

Supplementary tables and figure

Table S1. Baseline characteristics in the sensitivity analysis taking into account only patients with tocilizumab since 2014

N = 1887	TCZ-IV n=882	n	TCZ-SC n =1005	n	p
Total number of visits (median [IQR])	3 [1-5]		2 [1-4]		
Total patient-years	1346.7		11171.4		
Age, yr (median [IQR])	57.6 [48.3, 64.9]	882	57.4 [48.6, 65.4]	1005	0.86
Female gender, n (%)	689 (78.1)	882	825 (82.1)	1005	0.04
Ever smoker	192 (31.3)	613	197 (28.9)	682	0.37
BMI (median [IQR])	25.9 [22.9, 29.6]	714	26.2 [23.1, 29.6]	697	0.53
Disease duration, yr (median [IQR])	6.0 [2.7, 11.7]	714	6.7 [2.8, 13.0]	727	0.14
Seropositivity (RF and/or ACPA), n (%)	617 (81.8)	754	649 (81.4)	797	0.89
Previous bDMARDs, n (%)		704		698	0.40
None	240 (28.8)		306 (32.4)		
1	360 (43.2)		384 (40.7)		
2	171 (20.5)		181 (19.2)		
≥3	63 (7.6)		72 (7.6)		
Glucocorticoids	545 (63.3)	861	587 (60.9)	964	0.31
Glucocorticoid dose, mg/day (median, IQR)	5.0 [5.0, 10.0]	360	5.0 [5.0, 10.0]	347	0.56
Concomitant csDMARD		865		992	0.11
None	280 (32.4)		278 (28.0)		
MTX	270 (31.2)		308 (31.0)		
MTX + other csDMARDs	122 (14.1)		169 (17.0)		
Other than MTX	193 (22.3)		237 (23.9)		
DAS28 (median [IQR])	4.6 [3.4, 5.9]	882	4.1 [3.3, 5.5]	1005	<0.001
CDAI (median, [IQR])	17.0 [14.0, 29.0]	882	17.0 [15.1, 24.5]	1005	0.06
HAQ (median, [IQR])	1.0 [0.9, 1.6]	882	1.0 [1.0, 1.5]	1005	0.78
TJC (over 28 joints) (median, [IQR])	8.0 [3.0, 13.0]	741	6.0 [2.0, 11.0]	860	<0.001
SJC (over 28 joints) (median, [IQR])	6.0 [2.0, 10.0]	740	4.0 [2.0, 8.0]	863	<0.001
PGA (median, [IQR])	60.0 [10.0, 80.0]	627	59.0 [23.5, 78.0]	639	0.66
PhGA (median, [IQR])	40.0 [6.0, 65.0]	741	41.0 [13.0, 60.0]	837	0.22
ESR (mm/hour) (median, [IQR])	30.0 [12.0, 51.0]	582	22.0 [10.0, 40.5]	623	<0.001
CRP (median [IQR])	9.2 [3.0, 26.0]	602	6.7 [2.0, 19.0]	617	<0.001
Education category		377		353	0.23
0-10 years	128 (34.0)		124 (35.1)		
11-13 years	186 (49.3)		155 (43.9)		
>13 years	63 (16.7)		74 (21.0)		
Comorbidities	494 (62.6)	789	511 (58.7)	870	0.12

ACPA: anti-citrullinated protein antibody; bDMARDs: biological disease-modifying antirheumatic drugs; BMI: body mass index; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; CDAI: Clinical Disease Activity Index; DAS28: Disease Activity Score 28; ESR: erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire; IQR: interquartile range; MTX: methotrexate; PGA: patient global assessment; PhGA: Physician global assessment; RF: rheumatoid factor; SJC: swollen joint counts; TCZ-IV: intravenous tocilizumab; TCZ-SC: subcutaneous tocilizumab; TJC: tender joint counts

Table S2 Baseline characteristics in the sensitivity analysis taking into account switching or not between routes of delivery

N = 3448	TCZ-IV only n=2140	TCZ-IV2SC n=274	TCZ-SC only n=1016	TCZ-SC2IV n=18
Total number of visits (median [IQR])	3 [2, 7]	9 [6-11]	2 [1-4]	3 [5-6]
Total patient-years	64978.2	11116.1	11270.7	327.7
Age, yr (median [IQR])	56.8 [48.0, 64.8]	54.3 [42.9, 61.7]	57.3 [48.6, 65.3]	56.3 [45.9, 65.5]
Female gender, n (%)	1694 (79.2)	229 (83.6)	835 (82.2)	15 (83.3)
Ever smoker	405 (32.3)	51 (30.5)	197 (28.8)	5 (41.7)
BMI (median [IQR])	25.7 [22.6, 29.0]	25.1 [22.2, 29.5]	26.2 [23.0, 29.6]	27.3 [24.4, 29.4]
Disease duration, yr (median [IQR])	6.2 [2.7, 12.3]	5.8 [2.9, 11.9]	6.6 [2.7, 13.0]	8.2 [4.3, 14.1]
Seropositivity (RF and/or ACPA), n (%)	1372 (79.5)	200 (83.3)	649 (81.3)	14 (87.5)
Previous bDMARDs, n (%)				
None	626 (31.2)	66 (25.2)	317 (33.5)	2 (11.8)
1	811 (40.5)	110 (42.0)	380 (40.1)	7 (41.2)
2	403 (20.1)	71 (27.1)	179 (18.9)	6 (35.3)
≥3	164 (8.2)	15 (5.7)	71 (7.5)	2 (11.8)
Glucocorticoids	1244 (59.6)	192 (78.0)	597 (61.2)	8 (47.1)
Glucocorticoid dose, mg/day (median, IQR)	5.0 [5.0, 10.0]	5.0 [5.0, 10.0]	5.0 [5.0, 10.0]	8.0 [5.0, 9.0]
Concomitant csDMARD				
None	596 (28.4)	79 (29.3)	277 (27.6)	7 (38.9)
MTX	843 (40.1)	117 (43.3)	312 (31.1)	5 (27.8)
MTX + other csDMARDs	266 (12.7)	29 (10.7)	173 (17.3)	2 (11.1)
Other than MTX	397 (18.9)	45 (16.7)	240 (24.0)	4 (22.2)
DAS28 (median [IQR])	4.4 [3.3, 5.8]	5.5 [4.0, 6.6]	4.1 [3.3, 5.5]	5.0 [3.3, 5.5]
CDAI (median, [IQR])	17.0 [13.5, 27.0]	23.6 [13.6, 37.0]	17.0 [15.1, 24.5]	20.0 [9.1, 26.8]
HAQ (median, [IQR])	1.0 [0.9, 1.7]	1.4 [0.9, 1.9]	1.0 [1.0, 1.5]	1.1 [0.5, 1.6]
TJC (over 28 joints) (median, [IQR])	8.0 [3.0, 13.0]	10.0 [5.0, 15.0]	6.0 [2.0, 11.0]	6.5 [4.8, 8.8]
SJC (over 28 joints) (median, [IQR])	6.0 [2.0, 10.0]	7.0 [3.0, 11.0]	4.0 [2.0, 8.0]	5.0 [1.0, 6.5]
PGA (median, [IQR])	53.0 [8.0, 79.0]	70.0 [40.0, 80.0]	60.0 [25.0, 78.0]	50.0 [7.5, 65.0]
PhGA (median, [IQR])	40.0 [6.0, 63.0]	60.0 [35.0, 71.0]	41.0 [15.0, 60.0]	40.0 [4.5, 55.0]
ESR (mm/hour) (median, [IQR])	26.0 [10.0, 46.0]	29.5 [12.0, 44.8]	22.0 [10.0, 41.0]	36.0 [18.0, 58.0]
CRP (mg/L) (median, [IQR])	8.9 [3.0, 24.0]	13.0 [3.1, 35.0]	6.6 [2.0, 19.0]	11.0 [1.4, 43.0]
Education category				
0-10 years	350 (37.8)	44 (25.3)	126 (35.9)	1 (10.0)
11-13 years	437 (47.1)	101 (58.0)	153 (43.6)	5 (50.0)
>13 years	140 (15.1)	29 (16.7)	72 (20.5)	4 (40.0)
Comorbidities	1180 (60.9)	130 (68.4)	515 (58.5)	9 (52.9)

ACPA: anti-citrullinated protein antibody; bDMARDs: biological disease-modifying antirheumatic drugs; BMI: body mass index; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; CDAI: Clinical Disease Activity Index; DAS28: Disease Activity Score 28; ESR: erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire; IQR: interquartile range; MTX: methotrexate ; PGA: patient global assessment; PhGA: Physician global assessment; RF: rheumatoid factor; SJC: swollen joint counts; TCZ-IV: intravenous tocilizumab; TCZ-IV2SC: TCZ-IV switching to TCZ-SC; TCZ-SC: subcutaneous tocilizumab; TCZ-SC2IV; TCZ-SC switching to TCZ-IV; TJC: tender joint counts

Table S3. Multivariable analysis of drug discontinuation by delivery route stratifying or adjusting by year of treatment initiation only

	HR	95%CI	p
Stratification by year of treatment initiation			
TCZ-IV	--	--	--
TCZ-SC	0.98	0.85-1.12	0.73
Adjustment by year of treatment initiation (ref: 2009)			
TCZ-IV	--	--	--
TCZ-SC	0.93	0.82-1.06	0.27
2010	1.52	1.15-2.00	0.003
2011	1.52	1.16-2.00	0.002
2012	1.69	1.28-2.23	<0.001
2013	1.94	1.47-2.56	<0.001
2014	2.05	1.55-2.71	<0.001
2015	2.69	2.03-3.57	<0.001
2016	4.05	3.02-5.43	<0.001
2017-2018	9.09	6.57-12.56	<0.001

Table S4 Multivariable analysis of DAS28 over time			
	coeff	95%CI	p
Treatment at baseline			
TCZ-IV	--	--	
TCZ-SC	-0.15	-0.26--0.05	0.004
Time, yr	-0.93	-1.01--0.86	<0.001
Time-squared	0.25	0.23-0.28	<0.001
Time-cubed	-0.02	-0.02--0.02	<0.001
Age, yr	0.00	-0.00-0.00	0.68
Female gender	0.17	0.05-0.28	0.006
Disease duration, yr	0.00	-0.01-0.01	0.98
Seropositivity	-0.16	-0.28--0.04	0.01
BMI	0.01	0.00-0.01	0.25
Smoking	-0.02	-0.12-0.07	0.63
Glucocorticoid	0.21	0.14-0.28	<0.001
Concomitant csDMARD (base= none)			
Any csDMARD	0.06	-0.01-0.13	0.10
MTX	0.09	0.01-0.17	0.02
MTX + other csDMARDs	0.03	-0.11-0.17	0.68
Other than MTX	-0.02	-0.13-0.08	0.69
Previous bDMARDs (base = none)			
1	0.07	-0.04-0.18	0.22
2	0.06	-0.07-0.18	0.38
≥3	0.18	0.01-0.36	0.04
HAQ at baseline	0.45	0.39-0.52	<0.001
ESR	0.05	0.05-0.06	<0.001
Comorbidity	0.02	-0.08-0.12	0.73

bDMARDs: biological disease-modifying antirheumatic drugs; BMI: body mass index; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; CDAI: Clinical Disease Activity Index; ESR: erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire; MTX: methotrexate; TCZ-IV: intravenous tocilizumab; TCZ-SC: subcutaneous tocilizumab;

Table S5. Baseline characteristics of patients matched by propensity score and exact matching for category of CDAI, HAQ and erythrocyte sedimentation rate for the analysis of LUNDEX index

N = 1122	TCZ-IV n=561	TCZ-SC n =561	p
Age, yr (median [IQR])	56.7 [48.5, 64.8]	56.9 [47.9, 64.6]	0.87
Female gender, n (%)	448 (80.0)	438 (78.2)	0.51
Ever smoker	124 (32.9)	116 (33.4)	0.94
BMI (median [IQR])	26.2 [23.1, 29.7]	26.1 [23.0, 29.3]	0.59
Disease duration, yr (median [IQR])	6.3 [2.8, 11.8]	5.9 [2.3, 11.9]	0.41
Seropositivity (RF and/or ACPA), n (%)	380 (82.1)	370 (81.9)	1.00
Previous bDMARDs, n (%)			0.31
None	182 (34.4)	155 (29.1)	
1	215 (40.6)	229 (43.0)	
2	95 (18.0)	104 (19.5)	
≥3	37 (7.0)	44 (8.3)	
Glucocorticoids	344 (62.3)	315 (58.9)	0.27
Concomitant csDMARD			0.20
None	162 (29.4)	175 (31.7)	
MTX	162 (29.4)	180 (32.6)	
MTX + other csDMARDs	91 (16.5)	89 (16.1)	
Other than MTX	136 (24.7)	108 (19.6)	
CDAI (median, [IQR])	17.0 [14.0, 24.1]	17.0 [13.7, 24.8]	0.84
HAQ (median, [IQR])	1.0 [0.9, 1.5]	1.0 [0.9, 1.5]	0.50
ESR (mm/hour) (median, [IQR])	25.0 [9.0, 45.0]	25.0 [10.8, 43.0]	0.61
Comorbidities	294 (58.9)	320 (65.0)	0.05

ACPA: anti-citrullinated protein antibody; bDMARDs: biological disease-modifying antirheumatic drugs; BMI: body mass index; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; CDAI: Clinical Disease Activity Index; DAS28: Disease Activity Score 28; ESR: erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire; IQR: interquartile range; MTX: methotrexate; RF: rheumatoid factor; TCZ-IV: intravenous tocilizumab; TCZ-SC: subcutaneous tocilizumab; TJC: tender joint counts

Table S6. Median CDAI at baseline visit, last visit in all patients, and last visit before switch for patients switching between routes of delivery. The CDAI may vary from the CDAI described in Table 1 because no imputation was made when the variable was missing at the visit

	TCZ-IV only	TCZ-IV2SC	TCZ-SC only	TCZ-SC2IV
Baseline	25.0 (14-36.5)	30.7 (19.4-41.0)	22 (12.6-32.0)	24.5 (14-27.0)
Last visit before switch	-	8.0 (3.0-15.4)	-	6.6 (0.7-15.9)
At last visit	8.5 (3-18.0)	5.8 (2.9-9.4)	7.7 (3.5-14.0)	6.0 (3.4-8.4)
Values are median (interquartile range)				

Figure S1. Unadjusted Kaplan-Meier curves of drug discontinuation by route of administration taking into account only patients with tocilizumab since 2014. TCZ-IV, intravenous tocilizumab; TCZ-SC, subcutaneous tocilizumab

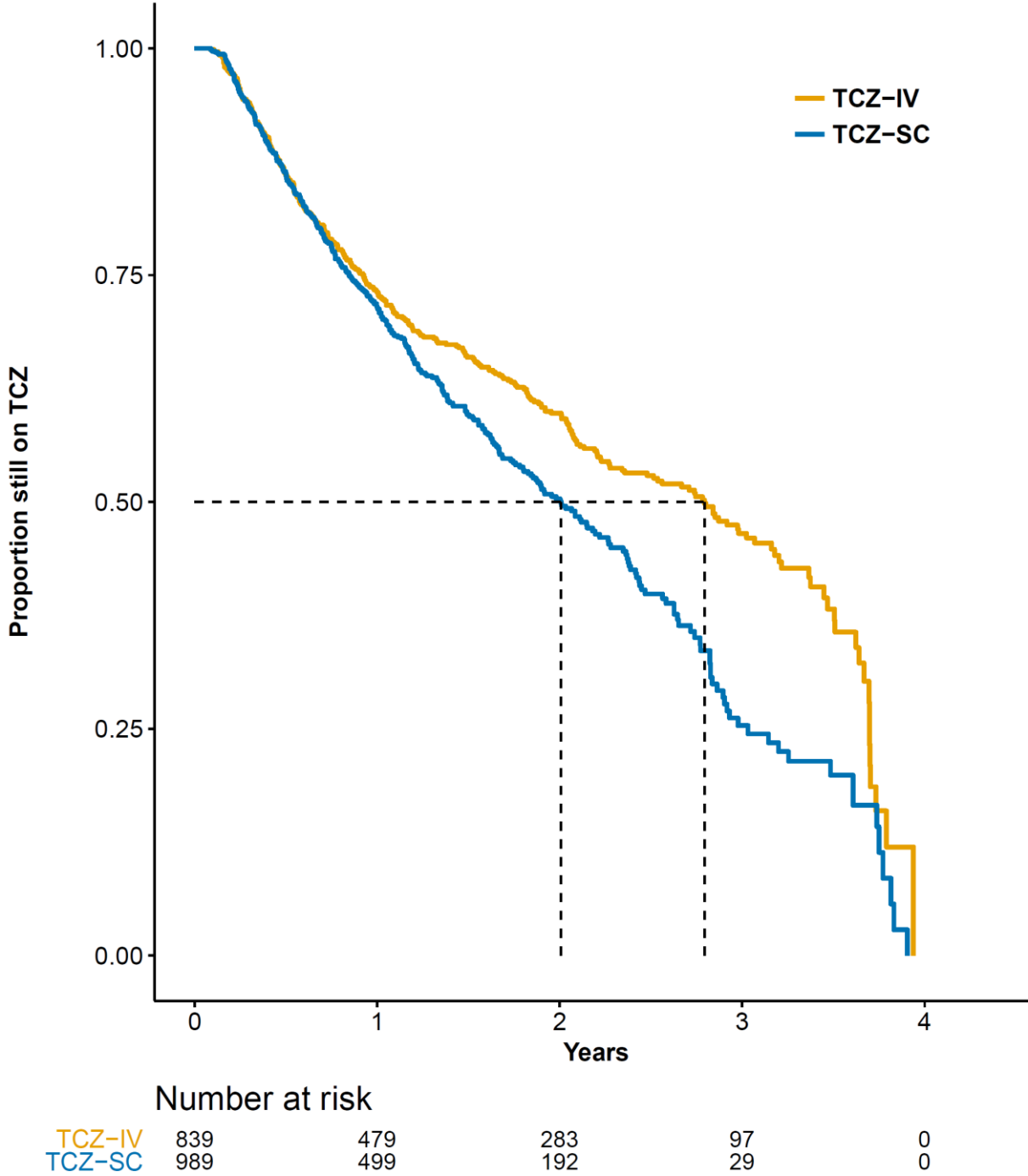
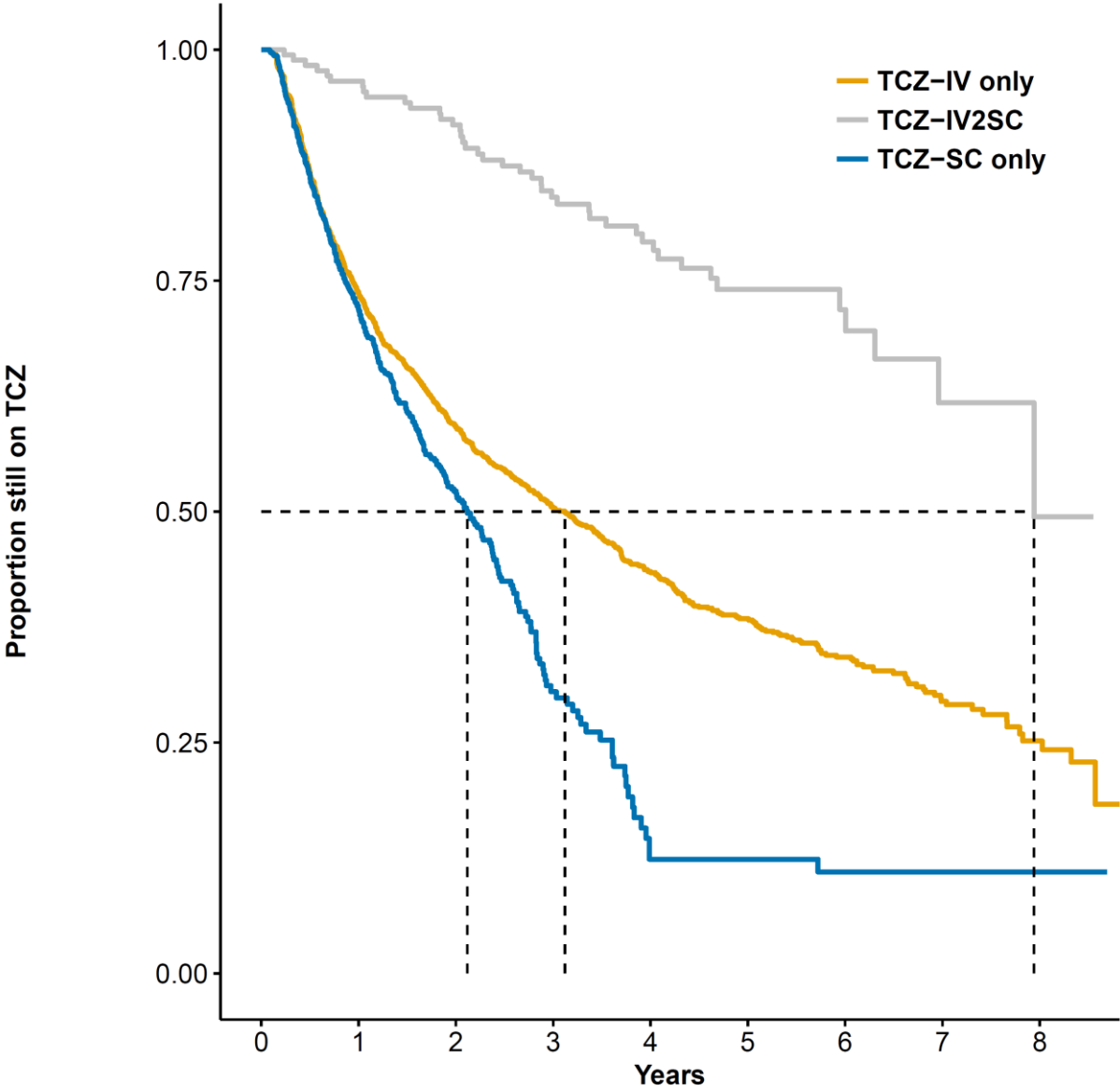


Figure S2. Unadjusted Kaplan-Meier curves of drug discontinuation by route of administration comparing patients who switched from intravenous to subcutaneous tocilizumab to patients who stayed on the same route of delivery. TCZ-IV: tocilizumab iv only, TCZ-IV2SC: patients switching from intravenous tocilizumab to subcutaneous tocilizumab, and TCZ-SC: tocilizumab subcutaneous



Number at risk

TCZ-IV only	2121	1358	941	641	427	273	169	87	28
TCZ-IV2SC	177	167	148	119	89	54	31	12	4
TCZ-SC only	1000	512	212	47	11	10	8	7	4