4)	23 (7.5)	259 (3.3)	0.092
Unstable angina	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.041	≤ 10	0 (0.0)	≤ 10	14 (0.2)	-0.028
Ventricular arrhythmia	≤ 10	≤ 10	≤ 10	16 (0.7)	-0.037	11 (0.9)	≤ 10	≤ 10	52 (0.7)	0.024
Stroke	18 (0.9)	11 (0.7)	≤ 10	16 (0.7)	0.026	11 (0.9)	≤ 10	≤ 10	45 (0.6)	0.035

	bDMARD-Experienced					bDMARD naïve				
Characteristics[a]	**Bari. Any[d] 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)**
Hemorrhagic	≤ 10	≤ 10	0 (0.0)	≤ 10	0.022	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.036
Ischemic	≤ 10	≤ 10	≤ 10	≤ 10	0.038	≤ 10	≤ 10	0 (0.0)	13 (0.2)	0.016
Unknown	14 (0.7)	≤ 10	≤ 10	12 (0.5)	0.026	≤ 10	≤ 10	≤ 10	33 (0.4)	0.039
TIA	≤ 10	0 (0.0)	≤ 10	≤ 10	0.004	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.032
Diabetes Mellitus[c]	211 (10.6)	163 (9.8)	47 (14.8)	239 (10.1)	0.019	110 (8.7)	71 (7.4)	39 (12.8)	645 (8.2)	0.018
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	71 (3.6)	56 (3.4)	15 (4.7)	75 (3.2)	0.023	52 (4.1)	32 (3.4)	20 (6.6)	207 (2.6)	0.082
AIDS/HIV	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.041	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.048
Antiphospholipid syndrome	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	
SLE	17 (0.9)	15 (0.9)	≤ 10	≤ 10	0.082	14 (1.1)	11 (1.2)	≤ 10	46 (0.6)	0.057

	bDMARD-Experienced					bDMARD naïve				
Characteristics[a]	**Bari. Any[d] 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)**
Primary Sjogren Syndrome	56 (2.8)	42 (2.5)	14 (4.4)	68 (2.9)	-0.002	43 (3.4)	25 (2.6)	18 (5.9)	159 (2.0)	0.085
Liver or pancreatic disorder[c]	70 (3.5)	54 (3.3)	15 (4.7)	76 (3.2)	0.018	29 (2.3)	21 (2.2)	≤ 10	177 (2.3)	0.003
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 (0.0)	19 (0.8)	-0.094	≤ 10	≤ 10	0 (0.0)	125 (1.6)	-0.121
RA Severity (CIRAS Index)					-0.096					-0.249
Mean (SD)	6.4 (1.3)	6.5 (1.3)	5.8 (1.4)	6.5 (1.4)		6.5 (1.5)	6.7 (1.4)	5.7 (1.4)	6.9 (1.6)	
Smoking (not available in SNDS)	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	
DMARDs, n (%)										
cDMARDs, during baseline period										
n, total (%)	1245 (62.8)	1055 (63.5)	187 (59.0)	1449 (61.0)	0.037	918 (72.9)	727 (76.1)	191 (62.6)	5856 (74.8)	-0.044
Mean (SD)	0.7 (0.6)	0.7 (0.6)	0.6 (0.6)	0.6 (0.5)	0.044	0.9 (0.7)	0.9 (0.6)	0.7 (0.7)	0.8 (0.6)	0.03
Median	1.0	1.0	1.0	1.0		1.0	1.0	1.0	1.0	
Min; Max	[0.0;4.0]	[0.0;4.0]	[0.0;3.0]	[0.0;3.0]		[0.0;4.0]	[0.0;4.0]	[0.0;3.0]	[0.0;4.0]	

	bDMARD-Experienced					bDMARD naïve				
Characteristics[a]	**Bari. Any[d] 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)**
>1 cDMARD concomitantly	59 (3.0)	51 (3.1)	≤ 10	63 (2.7)	0.020	116 (9.2)	90 (9.4)	26 (8.5)	517 (6.6)	0.097
Hydroxychloroquine	67 (3.4)	57 (3.4)	≤ 10	72 (3.0)	0.020	111 (8.8)	82 (8.6)	29 (9.5)	417 (5.3)	0.136
Chloroquine	≤ 10	0 (0.0)	≤ 10	≤ 10	0.004	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.023
Azathioprine	≤ 10	≤ 10	≤ 10	≤ 10	0.005	≤ 10	≤ 10	0 (0.0)	23 (0.3)	0.004
Leflunomide	215 (10.8)	185 (11.1)	30 (9.5)	196 (8.3)	0.088	195 (15.5)	160 (16.8)	35 (11.5)	814 (10.4)	0.152
Methotrexate	986 (49.7)	842 (50.7)	142 (44.8)	1181 (49.7)	0.000	693 (55.0)	548 (57.4)	145 (47.5)	4913 (62.8)	-0.158
Mycophenolate mofetil	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.041	≤ 10	≤ 10	0 (0.0)	≤ 10	0.031
Sulfasalazine	38 (1.9)	30 (1.8)	≤ 10	55 (2.3)	-0.028	71 (5.6)	53 (5.5)	18 (5.9)	376 (4.8)	0.037
Cyclosporin	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.029	≤ 10	≤ 10	≤ 10	≤ 10	0.05
Penicillamine	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.029	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.016
bDMARDs, during baseline period										
n, total (%)	1982 (100.0)	1661 (100.0)	317 (100.0)	2374 (100.0)	0.000	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Mean (SD)	1.1 (0.3)	1.1 (0.4)	1.1 (0.3)	1.1 (0.2)	0.238	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	-
Median	1.0	1.0	1.0	1.0		0.0	0.0	0.0	0.0	
Min; Max	[1.0;3.0]	[1.0;3.0]	[1.0;3.0]	[1.0;3.0]		[0.0;0.0]	[0.0;0.0]	[0.0;0.0]	[0.0;0.0]	
cDMARDs, concomitant	1076 (54.3)	920 (55.4)	153 (48.3)	1304 (54.9)	-0.013	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Adalimumab[b]	253 (12.8)	221 (13.3)	32 (10.1)	408 (17.2)	-0.124	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Certolizumab pegol[b]	157 (7.9)	139 (8.4)	18 (5.7)	150 (6.3)	0.062	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000

	bDMARD-Experienced					bDMARD naïve				
Characteristics[a]	**Bari. Any[d] 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)**
Etanercept[b]	359 (18.1)	305 (18.4)	53 (16.7)	664 (28.0)	-0.236	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Golimumab[b]	132 (6.7)	123 (7.4)	≤ 10	146 (6.1)	0.021	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Infliximab[b]	92 (4.6)	82 (4.9)	≤ 10	185 (7.8)	-0.131	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Rituximab	122 (6.2)	96 (5.8)	26 (8.2)	38 (1.6)	0.238	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Sarilumab	47 (2.4)	37 (2.2)	≤ 10	27 (1.1)	0.094	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Abatacept	556 (28.1)	445 (26.8)	108 (34.1)	490 (20.6)	0.173	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Tocilizumab	506 (25.5)	432 (26.0)	74 (23.3)	389 (16.4)	0.226	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Anakinra	16 (0.8)	11 (0.7)	≤ 10	17 (0.7)	0.011	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
TNFi naïve at baseline	1982 (100.0)	1661 (100.0)	317 (100.0)	2374 (100.0)	0.36	1260 (100.0)	955 (100.0)	305 (100.0)	7828 (100.0)	0.000
≥ 1 dispensing of bDMARD within 730 days before index date (excluded), n (%)	1982 (100.0)	1661 (100.0)	317 (100.0)	2374 (100.0)		453 (36.0)	337 (35.3)	116 (38.0)	2006 (25.6)	0.225
Other prescription medications during baseline period, n (%)										
Antibiotics	867 (43.7)	721 (43.4)	144 (45.4)	1020 (43.0)	0.016	502 (39.8)	352 (36.9)	150 (49.2)	2860 (36.5)	0.068
Antidiabetic agents	206 (10.4)	161 (9.7)	44 (13.9)	226 (9.5)	0.029	104 (8.3)	68 (7.1)	36 (11.8)	602 (7.7)	0.021
Insulins	80 (4.0)	61 (3.7)	19 (6.0)	83 (3.5)	0.028	38 (3.0)	26 (2.7)	12 (3.9)	216 (2.8)	0.015
Non-insulins	164 (8.3)	131 (7.9)	32 (10.1)	182 (7.7)	0.023	88 (7.0)	58 (6.1)	30 (9.8)	506 (6.5)	0.021
Cardiovascular										

	bDMARD-Experienced					bDMARD naïve				
Characteristics[a]	**Bari. Any[d] 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)**
Antithrombotic agents	295 (14.9)	209 (12.6)	85 (26.8)	332 (14.0)	0.026	211 (16.7)	131 (13.7)	80 (26.2)	1067 (13.6)	0.087
Anticoagulant	69 (3.5)	46 (2.8)	23 (7.3)	85 (3.6)	-0.005	73 (5.8)	38 (4.0)	35 (11.5)	380 (4.9)	0.042
Antiplatelet	239 (12.1)	170 (10.2)	68 (21.5)	262 (11.0)	0.032	157 (12.5)	102 (10.7)	55 (18.0)	740 (9.5)	0.096
Antihypertensives	693 (35.0)	512 (30.8)	179 (56.5)	779 (32.8)	0.046	426 (33.8)	258 (27.0)	168 (55.1)	2154 (27.5)	0.137
Angiotensin converting enzyme inhibitors (ACE)	187 (9.4)	141 (8.5)	46 (14.5)	216 (9.1)	0.012	100 (7.9)	59 (6.2)	41 (13.4)	627 (8.0)	-0.003
Angiotensin receptor blockers (ARB)	257 (13.0)	185 (11.1)	72 (22.7)	323 (13.6)	-0.019	168 (13.3)	105 (11.0)	63 (20.7)	863 (11.0)	0.071
Beta blocker	287 (14.5)	207 (12.5)	79 (24.9)	323 (13.6)	0.025	202 (16.0)	119 (12.5)	83 (27.2)	884 (11.3)	0.138
Calcium channel blocker	209 (10.5)	149 (9.0)	58 (18.3)	236 (9.9)	0.02	127 (10.1)	67 (7.0)	60 (19.7)	576 (7.4)	0.097
Nitrates	19 (1.0)	≤ 10	11 (3.5)	24 (1.0)	-0.005	12 (1.0)	≤ 10	≤ 10	62 (0.8)	0.017
Acyclovir	≤ 10	≤ 10	≤ 10	20 (0.8)	-0.064	≤ 10	≤ 10	≤ 10	39 (0.5)	0.018
ValAcyclovir	88 (4.4)	69 (4.2)	19 (6.0)	111 (4.7)	-0.011	35 (2.8)	24 (2.5)	11 (3.6)	207 (2.6)	0.008
Hormonal	272 (13.7)	246 (14.8)	26 (8.2)	360 (15.2)	-0.041	134 (10.6)	109 (11.4)	25 (8.2)	1138 (14.5)	-0.118
HRT	162 (8.2)	143 (8.6)	19 (6.0)	186 (7.8)	0.013	83 (6.6)	66 (6.9)	17 (5.6)	498 (6.4)	0.009
Oral Contraceptives	110 (5.5)	102 (6.1)	≤ 10	171 (7.2)	-0.068	47 (3.7)	41 (4.3)	≤ 10	602 (7.7)	-0.171
SERMs	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.016	≤ 10	≤ 10	≤ 10	26 (0.3)	-0.003

	bDMARD-Experienced					bDMARD naïve				
Characteristics[a]	**Bari. Any[d] 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)**
Topic with progestogens and/or estrogens	≤ 10	≤ 10	0 (0.0)	≤ 10	0.001	≤ 10	≤ 10	0 (0.0)	51 (0.7)	-0.078
Lipid-lowering agents	340 (17.2)	256 (15.4)	83 (26.2)	371 (15.6)	0.041	215 (17.1)	138 (14.5)	77 (25.2)	1012 (12.9)	0.116
HMG CoA reductase inhibitors	274 (13.8)	204 (12.3)	69 (21.8)	299 (12.6)	0.036	176 (14.0)	111 (11.6)	65 (21.3)	819 (10.5)	0.107
Fibrates	32 (1.6)	25 (1.5)	≤ 10	32 (1.3)	0.022	11 (0.9)	≤ 10	≤ 10	81 (1.0)	-0.017
Bile acid sequestrants	≤ 10	≤ 10	≤ 10	≤ 10	0.004	≤ 10	≤ 10	≤ 10	24 (0.3)	0.015
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	15 (0.8)	13 (0.8)	≤ 10	20 (0.8)	-0.01	11 (0.9)	≤ 10	≤ 10	69 (0.9)	-0.001
Lipid modifying agents, combinations	22 (1.1)	18 (1.1)	≤ 10	30 (1.3)	-0.014	24 (1.9)	19 (2.0)	≤ 10	70 (0.9)	0.086
Rheumatoid arthritis-related										
Aspirin	31 (1.6)	22 (1.3)	≤ 10	32 (1.3)	0.018	≤ 10	≤ 10	≤ 10	85 (1.1)	-0.03
Cox-2 Inhibitor	114 (5.8)	103 (6.2)	≤ 10	154 (6.5)	-0.031	64 (5.1)	53 (5.5)	11 (3.6)	487 (6.2)	-0.05
NSAIDs	699 (35.3)	617 (37.1)	81 (25.6)	956 (40.3)	-0.103	463 (36.7)	378 (39.6)	85 (27.9)	3230 (41.3)	-0.093
Glucocorticosteroid	1429 (72.1)	1190 (71.6)	236 (74.4)	1453 (61.2)	0.233	930 (73.8)	692 (72.5)	238 (78.0)	5256 (67.1)	0.147
Vaccines	532 (26.8)	413 (24.9)	119 (37.5)	598 (25.2)	0.038	426 (33.8)	314 (32.9)	112 (36.7)	3198 (40.9)	-0.146

	bDMARD-Experienced					bDMARD naïve				
Characteristics[a]	**Bari. Any[d] 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)**
Antineoplastic agents	≤ 10	≤ 10	≤ 10	11 (0.5)	-0.045	≤ 10	≤ 10	≤ 10	14 (0.2)	0.072

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; HIV = human immunodeficiency virus; HRT = hormone replacement therapy; MACE = major adverse cardiovascular event, defined based on primary hospital discharge diagnosis codes for acute myocardial infarction, ischemic or hemorrhagic stroke; Max = maximum; 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. = standardized difference; TB = tuberculosis; 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

[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

Table 6.81. bDMARD-Experienced and bDMARD naïve: Clinical history at baseline - Unmatched cohort [SNDS]

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

Table 6.82. bDMARD-Experienced and bDMARD naïve: Clinical history at baseline - VTE cohort, Matched [SNDS]

	bDMARD-Experienced					bDMARD naïve				
Characteristics[b]	**Bari. Any[e] 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)**
Clinical conditions during baseline period, n (%)										
Cancer, excluding NMSC	37 (2.3)	29 (2.1)	≤ 10	47 (2.9)	-0.039	50 (4.0)	34 (3.6)	16 (5.2)	45 (3.6)	0.021
NMSC	≤ 10	0 (0.0)	≤ 10	≤ 10	0.02	≤ 10	≤ 10	≤ 10	≤ 10	0.000
Chronic lung disease, excluding cystic fibrosis[d]	208 (13.0)	162 (12.0)	45 (18.1)	185 (11.6)	0.044	173 (13.7)	116 (12.1)	57 (18.7)	166 (13.2)	0.016
Cardiovascular conditions										
Atrial arrhythmia/fibrillation	14 (0.9)	≤ 10	≤ 10	≤ 10	0.029	14 (1.1)	≤ 10	≤ 10	≤ 10	0.033
Cardiovascular revascularization procedure	≤ 10	≤ 10	≤ 10	≤ 10	-0.012	≤ 10	≤ 10	≤ 10	≤ 10	-0.015
Congestive Heart Failure,hospitalized	≤ 10	≤ 10	≤ 10	≤ 10	0.019	≤ 10	≤ 10	≤ 10	≤ 10	-0.023
Coronary artery disease	62 (3.9)	41 (3.0)	21 (8.5)	62 (3.9)	0.000	65 (5.2)	42 (4.4)	23 (7.5)	52 (4.1)	0.049
Unstable angina	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.05	≤ 10	0 (0.0)	≤ 10	≤ 10	0.000
Ventricular arrhythmia	≤ 10	≤ 10	≤ 10	14 (0.9)	-0.064	11 (0.9)	≤ 10	≤ 10	12 (1.0)	-0.008
Stroke	15 (0.9)	≤ 10	≤ 10	13 (0.8)	0.013	11 (0.9)	≤ 10	≤ 10	≤ 10	0.009

	bDMARD-Experienced					bDMARD naïve				
Characteristics[b]	**Bari. Any[e] 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)**
Hemorrhagic	≤ 10	≤ 10	0 (0.0)	≤ 10	0.000	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.056
Ischemic	≤ 10	≤ 10	≤ 10	≤ 10	0.029	≤ 10	≤ 10	0 (0.0)	≤ 10	0.000
Unknown	13 (0.8)	≤ 10	≤ 10	≤ 10	0.022	≤ 10	≤ 10	≤ 10	≤ 10	0.043
TIA	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0.035	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.040
Diabetes Mellitus[d]	170 (10.6)	135 (10.0)	34 (13.7)	168 (10.5)	0.004	110 (8.7)	71 (7.4)	39 (12.8)	116 (9.2)	-0.017
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	49 (3.1)	39 (2.9)	≤ 10	57 (3.6)	-0.028	52 (4.1)	32 (3.4)	20 (6.6)	49 (3.9)	0.012
AIDS/HIV	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.040
Antiphospholipid syndrome	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	
SLE	11 (0.7)	11 (0.8)	0 (0.0)	≤ 10	0.053	14 (1.1)	11 (1.2)	≤ 10	≤ 10	0.051
Primary Sjogren Syndrome	39 (2.4)	29 (2.1)	≤ 10	53 (3.3)	-0.052	43 (3.4)	25 (2.6)	18 (5.9)	41 (3.3)	0.009

	bDMARD-Experienced					bDMARD naïve				
Characteristics[b]	**Bari. Any[e] 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)**
Liver or pancreatic disorder[d]	58 (3.6)	47 (3.5)	11 (4.4)	52 (3.3)	0.021	29 (2.3)	21 (2.2)	≤ 10	35 (2.8)	-0.030
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 (0.0)	≤ 10	-0.025	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.012
RA Severity (CIRAS Index)					0.041					-0.031
Mean (± SD)	6.5 (1.3)	6.6 (1.3)	5.9 (1.4)	6.4 (1.3)		6.5 (1.5)	6.7 (1.4)	5.7 (1.4)	6.5 (1.5)	
Smoking (not available in SNDS)	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	
DMARDs, n (%)										
cDMARDs, during baseline period										
n, total (%)	1020 (63.8)	872 (64.6)	147 (59.3)	963 (60.2)	0.073	918 (72.9)	727 (76.1)	191 (62.6)	933 (74.0)	-0.027
Mean (SD)	0.7 (0.6)	0.7 (0.5)	0.6 (0.6)	0.6 (0.5)	0.069	0.9 (0.7)	0.9 (0.6)	0.7 (0.7)	0.9 (0.6)	0.003
Median	1.0	1.0	1.0	1.0		1.0	1.0	1.0	1.0	
Min; Max	[0.0;4.0]	[0.0;4.0]	[0.0;3.0]	[0.0;3.0]		[0.0;4.0]	[0.0;4.0]	[0.0;3.0]	[0.0;4.0]	
>1 cDMARD concomitantly	44 (2.8)	40 (3.0)	≤ 10	43 (2.7)	0.004	116 (9.2)	90 (9.4)	26 (8.5)	89 (7.1)	0.078
Hydroxychloroquine	51 (3.2)	45 (3.3)	≤ 10	58 (3.6)	-0.024	111 (8.8)	82 (8.6)	29 (9.5)	106 (8.4)	0.014

	bDMARD-Experienced					bDMARD naïve				
Characteristics[b]	**Bari. Any[e] 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)**
Chloroquine	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.04
Azathioprin	≤ 10	≤ 10	≤ 10	≤ 10	-0.049	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.013
Leflunomid	173 (10.8)	145 (10.7)	28 (11.3)	146 (9.1)	0.056	195 (15.5)	160 (16.8)	35 (11.5)	152 (12.1)	0.099
Methotrexate	819 (51.2)	706 (52.3)	112 (45.2)	761 (47.6)	0.073	693 (55.0)	548 (57.4)	145 (47.5)	741 (58.8)	-0.077
Mycophenolate mofetil	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.05	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0.04
Sulfasalazin	29 (1.8)	22 (1.6)	≤ 10	37 (2.3)	-0.035	71 (5.6)	53 (5.5)	18 (5.9)	70 (5.6)	0.004
Cyclosporin	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.035	≤ 10	≤ 10	≤ 10	0 (0.0)	0.056
Penicillamin	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.035	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
bDMARDs, during baseline period										
n, total (%)	1600 (100.0)	1350 (100.0)	248 (100.0)	1600 (100.0)	0.000	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Mean (SD)	1.1 (0.3)	1.1 (0.3)	1.1 (0.2)	1.1 (0.3)	-0.004	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.000
Median	1.0	1.0	1.0	1.0		0.0	0.0	0.0	0.0	
Min; Max	[1.0;3.0]	[1.0;3.0]	[1.0;3.0]	[1.0;3.0]		[0.0;0.0]	[0.0;0.0]	[0.0;0.0]	[0.0;0.0]	
cDMARDs, concomitant	909 (56.8)	781 (57.9)	127 (51.2)	847 (52.9)	0.078	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Adalimumab[c]	218 (13.6)	188 (13.9)	30 (12.1)	240 (15.0)	-0.039	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Certolizumab pegol[c]	119 (7.4)	107 (7.9)	12 (4.8)	114 (7.1)	0.012	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Etanercept[c]	332 (20.8)	280 (20.7)	51 (20.6)	348 (21.8)	-0.024	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Golimumab[c]	103 (6.4)	95 (7.0)	≤ 10	106 (6.6)	-0.008	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Infliximab[c]	80 (5.0)	72 (5.3)	≤ 10	85 (5.3)	-0.014	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000

	bDMARD-Experienced					bDMARD naïve				
Characteristics[b]	**Bari. Any[e] 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)**
Rituximab	57 (3.6)	44 (3.3)	13 (5.2)	38 (2.4)	0.07	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Sarilumab	25 (1.6)	18 (1.3)	≤ 10	21 (1.3)	0.021	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Abatacept	431 (26.9)	354 (26.2)	76 (30.6)	419 (26.2)	0.017	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Tocilizumab	358 (22.4)	305 (22.6)	53 (21.4)	355 (22.2)	0.005	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Anakinra	13 (0.8)	≤ 10	≤ 10	12 (0.8)	0.007	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
TNFi naïve at baseline	790 (49.4)	648 (48.0)	142 (57.3)	727 (45.4)	0.079	1260 (100.0)	955 (100.0)	305 (100.0)	1260 (100.0)	0.000
≥1 dispensing of bDMARD within 730 days before index date (excluded), n (%)	1600 (100.0)	1350 (100.0)	248 (100.0)	1600 (100.0)	0.000	453 (36.0)	337 (35.3)	116 (38.0)	369 (29.3)	0.143
Other prescription medications during baseline period, n (%)										
Antibiotics	687 (42.9)	576 (42.7)	110 (44.4)	695 (43.4)	-0.01	502 (39.8)	352 (36.9)	150 (49.2)	456 (36.2)	0.075
Antidiabetic agents	169 (10.6)	136 (10.1)	32 (12.9)	157 (9.8)	0.025	104 (8.3)	68 (7.1)	36 (11.8)	104 (8.3)	0.000
Insulins	63 (3.9)	50 (3.7)	13 (5.2)	56 (3.5)	0.023	38 (3.0)	26 (2.7)	12 (3.9)	38 (3.0)	0.000
Non-insulins	132 (8.3)	110 (8.1)	21 (8.5)	130 (8.1)	0.005	88 (7.0)	58 (6.1)	30 (9.8)	89 (7.1)	-0.003
Cardiovascular										
Antithrombotic agents	239 (14.9)	168 (12.4)	70 (28.2)	234 (14.6)	0.009	211 (16.7)	131 (13.7)	80 (26.2)	193 (15.3)	0.039

	bDMARD-Experienced					bDMARD naïve				
Characteristics[b]	**Bari. Any[e] 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)**
Anticoagulant	61 (3.8)	39 (2.9)	22 (8.9)	62 (3.9)	-0.003	73 (5.8)	38 (4.0)	35 (11.5)	70 (5.6)	0.010
Antiplatelet	188 (11.8)	134 (9.9)	53 (21.4)	182 (11.4)	0.012	157 (12.5)	102 (10.7)	55 (18.0)	130 (10.3)	0.068
Antihypertensives	538 (33.6)	396 (29.3)	140 (56.5)	576 (36.0)	-0.05	426 (33.8)	258 (27.0)	168 (55.1)	417 (33.1)	0.015
Angiotensin converting enzyme inhibitors (ACE)	150 (9.4)	111 (8.2)	39 (15.7)	157 (9.8)	-0.015	100 (7.9)	59 (6.2)	41 (13.4)	122 (9.7)	-0.062
Angiotensin receptor blockers (ARB)	194 (12.1)	136 (10.1)	58 (23.4)	250 (15.6)	-0.101	168 (13.3)	105 (11.0)	63 (20.7)	164 (13.0)	0.009
Beta blocker	223 (13.9)	162 (12.0)	60 (24.2)	240 (15.0)	-0.03	202 (16.0)	119 (12.5)	83 (27.2)	169 (13.4)	0.074
Calcium channel blocker	155 (9.7)	108 (8.0)	45 (18.1)	171 (10.7)	-0.033	127 (10.1)	67 (7.0)	60 (19.7)	128 (10.2)	-0.003
Nitrates	12 (0.8)	≤ 10	≤ 10	18 (1.1)	-0.039	12 (1.0)	≤ 10	≤ 10	13 (1.0)	-0.008
Acyclovir	≤ 10	≤ 10	≤ 10	15 (0.9)	-0.079	≤ 10	≤ 10	≤ 10	≤ 10	0.010
ValAcyclovir	70 (4.4)	53 (3.9)	17 (6.9)	73 (4.6)	-0.009	35 (2.8)	24 (2.5)	11 (3.6)	41 (3.3)	-0.028
Hormonal	229 (14.3)	209 (15.5)	20 (8.1)	221 (13.8)	0.014	134 (10.6)	109 (11.4)	25 (8.2)	152 (12.1)	-0.045
HRT	129 (8.1)	115 (8.5)	14 (5.6)	129 (8.1)	0	83 (6.6)	66 (6.9)	17 (5.6)	94 (7.5)	-0.034
Oral Contraceptives	100 (6.3)	93 (6.9)	≤ 10	91 (5.7)	0.024	47 (3.7)	41 (4.3)	≤ 10	53 (4.2)	-0.024
SERMs	≤ 10	≤ 10	0 (0.0)	≤ 10	0	≤ 10	≤ 10	≤ 10	≤ 10	0.015

	bDMARD-Experienced					bDMARD naïve				
Characteristics[b]	**Bari. Any[e] 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)**
Topic with progestogens and/or estrogens	≤ 10	≤ 10	0 (0.0)	≤ 10	0.067	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.033
Lipid-lowering agents	269 (16.8)	201 (14.9)	67 (27.0)	274 (17.1)	-0.008	215 (17.1)	138 (14.5)	77 (25.2)	181 (14.4)	0.074
HMG CoA reductase inhibitors	222 (13.9)	164 (12.1)	57 (23.0)	223 (13.9)	-0.002	176 (14.0)	111 (11.6)	65 (21.3)	139 (11.0)	0.089
Fibrates	26 (1.6)	19 (1.4)	≤ 10	23 (1.4)	0.015	11 (0.9)	≤ 10	≤ 10	18 (1.4)	-0.052
Bile acid sequestrants	≤ 10	≤ 10	≤ 10	≤ 10	-0.011	≤ 10	≤ 10	≤ 10	≤ 10	-0.012
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	11 (0.7)	≤ 10	≤ 10	14 (0.9)	-0.021	11 (0.9)	≤ 10	≤ 10	17 (1.3)	-0.045
Lipid modifying agents, combinations	14 (0.9)	12 (0.9)	≤ 10	23 (1.4)	-0.053	24 (1.9)	19 (2.0)	≤ 10	14 (1.1)	0.065
Rheumatoid arthritis-related										
Aspirin	26 (1.6)	18 (1.3)	≤ 10	20 (1.3)	0.032	≤ 10	≤ 10	≤ 10	13 (1.0)	-0.025
Cox-2 Inhibitor	93 (5.8)	85 (6.3)	≤ 10	93 (5.8)	0	64 (5.1)	53 (5.5)	11 (3.6)	77 (6.1)	-0.045
NSAIDs	579 (36.2)	508 (37.6)	70 (28.2)	633 (39.6)	-0.07	463 (36.7)	378 (39.6)	85 (27.9)	492 (39.0)	-0.048
Glucocorticosteroid	1096 (68.5)	920 (68.1)	174 (70.2)	1090 (68.1)	0.008	930 (73.8)	692 (72.5)	238 (78.0)	957 (76.0)	-0.049
Vaccines	440 (27.5)	342 (25.3)	98 (39.5)	380 (23.8)	0.086	426 (33.8)	314 (32.9)	112 (36.7)	454 (36.0)	-0.047

	bDMARD-Experienced					bDMARD naïve				
Characteristics[b]	**Bari. Any[e] 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)**
Antineoplastic agents	≤ 10	≤ 10	≤ 10	≤ 10	-0.061	≤ 10	≤ 10	≤ 10	≤ 10	0.076

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 6.83. bDMARD-Experienced and bDMARD naïve: Clinical history at baseline - VTE cohort, Matched [SNDS]

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

Table 6.84. bDMARD-Experienced and bDMARD naïve: Clinical history at baseline - MACE cohort, Matched [SNDS]

Characteristics[b]	bDMARD-Experienced					bDMARD naïve				
	Bari. Any[e] 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)
Clinical conditions during baseline period, n (%)										
Cancer, excluding NMSC	41 (2.6)	33 (2.4)	≤ 10	51 (3.2)	-0.037	49 (3.9)	33 (3.5)	16 (5.3)	49 (3.9)	0.000
NMSC	≤ 10	≤ 10	≤ 10	≤ 10	0.029	≤ 10	≤ 10	≤ 10	≤ 10	-0.018
Chronic lung disease, excluding cystic fibrosis[d]	216 (13.4)	168 (12.4)	48 (19.7)	178 (11.1)	0.072	171 (13.6)	115 (12.1)	56 (18.5)	159 (12.6)	0.028
Cardiovascular conditions										
Atrial arrhythmia/fibrillation	14 (0.9)	≤ 10	≤ 10	≤ 10	0.045	15 (1.2)	≤ 10	11 (3.6)	≤ 10	0.049
Cardiovascular revascularization procedure	≤ 10	0 (0.0)	≤ 10	≤ 10	-0.035	≤ 10	≤ 10	0 (0.0)	≤ 10	0.000
Congestive Heart Failure, hospitalized	≤ 10	≤ 10	≤ 10	≤ 10	0.000	≤ 10	≤ 10	≤ 10	≤ 10	-0.023
Coronary artery disease	54 (3.4)	35 (2.6)	19 (7.8)	69 (4.3)	-0.049	65 (5.2)	42 (4.4)	23 (7.6)	60 (4.8)	0.018
Unstable angina	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.035	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Ventricular arrhythmia	≤ 10	≤ 10	≤ 10	11 (0.7)	-0.076	11 (0.9)	≤ 10	≤ 10	≤ 10	0.018
Stroke	12 (0.7)	≤ 10	≤ 10	≤ 10	0.015	≤ 10	≤ 10	≤ 10	≤ 10	0.019

Characteristics[b]	bDMARD-Experienced					bDMARD naïve				
	Bari. Any[e] 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)
Hemorrhagic	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0.035	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Ischemic	≤ 10	≤ 10	≤ 10	≤ 10	0.000	≤ 10	≤ 10	0 (0.0)	≤ 10	0.023
Unknown	≤ 10	≤ 10	≤ 10	≤ 10	0.017	≤ 10	≤ 10	≤ 10	≤ 10	0.01
TIA	≤ 10	0 (0.0)	≤ 10	0 (0.0)	0.035	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Diabetes Mellitus[d]	175 (10.9)	139 (10.2)	35 (14.3)	168 (10.5)	0.014	109 (8.7)	71 (7.4)	38 (12.5)	110 (8.8)	-0.003
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	48 (3.0)	40 (2.9)	≤ 10	58 (3.6)	-0.035	51 (4.1)	32 (3.4)	19 (6.3)	48 (3.8)	0.012
AIDS/HIV	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.035	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.040
Antiphospholipid syndrome	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	
SLE	11 (0.7)	11 (0.8)	0 (0.0)	≤ 10	0.076	14 (1.1)	11 (1.2)	≤ 10	13 (1.0)	0.008

Characteristics[b]	bDMARD-Experienced					bDMARD naïve				
	Bari. Any[e] 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)
Primary Sjogren Syndrome	38 (2.4)	30 (2.2)	≤ 10	55 (3.4)	-0.063	42 (3.3)	25 (2.6)	17 (5.6)	36 (2.9)	0.028
Liver or pancreatic disorder[d]	55 (3.4)	42 (3.1)	13 (5.3)	49 (3.1)	0.021	28 (2.2)	20 (2.1)	≤ 10	35 (2.8)	-0.036
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 (0.0)	≤ 10	-0.061	≤ 10	≤ 10	0 (0.0)	11 (0.9)	-0.060
RA Severity (CIRAS Index)					0.03					-0.078
Mean (± SD)	6.5 (1.3)	6.6 (1.3)	5.9 (1.3)	6.4 (1.3)		6.5 (1.5)	6.7 (1.4)	5.7 (1.4)	6.6 (1.6)	
Smoking (not available in SNDS)	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	
DMARDs, n (%)										
cDMARDs, during baseline period										
n, total (%)	1018 (63.4)	868 (63.8)	148 (60.7)	973 (60.6)	0.058	916 (72.9)	727 (76.2)	189 (62.4)	946 (75.3)	-0.055
Mean (SD)	0.7 (0.5)	0.7 (0.5)	0.6 (0.5)	0.6 (0.5)	0.048	0.9 (0.7)	0.9 (0.6)	0.7 (0.7)	0.9 (0.6)	-0.038
Median	1.0	1.0	1.0	1.0		1.0	1.0	1.0	1.0	
Min; Max	[0.0;4.0]	[0.0;4.0]	[0.0;3.0]	[0.0;3.0]		[0.0;4.0]	[0.0;4.0]	[0.0;3.0]	[0.0;3.0]	

Characteristics[b]	bDMARD-Experienced					bDMARD naïve				
	Bari. Any[e] 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)
>1 cDMARD concomitantly	41 (2.6)	36 (2.6)	≤ 10	40 (2.5)	0.004	116 (9.2)	90 (9.4)	26 (8.6)	99 (7.9)	0.048
Hydroxychloroquine	45 (2.8)	39 (2.9)	≤ 10	59 (3.7)	-0.049	111 (8.8)	82 (8.6)	29 (9.6)	94 (7.5)	0.049
Chloroquine	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.035	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.04
Azathioprin	≤ 10	≤ 10	≤ 10	≤ 10	0.012	≤ 10	≤ 10	0 (0.0)	≤ 10	0
Leflunomid	152 (9.5)	130 (9.6)	22 (9.0)	167 (10.4)	-0.031	193 (15.4)	160 (16.8)	33 (10.9)	186 (14.8)	0.016
Methotrexate	837 (52.1)	718 (52.8)	117 (48.0)	756 (47.1)	0.101	693 (55.1)	548 (57.4)	145 (47.9)	745 (59.3)	-0.084
Mycophenolate mofetil	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.050	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0.04
Sulfasalazin	28 (1.7)	22 (1.6)	≤ 10	34 (2.1)	-0.027	71 (5.6)	53 (5.6)	18 (5.9)	76 (6.0)	-0.017
Cyclosporin	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.035	≤ 10	≤ 10	≤ 10	0 (0.0)	0.057
Penicillamin	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.035	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
bDMARDs, during baseline period										
n, total (%)	1606 (100.0)	1360 (100.0)	244 (100.0)	1606 (100.0)	0.000	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Mean (SD)	1.1 (0.3)	1.1 (0.3)	1.1 (0.2)	1.1 (0.3)	-0.020	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.000
Median	1.0	1.0	1.0	1.0		0.0	0.0	0.0	0.0	
Min; Max	[1.0;3.0]	[1.0;3.0]	[1.0;3.0]	[1.0;3.0]		[0.0;0.0]	[0.0;0.0]	[0.0;0.0]	[0.0;0.0]	
cDMARDs, concomitant	895 (55.7)	768 (56.5)	125 (51.2)	876 (54.5)	0.024	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Adalimumab[c]	218 (13.6)	188 (13.8)	30 (12.3)	239 (14.9)	-0.037	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Certolizumab pegol[c]	122 (7.6)	109 (8.0)	13 (5.3)	115 (7.2)	0.017	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000

Characteristics[b]	bDMARD-Experienced					bDMARD naïve				
	Bari. Any[e] 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)
Etanercept[c]	325 (20.2)	276 (20.3)	49 (20.1)	350 (21.8)	-0.038	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Golimumab[c]	102 (6.4)	95 (7.0)	≤ 10	101 (6.3)	0.003	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Infliximab[c]	81 (5.0)	72 (5.3)	≤ 10	81 (5.0)	0.000	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Rituximab	63 (3.9)	50 (3.7)	13 (5.3)	37 (2.3)	0.093	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Sarilumab	25 (1.6)	19 (1.4)	≤ 10	23 (1.4)	0.01	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Abatacept	427 (26.6)	352 (25.9)	74 (30.3)	429 (26.7)	-0.003	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Tocilizumab	355 (22.1)	303 (22.3)	52 (21.3)	353 (22.0)	0.003	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Anakinra	14 (0.9)	≤ 10	≤ 10	13 (0.8)	0.007	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
TNFi naïve at baseline	799 (49.8)	658 (48.4)	140 (57.4)	739 (46.0)	0.075	1257 (100.0)	954 (100.0)	303 (100.0)	1257 (100.0)	0.000
≥1 dispensing of bDMARD within 730 days before index date (excluded), n (%)	1606 (100.0)	1360 (100.0)	244 (100.0)	1606 (100.0)	0.000	451 (35.9)	336 (35.2)	115 (38.0)	306 (24.3)	0.254
Other prescription medications during baseline period, n (%)										
Antibiotics	689 (42.9)	578 (42.5)	110 (45.1)	695 (43.3)	-0.008	502 (39.9)	352 (36.9)	150 (49.5)	486 (38.7)	0.026
Antidiabetic agents	169 (10.5)	134 (9.9)	34 (13.9)	159 (9.9)	0.021	103 (8.2)	68 (7.1)	35 (11.6)	102 (8.1)	0.003
Insulins	70 (4.4)	54 (4.0)	16 (6.6)	55 (3.4)	0.048	38 (3.0)	26 (2.7)	12 (4.0)	39 (3.1)	-0.005
Non-insulins	130 (8.1)	106 (7.8)	23 (9.4)	134 (8.3)	-0.009	87 (6.9)	58 (6.1)	29 (9.6)	87 (6.9)	0.000
Cardiovascular										

Characteristics[b]	bDMARD-Experienced					bDMARD naïve				
	Bari. Any[e] 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)
Antithrombotic agents	227 (14.1)	163 (12.0)	63 (25.8)	243 (15.1)	-0.028	208 (16.5)	130 (13.6)	78 (25.7)	200 (15.9)	0.017
Anticoagulant	54 (3.4)	36 (2.6)	18 (7.4)	58 (3.6)	-0.014	72 (5.7)	38 (4.0)	34 (11.2)	60 (4.8)	0.043
Antiplatelet	182 (11.3)	131 (9.6)	50 (20.5)	197 (12.3)	-0.029	155 (12.3)	101 (10.6)	54 (17.8)	148 (11.8)	0.017
Antihypertensives	539 (33.6)	404 (29.7)	134 (54.9)	569 (35.4)	-0.039	423 (33.7)	257 (26.9)	166 (54.8)	403 (32.1)	0.034
Angiotensin converting enzyme inhibitors (ACE)	150 (9.3)	114 (8.4)	36 (14.8)	145 (9.0)	0.011	101 (8.0)	59 (6.2)	42 (13.9)	111 (8.8)	-0.029
Angiotensin receptor blockers (ARB)	203 (12.6)	148 (10.9)	55 (22.5)	249 (15.5)	-0.082	165 (13.1)	104 (10.9)	61 (20.1)	160 (12.7)	0.012
Beta blocker	214 (13.3)	159 (11.7)	54 (22.1)	247 (15.4)	-0.059	200 (15.9)	118 (12.4)	82 (27.1)	187 (14.9)	0.029
Calcium channel blocker	158 (9.8)	110 (8.1)	47 (19.3)	162 (10.1)	-0.008	126 (10.0)	67 (7.0)	59 (19.5)	113 (9.0)	0.035
Nitrates	12 (0.7)	≤ 10	≤ 10	21 (1.3)	-0.056	11 (0.9)	≤ 10	≤ 10	13 (1.0)	-0.016
Acyclovir	≤ 10	≤ 10	≤ 10	12 (0.7)	-0.06	≤ 10	≤ 10	≤ 10	≤ 10	0.000
Valacyclovir	72 (4.5)	56 (4.1)	16 (6.6)	71 (4.4)	0.003	35 (2.8)	24 (2.5)	11 (3.6)	39 (3.1)	-0.019
Hormonal	220 (13.7)	203 (14.9)	17 (7.0)	233 (14.5)	-0.023	134 (10.7)	109 (11.4)	25 (8.3)	145 (11.5)	-0.028
HRT	122 (7.6)	110 (8.1)	12 (4.9)	131 (8.2)	-0.021	83 (6.6)	66 (6.9)	17 (5.6)	79 (6.3)	0.013
Oral Contraceptives	96 (6.0)	90 (6.6)	≤ 10	95 (5.9)	0.003	47 (3.7)	41 (4.3)	≤ 10	61 (4.9)	-0.055
SERMs	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.011	≤ 10	≤ 10	≤ 10	≤ 10	-0.025

Characteristics[b]	bDMARD-Experienced					bDMARD naïve				
	Bari. Any[e] 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)
Topic with progestogens and/or estrogens	≤ 10	≤ 10	0 (0.0)	≤ 10	0.011	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.033
Lipid-lowering agents	263 (16.4)	200 (14.7)	62 (25.4)	284 (17.7)	-0.035	213 (16.9)	137 (14.4)	76 (25.1)	191 (15.2)	0.048
HMG CoA reductase inhibitors	216 (13.4)	163 (12.0)	52 (21.3)	232 (14.4)	-0.029	175 (13.9)	110 (11.5)	65 (21.5)	159 (12.6)	0.038
Fibrates	22 (1.4)	16 (1.2)	≤ 10	23 (1.4)	-0.005	≤ 10	≤ 10	≤ 10	≤ 10	0.009
Bile acid sequestrants	≤ 10	≤ 10	≤ 10	≤ 10	0.011	≤ 10	≤ 10	≤ 10	≤ 10	0.000
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	≤ 10	≤ 10	≤ 10	15 (0.9)	-0.035	11 (0.9)	≤ 10	≤ 10	≤ 10	0.038
Lipid modifying agents, combinations	18 (1.1)	15 (1.1)	≤ 10	23 (1.4)	-0.028	24 (1.9)	19 (2.0)	≤ 10	15 (1.2)	0.058
Rheumatoid arthritis-related										
Aspirin	26 (1.6)	18 (1.3)	≤ 10	21 (1.3)	0.026	≤ 10	≤ 10	≤ 10	12 (1.0)	-0.017
Cox-2 Inhibitor	93 (5.8)	86 (6.3)	≤ 10	98 (6.1)	-0.013	64 (5.1)	53 (5.6)	11 (3.6)	63 (5.0)	0.004
NSAIDs	590 (36.7)	520 (38.2)	70 (28.7)	638 (39.7)	-0.062	461 (36.7)	378 (39.6)	83 (27.4)	457 (36.4)	0.007
Glucocorticosteroid	1105 (68.8)	935 (68.8)	169 (69.3)	1082 (67.4)	0.031	927 (73.7)	691 (72.4)	236 (77.9)	954 (75.9)	-0.05
Vaccines	446 (27.8)	349 (25.7)	97 (39.8)	382 (23.8)	0.091	426 (33.9)	314 (32.9)	112 (37.0)	440 (35.0)	-0.023

Characteristics[b]	bDMARD-Experienced					bDMARD naïve				
	Bari. Any[e] 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)
Antineoplastic agents	≤ 10	≤ 10	≤ 10	11 (0.7)	-0.064	≤ 10	≤ 10	≤ 10	≤ 10	0.060

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 6.85. bDMARD-Experienced and bDMARD naïve: Clinical history at baseline - MACE cohort, Matched [SNDS]

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

Table 6.86. bDMARD-Experienced and bDMARD naïve: Clinical history at baseline - Incident Serious Infection cohort, Matched [SNDS]

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)
Clinical conditions during baseline period, n (%)										
Cancer, excluding NMSC	34 (2.1)	27 (2.0)	≤ 10	48 (2.9)	-0.055	58 (4.4)	37 (3.8)	21 (6.3)	53 (4.0)	0.019
NMSC	≤ 10	≤ 10	≤ 10	≤ 10	0.016	≤ 10	≤ 10	≤ 10	≤ 10	-0.017
Chronic lung disease, excluding cystic fibrosis[d]	222 (13.5)	166 (12.1)	56 (21.2)	191 (11.6)	0.057	185 (14.0)	123 (12.5)	62 (18.6)	195 (14.8)	-0.022
Cardiovascular conditions										
Atrial arrhythmia/fibrillation	21 (1.3)	12 (0.9)	≤ 10	25 (1.5)	-0.021	38 (2.9)	13 (1.3)	25 (7.5)	32 (2.4)	0.028
Cardiovascular revascularization procedure	≤ 10	≤ 10	≤ 10	≤ 10	-0.035	≤ 10	≤ 10	≤ 10	≤ 10	-0.015
Congestive Heart Failure, hospitalized	≤ 10	≤ 10	≤ 10	≤ 10	0.029	≤ 10	≤ 10	≤ 10	≤ 10	-0.010
Coronary artery disease	64 (3.9)	43 (3.1)	21 (8.0)	77 (4.7)	-0.039	70 (5.3)	45 (4.6)	25 (7.5)	54 (4.1)	0.057
Unstable angina	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.061	≤ 10	0 (0.0)	≤ 10	≤ 10	-0.052

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)
Ventricular arrhythmia	≤ 10	≤ 10	≤ 10	12 (0.7)	-0.015	12 (0.9)	≤ 10	≤ 10	20 (1.5)	-0.055
Stroke	19 (1.2)	13 (0.9)	≤ 10	18 (1.1)	0.006	14 (1.1)	≤ 10	≤ 10	≤ 10	0.032
Hemorrhagic	≤ 10	≤ 10	0 (0.0)	≤ 10	0.020	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Ischemic	≤ 10	≤ 10	≤ 10	≤ 10	0.020	≤ 10	≤ 10	≤ 10	≤ 10	0.028
Unknown	14 (0.9)	11 (0.8)	≤ 10	12 (0.7)	0.014	11 (0.8)	≤ 10	≤ 10	≤ 10	0.027
TIA	≤ 10	0 (0.0)	≤ 10	≤ 10	-0.020	≤ 10	0 (0.0)	≤ 10	≤ 10	0.000
Diabetes Mellitus[d]	165 (10.0)	127 (9.2)	37 (14.0)	167 (10.2)	-0.004	125 (9.5)	78 (7.9)	47 (14.1)	127 (9.6)	-0.005
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	51 (3.1)	43 (3.1)	≤ 10	65 (4.0)	-0.046	58 (4.4)	34 (3.5)	24 (7.2)	50 (3.8)	0.031
AIDS/HIV	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.035	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.055

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)
Antiphospholipid syndrome	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	
SLE	16 (1.0)	15 (1.1)	≤ 10	≤ 10	0.094	14 (1.1)	11 (1.1)	≤ 10	14 (1.1)	0.000
Primary Sjogren Syndrome	36 (2.2)	28 (2.0)	≤ 10	61 (3.7)	-0.09	49 (3.7)	27 (2.7)	22 (6.6)	36 (2.7)	0.056
Liver or pancreatic disorder[d]	55 (3.3)	43 (3.1)	11 (4.2)	55 (3.3)	0.000	30 (2.3)	21 (2.1)	≤ 10	39 (3.0)	-0.043
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 (0.0)	≤ 10	-0.068	≤ 10	≤ 10	0 (0.0)	≤ 10	-0.042
RA Severity (CIRAS Index)					0.022					-0.036
Mean (± SD)	6.4 (1.3)	6.6 (1.3)	5.8 (1.3)	6.4 (1.3)		6.4 (1.5)	6.7 (1.4)	5.7 (1.4)	6.5 (1.5)	
Smoking (not available in SNDS)	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	
DMARDs, n (%)										
cDMARDs, during baseline period										
n, total (%)	1047 (63.7)	888 (64.5)	156 (59.1)	996 (60.6)	0.064	948 (71.9)	747 (75.8)	201 (60.2)	1003 (76.0)	-0.095

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)
Mean (SD)	0.7 (0.5)	0.7 (0.5)	0.6 (0.6)	0.6 (0.5)	0.064	0.8 (0.7)	0.9 (0.6)	0.7 (0.7)	0.9 (0.6)	-0.072
Median	1.0	1.0	1.0	1.0		1.0	1.0	1.0	1.0	
Min; Max	[0.0;4.0]	[0.0;4.0]	[0.0;3.0]	[0.0;3.0]		[0.0;4.0]	[0.0;4.0]	[0.0;3.0]	[0.0;4.0]	
>1 cDMARD concomitantly	43 (2.6)	38 (2.8)	≤ 10	37 (2.3)	0.024	117 (8.9)	89 (9.0)	28 (8.4)	122 (9.2)	-0.013
Hydroxychloroquine	48 (2.9)	42 (3.1)	≤ 10	58 (3.5)	-0.035	113 (8.6)	82 (8.3)	31 (9.3)	106 (8.0)	0.019
Chloroquine	≤ 10	0 (0.0)	≤ 10	≤ 10	0.000	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Azathioprin	≤ 10	≤ 10	≤ 10	≤ 10	0.02	≤ 10	≤ 10	≤ 10	≤ 10	0.044
Leflunomid	156 (9.5)	134 (9.7)	22 (8.3)	168 (10.2)	-0.025	203 (15.4)	166 (16.9)	37 (11.1)	210 (15.9)	-0.015
Methotrexate	856 (52.1)	730 (53.1)	124 (47.0)	779 (47.4)	0.094	713 (54.1)	562 (57.1)	151 (45.2)	783 (59.4)	-0.107
Mycophenolate mofetil	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.049	≤ 10	≤ 10	0 (0.0)	0 (0.0)	0.039
Sulfasalazin	32 (1.9)	23 (1.7)	≤ 10	29 (1.8)	0.014	72 (5.5)	54 (5.5)	18 (5.4)	69 (5.2)	0.010
Cyclosporin	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000	≤ 10	≤ 10	≤ 10	0 (0.0)	0.055
Penicillamin	0 (0.0)	0 (0.0)	0 (0.0)	≤ 10	-0.035	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
bDMARDs, during baseline period										
n, total (%)	1643 (100.0)	1376 (100.0)	264 (100.0)	1643 (100.0)	0.000	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Mean (SD)	1.1 (0.3)	1.1 (0.3)	1.0 (0.2)	1.1 (0.3)	-0.047	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.000
Median	1.0	1.0	1.0	1.0		0.0	0.0	0.0	0.0	
Min; Max	[1.0;3.0]	[1.0;3.0]	[1.0;2.0]	[1.0;3.0]		[0.0;0.0]	[0.0;0.0]	[0.0;0.0]	[0.0;0.0]	

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)
cDMARDs, concomitant	933 (56.8)	798 (58.0)	132 (50.0)	894 (54.4)	0.048	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Adalimumab[c]	216 (13.1)	190 (13.8)	26 (9.8)	241 (14.7)	-0.044	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Certolizumab pegol[c]	115 (7.0)	102 (7.4)	13 (4.9)	124 (7.5)	-0.021	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Etanercept[c]	326 (19.8)	278 (20.2)	48 (18.2)	359 (21.9)	-0.05	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Golimumab[c]	106 (6.5)	99 (7.2)	≤ 10	107 (6.5)	-0.003	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Infliximab[c]	82 (5.0)	74 (5.4)	≤ 10	81 (4.9)	0.003	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Rituximab	58 (3.5)	43 (3.1)	15 (5.7)	37 (2.3)	0.076	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Sarilumab	32 (1.9)	27 (2.0)	≤ 10	25 (1.5)	0.033	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Abatacept	446 (27.1)	353 (25.7)	91 (34.5)	441 (26.8)	0.007	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Tocilizumab	372 (22.6)	312 (22.7)	60 (22.7)	356 (21.7)	0.024	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
Anakinra	≤ 10	≤ 10	≤ 10	13 (0.8)	-0.022	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.000
TNFi naïve at baseline	831 (50.6)	665 (48.3)	165 (62.5)	751 (45.7)	0.098	1319 (100.0)	985 (100.0)	334 (100.0)	1319 (100.0)	0.000
>=1 dispensing of bDMARD within 730 days before index date (excluded), n (%)	1643 (100.0)	1376 (100.0)	264 (100.0)	1643 (100.0)	0.000	485 (36.8)	350 (35.5)	135 (40.4)	340 (25.8)	0.239
Other prescription medications during baseline period, n (%)										