JAKi – Final Report

The data included in the current report are based on the ARTIS linkage (Karolinska Institutet). ARTIS has linked the data from the Swedish Rheumatology Quality register (SRQ) to data from the Swedish National Health Registers. In particular, for this report, data from the National Patient Register (NPR) and the Prescribed Drug Register (PDR) have been used. Additionally, information on education and country of birth have been collected from LISA (Longitudinal integrated database for health insurance and labour market studies) and from the Swedish Population Register. Also, information on county of residence in 2018 have been collected from LISA.

The data on prescription of biological disease-modifying antirheumatic drugs (bDMARD) and targeted synthetic disease-modifying antirheumatic drugs (tsDMARD) are collected in PDR since July 2005. The dataset includes a record for each dispensation, including information on dispensation date, ATC code, and Defined Daily Doses (DDDs).

Line of treatment have been assigned based on the whole dataset from 1999 (SRQ) and PDR (2005), although this report is based on JAKi and bDMARDs prescribed between 1st May 2017 and 31st December 2019.
To preserve privacy, all cells containing between one and five individuals will be presented as "<5".

Contents

Table 1. Number of JAKi or any bDMARD treatments initiated by rheumatoid arthritis patients 2017-2019, by line of therapy, age, gender, educational level, and country of birth (n=13 624)

	All		No previous b/tsDMARD		1 previous b/tsDMARD		2 previous b/tsDMARD		3 or more previous b/tsDMARD	
	JAKi	bDMARD	JAKi	bDMARD	JAKi	bDMARD	JAKi	bDMARD	JAKi	bDMARD
All	2310	11314	283	4272	344	2711	444	1744	1239	2587
Age										
0-18	<5	70	0	29	0	16	<5	13	<5	12
18-34	111	918	8	383	18	221	16	127	69	187
35-44	183	1314	17	488	27	284	36	197	103	345
45-54	467	2173	29	798	68	520	103	316	267	539
55-64	618	2763	59	1028	98	651	115	461	346	623
65-74	600	2776	84	1033	89	694	117	445	310	604
75+	327	1300	86	513	44	325	56	185	141	277
Gender										
Female	1871	8771	208	3196	262	2092	355	1368	1046	2115
Male	439	2543	75	1076	82	619	89	376	193	472
Educational level										
≤9 years	440	2064	77	821	68	480	78	317	217	446
10-12 years	1106	5287	112	1973	168	1266	202	808	624	1240
>12 years	754	3798	91	1393	106	927	162	598	395	880
Missing	10	165	<5	85	<5	38	<5	21	<5	21
Country of birth										
Sweden	1983	9542	238	3575	285	2268	374	1449	1086	2250
Scandinavia	105	552	10	201	17	138	24	98	54	115
Europe	99	490	15	202	17	126	20	81	47	81
Other	123	730	20	294	25	179	26	116	52	141

Table 2. Number of treatments with JAKi or bDMARD initiated by non-RA rheumatologic* patients 2017-2019, by line of therapy, age, gender, educational level, and country of birth (n=17 336)

	All		No previous b/tsDMARD		1 previous b/tsDMARD		2 previous b/tsDMARD		3 or more previous b/tsDMARD	
	JAKi	bDMARD	JAKi	bDMARD	JAKi	bDMARD	JAKi	bDMARD	JAKi	bDMARD
All	852	16484	58	6176	111	4127	129	2482	554	3699
Age										
0-18	12	967	<5	536	<5	272	<5	91	5	68
18-34	179	3518	7	1341	23	859	22	534	127	784
35-44	128	3056	10	1096	10	758	21	451	87	751
45-54	197	3851	7	1334	18	990	31	601	141	926
55-64	193	2977	17	1052	30	731	26	461	120	733
65-74	111	1688	13	658	18	407	20	278	60	345
75+	32	427	<5	159	9	110	6	66	14	92
Gender										
Female	614	9217	43	3257	78	2311	90	1416	403	2233
Male	238	7267	15	2919	33	1816	39	1066	151	1466
Educational level										
≤9 years	147	2447	10	880	26	612	22	400	89	555
10-12 years	397	7659	27	2707	50	1936	57	1206	263	1810
>12 years	294	5451	18	2057	32	1341	48	792	196	1261
Missing	14	927	<5	532	<5	238	<5	84	6	73
Country of birth										
Sweden	765	14526	43	5386	101	3640	117	2178	504	3322
Scandinavia	28	438	5	178	<5	108	<5	67	15	85
Europe	19	610	<5	269	<5	155	<5	83	11	103
Other	40	909	6	342	<5	224	6	154	24	189

*Non-RA rheumatologic patients includes patients diagnosed with PsA, SpA, AS, mono/polyarthritis, or JIA.

Table 3. Number of treatments with JAKi initiated by eligible* rheumatoid arthritis patients and p-values from of a logistic regression to evaluate which characteristics are associated with JAKi prescription instead of a bDMARD prescription in 2017-2019, by line of therapy, age, gender, educational level, and disease activity score (DAS28) at baseline. (n=4448)

This table is based only on data from SRQ, and with no missing data on DAS28 in the period (90 days) before start of a new treatment.

		JAKi	bDMARD	p-value¤
All		972	3476	
Age				
	0-18	0 (0.00%)	<5 (0.03%)	-
	18-34	42 (4.32%)	241 (6.93%)	<0.001
	35-44	67 (6.89%)	344 (9.90%)	0,003
	45-54	184 (18.93%)	671 (19.30%)	0,23
	55-64	293 (30.14%)	914 (26.29%)	Ref
	65-74	261 (26.85%)	909 (26.15%)	0,68
	75+	125 (12.86%)	396 (11.39%)	0,12
Gender				
	Female	809 (83.23%)	2761 (79.43%)	Ref
	Male	163 (16.77%)	715 (20.57%)	0,33
Educational level				
	≤9 years	185 (19.03%)	669 (19.25%)	0,76
	10-12 years	485 (49.90%)	1694 (48.73%)	Ref
	>12 years	301 (30.97%)	1088 (31.30%)	0,89
	Missing	<5 (0.10%)	25 (0.72%)	0,32
Disease activity (DAS28) at start of new treatment				
	Moderate disease activity (3.2-5.1)	565 (58.13%)	2081 (59.87%)	0,10
	High disease activity (>5.1)	407 (41.87%)	1395 (40.13%)	Ref
Line of treatment				
	First line	90 (9.26%)	1492 (42.92%)	<0.001
	Second line	149 (15.33%)	748 (21.52%)	Ref
	Third line	184 (18.93%)	486 (13.98%)	<0.001
	Fourth+ line	549 (56.48%)	750 (21.58%)	<0.001

*Patients are considered to be eligible to start JAKi treatment if they have RA, they have been treated with at least one cs/bDMARD, they are changing to a new substance, and DAS28>=3.2 (moderate or high) at the time of treatment change. Of the 13 624 RA patients, only 5 886 had a non-missing value for DAS28.

¤ P-values are from a logistic model mutually adjusted for all the variables in the table, and further adjusted for line of treatment. The logistic model has been restricted to patients >=18 years of age.

Table 3b. Number of treatments with JAKi initiated by eligible* rheumatoid arthritis patients and p-values from of a logistic regression to evaluate which characteristics are associated with JAKi prescription instead of a bDMARD prescription in 2017-2019, by line of therapy, age, gender, and educational level at baseline. (n=11 479)

		JAKi	bDMARD	p-value¤
All		2264	9215	
Age				
	0-18	<5 (0.18%)	60 (0.65%)	-
	18-34	108 (4.77%)	736 (7.99%)	<0.001
	35-44	177 (7.82%)	999 (10.84%)	<0.001
	45-54	459 (20.27%)	1775 (19.26%)	0,56
	55-64	604 (26.68%)	2289 (24.84%)	Ref
	65-74	591 (26.10%)	2268 (24.61%)	0,74
	75+	321 (14.18%)	1088 (11.81%)	0,02
Gender				
	Female	1835 (81.05%)	7171 (77.82%)	Ref
	Male	429 (18.95%)	2044 (22.18%)	0,33
Educational level				
	≤9 years	432 (19.08%)	1695 (18.39%)	0,27
	10-12 years	1081 (47.75%)	4356 (47.27%)	Ref
	>12 years	741 (32.73%)	3027 (32.85%)	0,48
	Missing	10 (0.44%)	137 (1.49%)	0,18
Line of treatment				
	First line	276 (12.19%)	4038 (43.82%)	<0.001
	Second line	342 (15.11%)	2066 (22.42%)	Ref
	Third line	438 (19.35%)	1283 (13.92%)	<0.001
	Fourth+ line	1208 (53.36%)	1828 (19.84%)	<0.001

*Patients are considered to be eligible to start JAKi treatment if they have RA, they have been treated with at least one cs/bDMARD and they are changing to a new substance.
¤ P-values are from a logistic model mutually adjusted for all the variables in the table, and further adjusted for line of treatment. The logistic model has been restricted to patients >=18 years of age.

Table 4. Number of treatments with JAKi or bDMARD 2017-2019 (all indications), by line of therapy and län (n=40 445)

	All		No previous b/tsDMARD		1 previous b/tsDMARD		2 previous b/tsDMARD		3 or more previous b/tsDMARD	
Lan	**JAKi**	**bDMARD**	**JAKi**	**bDMARD**	**JAKi**	**bDMARD**	**JAKi**	**bDMARD**	**JAKi**	**bDMARD**
Blekinge	68	437	15	132	8	96	8	72	37	137
Dalarna	46	731	<5	282	<5	168	6	100	36	181
Gotland	20	335	0	124	0	87	<5	59	17	65
Gävleborg	100	915	8	345	13	231	23	150	56	189
Halland	88	844	10	335	9	219	20	117	49	173
Jämtland	47	354	<5	106	<5	81	5	58	38	109
Jönköping	47	671	<5	294	5	145	8	87	32	145
Kalmar	85	761	6	268	<5	162	9	123	66	208
Kronoberg	51	588	9	247	<5	150	13	74	25	117
Norrbotten	82	857	6	269	8	208	11	133	57	247
Skåne	401	3462	33	1280	48	829	76	548	244	805
Stockholm	809	6879	115	2512	141	1641	139	1079	414	1647
Södermanland	134	830	6	331	28	212	27	137	73	150
Uppsala	56	882	<5	300	5	215	6	143	43	224
Värmland	160	720	40	248	24	195	29	111	67	166
Västerbotten	66	594	<5	237	8	152	11	83	43	122
Västernorrland	105	833	13	291	17	227	23	132	52	183
Västmanland	39	967	<5	366	<5	253	<5	140	32	208
Västra Götaland	387	3851	28	1576	60	1010	84	561	215	704
Örebro	92	779	12	271	19	200	19	128	42	180
Östergötland	268	1348	24	577	47	318	45	171	152	282

Table 5. Indication among patients initiating treatment with Olumiant or Xeljanz 2017-2019. (n=3 444)

	N° patients initiated							
	2017-2019		2017		2018		2019	
Indication*	Olumiant	Xeljanz	Olumiant	Xeljanz	Olumiant	Xeljanz	Olumiant	Xeljanz
RA	1875	435	281	133	846	134	748	168
PsA	88	286	11	5	35	88	42	193
SpA	44	46	6	<5	13	15	25	29
AS	17	22	<5	0	7	10	9	12
Mono/poly-arthritis UNS	94	46	10	6	47	14	37	26
JIA	155	54	26	9	67	21	62	24
Ulcerative colitis	0	178	0	<5	0	38	0	138
Crohns´ disease	<5	10	-	-	0	<5	<5	8
Other non-rheumatic diagnosis	52	41	8	5	11	15	33	21

*RA=M05,M06, Psa=L40.5 or M07.0-3, SpA=M46.8, AS=M45, Mono/polyarthritis=M12.3, M13, JIA=M08, M09, UC=K51, CD=K50. The diagnoses was assigned based on SRQ and, for those who are not listed in SRQ, through the National Patient Register.

Table 5a. Indication among patients initiating treatment with Olumiant or Xeljanz 2017-2019, by line of treatment. (n= 3 162)

	All		No previous bDMARD		1 previous bDMARD		2 previous bDMARD		3 or more previous bDMARD	
Indication*	Olumiant	Xeljanz	Olumiant	Xeljanz	Olumiant	Xeljanz	Olumiant	Xeljanz	Olumiant	Xeljanz
RA	1875	435	250	33	299	45	378	66	948	291
PsA	88	286	5	9	11	41	19	47	53	189
SpA	44	46	<5	<5	<5	<5	<5	5	35	35
AS	17	22			<5	<5	<5	<5	12	16
Mono/poly-arthritis UNS	94	46	28	5	15	9	19	10	32	22
JIA	155	54	5	0	21	<5	14	7	115	45

*RA=M05,M06, Psa=L40.5 or M07.0-3, SpA=M46.8, AS=M45, Mono/polyarthritis=M12.3, M13, JIA=M08, M09. IBD was not included due to the different treatment strategy

Table 6. Number of patients with rheumatoid arthritis switching from a TNFi as first, second or third ever bDMARD to another molecule, 2017-2019. (n=5 848)

Line of TNF	Following treatment	N
First	TNFi	1826
First	JAKi	277
First	IL-6	143
First	B-cell	168
First	T-cell	234
First	Other	26
Second	TNFi	839
Second	JAKi	260
Second	IL-6	136
Second	B-cell	99
Second	T-cell	168
Second	Other	30
Third	TNFi	393
Third	JAKi	130
Third	IL-6	72
Third	B-cell	37
Third	T-cell	95
Third	Other	11

Table 7. Treatment sequence of patients with rheumatoid arthritis starting a JAKi and bDMARD treatment 2017-2019 (n=13 624)

	All		2017		2018		2019	
	JAKi	bDMARD	JAKi	bDMARD	JAKi	bDMARD	JAKi	bDMARD
Number of previous bDMARD treatments								
0	283	4272	29	1082	122	1730	132	1460
1-2	788	4455	122	1109	347	1615	319	1731
3-4	659	1706	112	433	299	622	248	651
5+	580	881	151	173	212	317	217	391
Number of previousTNFi treatments								
0	397	904	43	267	177	357	177	280
1-2	1275	7847	227	1895	540	3016	508	2936
3-4	519	2015	112	518	217	713	190	784
5+	119	548	32	117	46	198	41	233
Number of previous non-TNFi treatments								
0	922	2470	125	697	397	966	400	807
1-2	971	1596	173	424	438	571	360	601
3-4	355	304	99	39	122	110	134	155
5+	62	76	17	6	23	24	22	46
Number of previous csDMARD treatments								
0	62	391	14	108	28	156	20	127
1-2	715	4759	115	1135	291	1845	309	1779
3+	1533	6164	285	1554	661	2283	587	2327
Treatment sequence (treatment preceding the use of JAKi)								
No previous bDMARD	283	4272	29	1082	122	1730	132	1460
At least one previous TNFi but no previous nTNFi	639	1835	96	503	275	700	268	632
At least one previous nTNFi, but no previous TNFi	114	269	14	73	55	91	45	105
At least one previous TNFi and one previous nTNFi	1274	1707	275	396	528	614	471	697
At least one previous JAKi[§]	239	575	14	17	86	200	139	358

[§]These patients might have had other TNFi or nTNFi treatments

Table 7b. Treatment sequence of non-RA rheumatologic patients starting a JAKi and bDMARD treatment 2017-2019 (n=17 336)

	All		2017		2018		2019	
	JAKi	bDMARD	JAKi	bDMARD	JAKi	bDMARD	JAKi	bDMARD
Number of previous bDMARD treatments								
0	58	6176	5	1640	22	2665	31	1871
1-2	240	6609	10	1516	83	2521	147	2572
3-4	254	2470	21	587	102	883	131	1000
5+	300	1229	40	267	110	443	150	519
Number of previousTNFi treatments								
0	81	920	7	246	28	386	46	288
1-2	388	10957	28	2678	145	4442	215	3837
3-4	265	3388	31	806	96	1249	138	1333
5+	118	1219	10	280	48	435	60	504
Number of previous non-TNFi treatments								
0	305	3287	18	821	112	1312	175	1154
1-2	402	1502	32	333	150	559	220	610
3-4	121	198	25	39	47	65	49	94
5+	24	49	<5	6	8	15	15	28
Number of previous csDMARD treatments								
0	43	3376	<5	870	17	1359	24	1147
1-2	308	7850	25	1865	104	3153	179	2832
3+	501	5258	49	1275	196	2000	256	1983
Treatment sequence (treatment preceding the use of JAKi)								
No previous bDMARD	58	6176	5	1640	22	2665	31	1871
At least one previous TNFi but no previous nTNFi	247	2585	13	617	90	1013	144	955
At least one previous nTNFi, but no previous TNFi	23	218	<5	42	6	87	15	89
At least one previous TNFi and one previous nTNFi	524	1531	56	336	199	552	269	643
At least one previous JAKi[§]	66	271	<5	<5	27	68	35	201

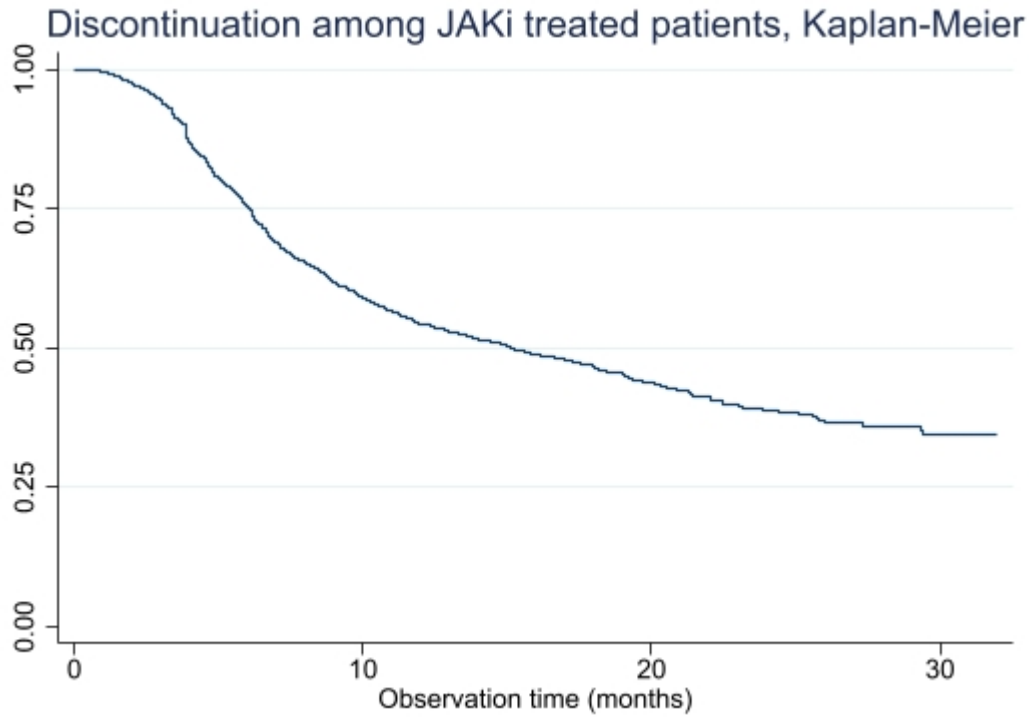
[§]These patients might have had other TNFi or nTNFi treatments

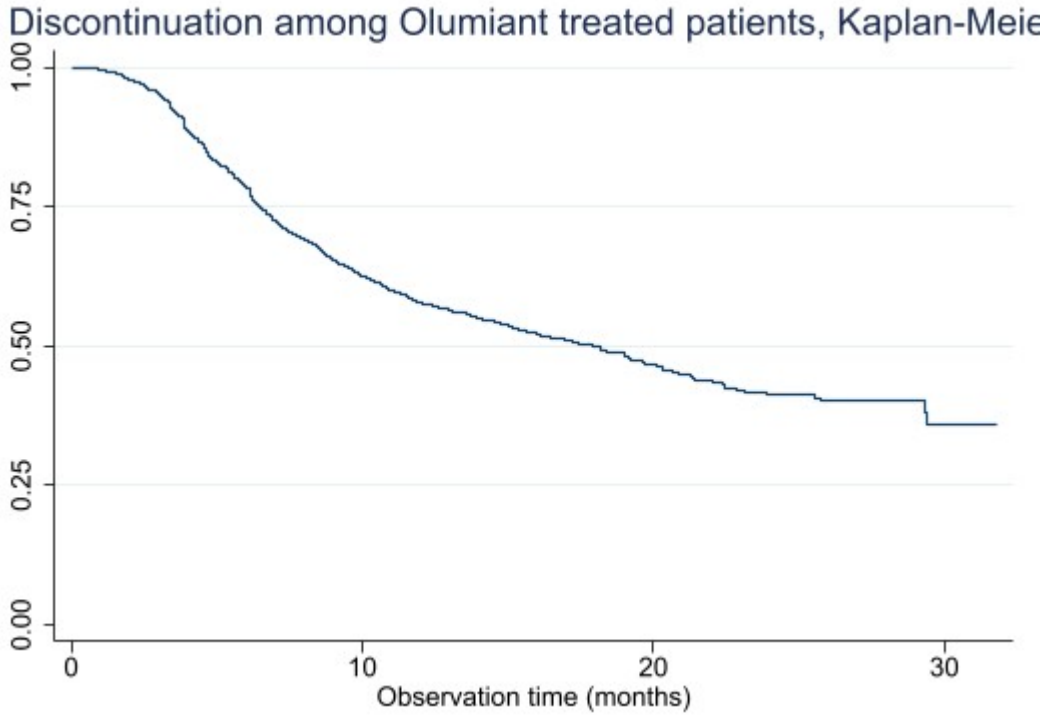
Table 8. Number of patients starting Olumiant or Xeljanz, by quarter of year and by diagnosis. (n=3 002)

	RA		SpA		IBD*	
	Olumiant	**Xeljanz**	**Olumiant**	**Xeljanz**	**Olumiant**	**Xeljanz**
Q2 2017	24	38	<5	<5		
Q3 2017	55	53	5	<5		
Q4 2017	202	42	11	<5	0	<5
Q1 2018	198	21	15	5	0	<5
Q2 2018	235	32	18	10	0	7
Q3 2018	186	31	12	40	0	7
Q4 2018	227	50	10	58	0	22
Q1 2019	213	38	18	66	0	68
Q2 2019	210	43	13	62	0	45
Q3 2019	171	49	24	49	<5	12
Q4 2019	154	38	21	57	0	21

***PsA includes also PsA and AS, and IBD includes UC and CD**

Figure 1. Kaplan-Meier curve of time on JAKi treatment, and separately for Olumiant and Xeljanz. The curves are crude, and therefore differences might be due to differences in the patients characteristics.




Discontinuation among Olumiant treated patients, Kaplan-Meie
1.00
0.75
0.50
0.25
0.00
0
10
20
30
Observation time (months)

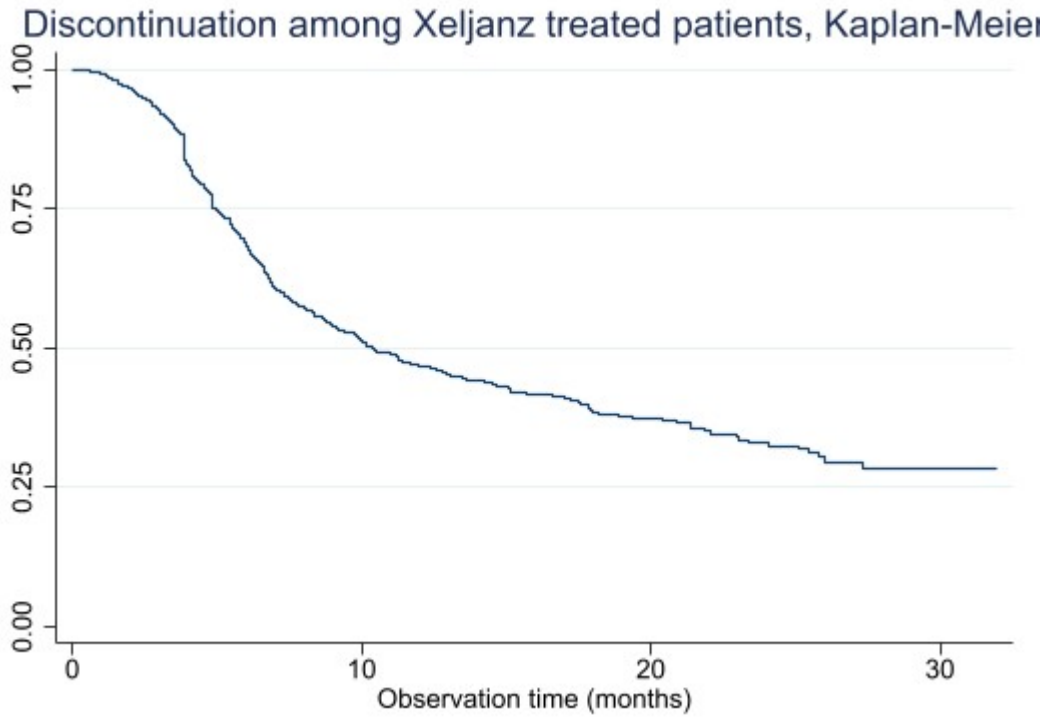

Discontinuation among Xeljanz treated patients, Kaplan-Meier
1.00
0.75
0.50
0.25
0.00
0
10
20
30
Observation time (months)

Table 9. Cause of treatment discontinuation and treatment outcome at 3 and 12 months among patients with rheumatoid arthritis treated with JAKi and with available data in SRQ, 2017-2019 (n=2179)

	JAKi
All	
Reason of discontinuation	
Adverse event	182 (31.01%)
Inefficacy	277 (47.19%)
Pregnancy	<5 (0.17%)
Other	127 (21.64%)
Baseline DAS28	
Remission (<2.6)	44 (4.55%)
Low disease activity (2.6-3.2)	71 (7.35%)
Moderate disease activity (3.2-5.1)	482 (49.90%)
High disease activity (>5.1)	369 (38.20%)
Outcome at 3* Months	
Proportion still on therapy…	894 (49.47%)
and EULAR good response^	45 (20.45%)
or DAS28 < 2.6	57 (15.20%)
or ΔHAQ < -0.2	104 (40%)
Outcome at 12 Months	
Proportion still on therapy…	618 (56.59%)
and EULAR good response	27 (19.29%)
or DAS28 < 2.6	32 (14.04%)
or ΔHAQ < -0.2	59 (39.07%)

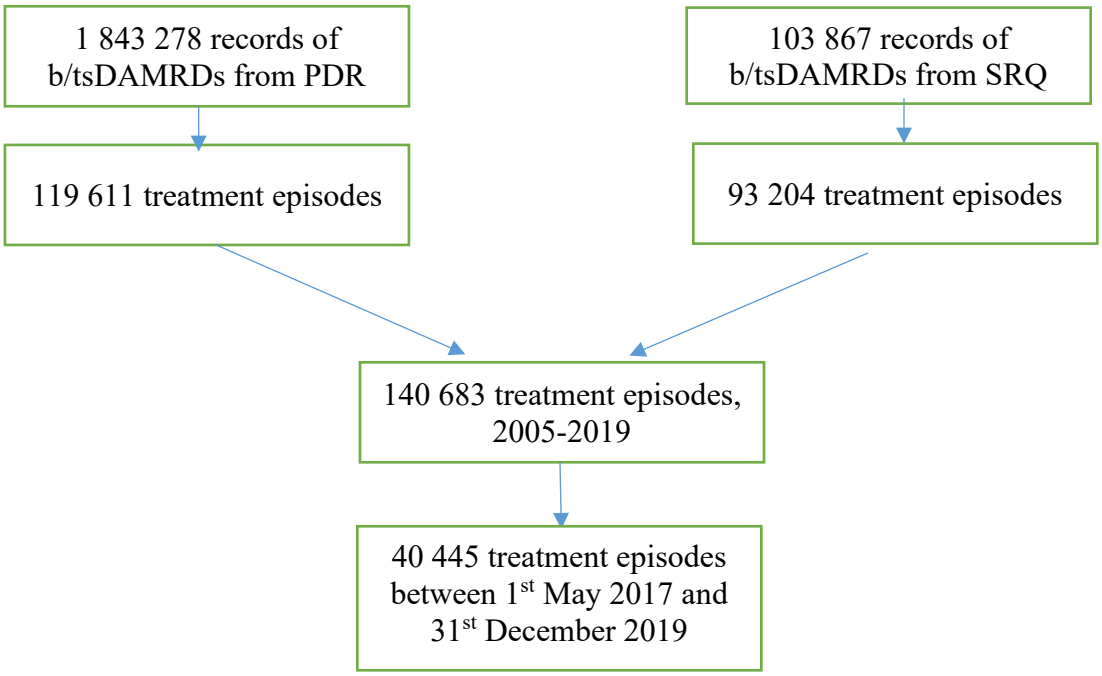
* 3 months data from visit closest to 90 days, between 60 and 183 days; 12 months data from visit closest to 365, between 275 and 455 day, baseline data from visit closet to 0 between -30 and +30. Only patients with enough follow-up time were included in the analyses (for the 3 months, only patients until 1st July 2019 (n=2750), for the 12 months until 2nd October 2018 (n=1454)). The percentages of EULAR good response, DAS28 and HAQ are based on patient with no missing value for the respective variable.
^ The EULAR good response is defined as having DAS28≤3.2 at the endpoint (in this case at 3 or 12 months), and an improvement between the baseline and the endpoint in DAS28 of ≤ 1.2 (Ref.
The Disease Activity Score and the EULAR response criteria. Fransen J, van Riel PL.Rheum Dis Clin North Am. 2009 Nov;35(4):745-57, vii-viii.).

ADDENDUM

We have selected all prescriptions of b/tsDMARD from the PDR and the SRQ, using the following ATC codes:

- Tumor necrosis factor inhibitors (TNFi): L04AB01, L04AB02, L04AB04, L04AB05, L04AB06
- IL-6: L04AC07, L04AC14
- B-cell: L01XC02, L04AA26
- T-cell: L04AA24
- Other Non TNFi bDMARDs: L04AC03, L04AC05, L04AC08, L04AC10, L04AC13
- JAKi included in the report: L04AA37, L04AA29
- other tsDMARDs: L04AA32, L04AA44 (used to calculate line of treatments)

We have collapsed the prescriptions to create treatment episodes: a treatment episode starts when the first prescription of the treatment begins and continues until either a different drug is started or there is a gap of more than 183 days between the end of the previous prescription and the start of the next. Based on the date of drug dispensation and the DDDs (the assumed average maintenance dose per day for a drug used for its main indication in adults), we were able to estimate the end date for each dispensing (date dispensed plus DDD). The data from the PDR are then combined with the highly overlapping data (clinical start and stop dates) on b/tsDMARD from SRQ, as entered by the rheumatologist. Data on infusion drugs are not included in the PDR, solely in SRQ.



SRQ has been the main source of data for the definition of the rheumatological diagnosis. If two different diagnosis were recorded, and since we wanted to have only one diagnosis for each patient, we assigned the diagnosis according to the following hierarchy, with rheumatoid arthritis (RA, ICD code: M05, M06) as the first choice, followed by psoriatic arthritis (PsA, ICD code: L40.5 or M07.0-3), spondyloarthritis (SpA, ICD code: M46.8), ankylosing spondylitis (AS, ICD code: M45), mono/polyarthritis (ICD code: M12.3, M13), juvenile idiopathic arthritis (JIA, ICD code: M08, M09), ulcerative colitis (UC, ICD code: K51), and Crohns´ disease (CD, ICD code: K50). If the patient was not included in the SRQ, the diagnosis was based on data from the NPR, following the same hierarchy . One ICD code, either as main or secondary diagnosis, was sufficient to be assigned to the respective diagnosis (i.e. a patient diagnosed with RA only once as secondary diagnosis was defined to be an RA patient in this report, despite potentially

also having received other diagnosis). This approach has been used in order to avoid to erroneously assign a patient using JAKi to a disease that was not on label.

The final dataset, including 40 445 treatment episodes, has been the bases for all tables. The same patient can have more than one treatment episodes.