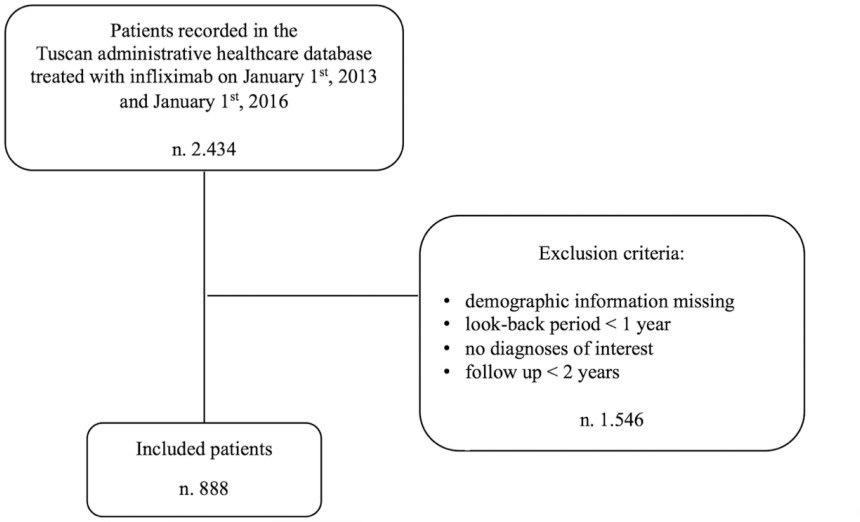
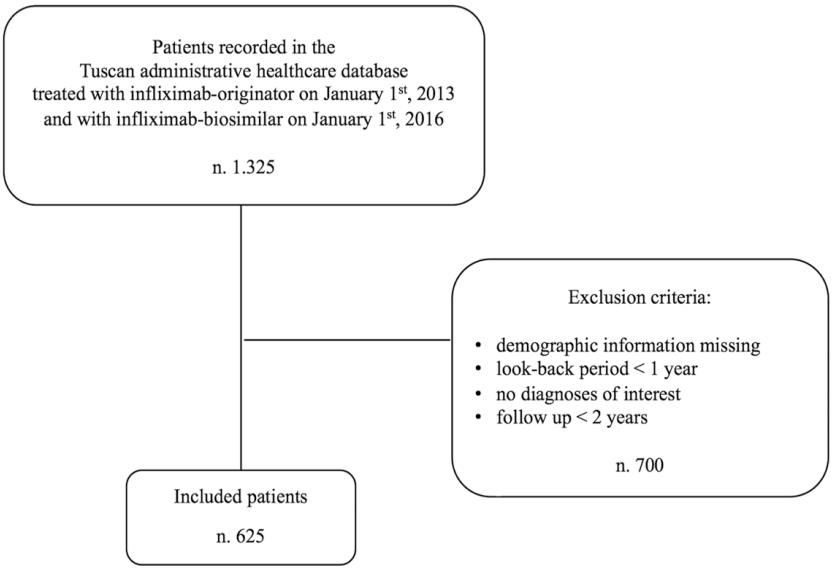
Supplementary file



Supplementary Fig. S1. Flow chart of patient selection; first analysis.



Supplementary Fig. S2. Flow chart of patient selection; second analysis.

Supplementary Table S1. Characteristics of included patients before Propensity Score matching; the first analysis.

	Unmatched		
	2013 [¶]	2016 [¶]	*p*-value [#]
Patients, n	454	434	
Male, n (%)	268 (59.0)	256 (59.0)	1.000
Age, mean (SD)	39.22 (17.23)	40.03 (17.75)	0.493
Duration of treatment in years, mean (SD)	1.81 (1.91)	3.07 (2.76)	<0.001
Disease, n (%)			0.005
Only one disease			
Rheumatoid arthritis	57 (12.6)	47 (10.8)	
Psoriatic arthritis	39 (8.6)	35 (8.1)	
Ankylosing spondylitis	81 (17.8)	79 (18.2)	
Ulcerative colitis	41 (9.0)	48 (11.1)	
Crohn's disease	35 (7.7)	53 (12.2)	
Psoriasis	34 (7.5)	12 (2.8)	
Two diseases			
Two gastroenterological diseases	31 (6.8)	48 (11.1)	
Two rheumatologic diseases	33 (7.3)	33 (7.6)	
Gastroenterological and dermatological diseases	4 (0.9)	2 (0.5)	
Rheumatologic and dermatological diseases	40 (8.8)	23 (5.3)	
Rheumatologic and gastroenterological diseases	34 (7.5)	24 (5.5)	
≥3 diseases			
Multiple diseases	25 (5.5)	30 (6.9)	

[¶]The 2013 cohort and 2016 cohort included patients treated with infliximab on January 1st, 2013 and January 1st, 2016, respectively.
[#]p-values were estimated by t-test and chi-squared test for comparing means and proportions, respectively
n: number; SD: standard deviation.

Supplementary Table S2. Distribution of persistent patients stratified by diseases; the first analysis.

	Matched [§]	
	2013 [¶]	2016 [¶]
Patients, n		
Overall	303	303
Persistent	157	148
Only one disease		
Rheumatoid arthritis	26	20
Psoriatic arthritis	8	13
Ankylosing spondylitis	27	31
Ulcerative colitis	9	5
Crohn's disease	13	19
Psoriasis	4	6
Two diseases		
Two gastroenterological	16	17
Two rheumatologic	18	4
Gastroenterological and dermatological	2	2
Rheumatologic and dermatological	12	12
Rheumatologic and gastroenterological	9	8
Multiple diseases		
Three or more	13	11

[§]Patients were matched for gender, age, disease, and duration of infliximab treatment in years.
[¶]The 2013 cohort included patients treated with infliximab on January 1st, 2013 and the 2016 cohort included those treated with infliximab on January 1st, 2016.

Supplementary Table S3. Most common causes for Emergency Department admission and hospitalisation in the matched cohorts; the first and second analyses.

	First analysis		Second analysis	
	2013 ¶	2016 ¶	Originator*	Biosimilar*
Patients, n	303	303	265	169
Patients with at least one ED admission or hospitalisation, n (%)	171 (56.4)	176 (58.1)	153 (57.7)	94 (55.6)
Patients with at least one ED admission or hospitalisation for kidney injuries, n (%)	7 (2.3)	1 (0.3)	7 (2.6)	1 (0.6)
Patients with at least one ED admission or hospitalisation for infections, n (%)	16 (5.3)	27 (8.9)	18 (6.8)	13 (7.7)
Patients with at least one ED admission or hospitalisation for neoplasm, n (%)	-	-	-	-
Patients with at least one ED admission or hospitalisation for cardiovascular disorders, n (%)	20 (6.6)	27 (8.9)	18 (6.8)	12 (7.1)

¶The 2013 cohort included patients treated with infliximab on January 1st, 2013 and the 2016 cohort included those treated with infliximab on January 1st, 2016.
*The originator cohort included patients treated with infliximab-originator on January 1st, 2013 and the biosimilar cohort included those treated with infliximab-biosimilar on January 1st, 2016.
n: number; ED: Emergency Department.

Supplementary Table S4. Minimum detectable odds-ratio with 80% power; the first analysis.

	2013 ¶,§	2016 cohort ¶					
	n (%)	Overall §,a n (%)	Minimum detectable OR[C]	Originator[b] n (%)	Minimum detectable OR[C]	Biosimilar[c] n (%)	Minimum detectable OR[C]
All patients	303	303		169		134	
Persistent patients	157 (51.8)	148 (48.8)	0.63 / 1.59	89 (52.7)	0.58 / 1.73	59 (44.0)	0.56 / 1.80
Patients with at least one ED admission or hospitalisation	171 (56.4)	176 (58.1)	0.63 / 1.60	100 (59.2)	0.58 / 1.74	76 (56.7)	0.56 / 1.82
Patients with at least one ED admission	117 (38.6)	135 (44.6)	0.62 / 1.58	78 (46.2)	0.56 / 1.73	57 (42.5)	0.54 / 1.80
Patients with at least one hospitalisation	111 (36.6)	115 (38.0)	0.61 / 1.59	64 (37.9)	0.56 / 1.73	51 (38.1)	0.54 / 1.81
Patients with at least one specialist visit	210 (69.3)	242 (79.9)	0.62 / 1.69	137 (81.1)	0.57 / 1.85	105 (78.4)	0.54 / 1.94
Patients with at least one rheumatologic visit	111 (36.6)	139 (45.9)	0.61 / 1.59	96 (56.8)	0.56 / 1.73	43 (32.1)	0.54 / 1.81
Patients with at least one gastroenterological visit	89 (29.4)	93 (30.7)	0.59 / 1.62	38 (22.5)	0.53 / 1.77	55 (41.0)	0.51 / 1.86
Patients with at least one dermatological visit	72 (23.8)	92 (30.4)	0.56 / 1.66	46 (27.2)	0.51 / 1.83	56 (34.3)	0.48 / 1.92

¶The 2013 cohort and 2016 cohort included patients treated with infliximab on January 1st, 2013 and January 1st, 2016, respectively.
§Patients were matched for gender, age, disease, and duration of infliximab tre≠atment in years.
[a]comparison between the overall 2016 cohort and the 2013 cohort; [b]comparison between the 2016 infliximab-originator cohort and the 2013 cohort (infliximab-originator only); [c]comparison between the 2016 infliximab-biosimilar cohort and the 2013 cohort.
[C]Using a one-sided test at the alpha = 5% level.
ED: Emergency Department; n: number; OR: odds ratio.

Supplementary Table S5. Characteristics of included patients before Propensity Score matching; the second analysis.

	Unmatched		*p*-value [#]
	Originator [¶]	Biosimilar [¶]	
Patients, n	454	171	
Male, n (%)	268 (59.0)	95 (55.6)	0.488
Age, mean (SD)	39.2 (17.23)	36.4 (17.31)	0.070
Duration of treatment in years, mean (SD)	1.8 (1.91)	2.2 (2.92)	0.066
Disease, n (%)			<0.001
Only one disease			
Rheumatoid arthritis	57 (12.6)	15 (8.8)	
Psoriatic arthritis	39 (8.6)	10 (5.8)	
Ankylosing spondylitis	81 (17.8)	14 (8.2)	
Ulcerative colitis	41 (9.0)	29 (17.0)	
Crohn's disease	35 (7.7)	28 (16.4)	
Psoriasis	34 (7.5)	7 (4.1)	
Two diseases			
Two gastroenterological diseases	31 (6.8)	22 (12.9)	
Two rheumatologic diseases	33 (7.3)	10 (5.8)	
Gastroenterological and dermatological diseases	4 (0.9)	2 (1.2)	
Rheumatologic and dermatological diseases	40 (8.8)	15 (8.8)	
Rheumatologic and gastroenterological diseases	34 (7.5)	9 (5.3)	
≥ 3 diseases			
Multiple diseases	25 (5.5)	10 (5.8)	

[¶]The originator cohort included patients treated with infliximab-originator on January 1st, 2013 and the biosimilar cohort included those treated with infliximab-biosimilar on January 1st, 2016.
[#]*p*-values were estimated by t-test and chi-squared test for comparing means and proportions, respectively.
n: number; SD: standard deviation.

Supplementary Table S6. Distribution of persistent patients stratified by diseases; the second analysis.

	Matched [§]	
	Originator [¶]	Biosimilar [¶]
Patients, n		
Overall	265	169
Persistent	145	78
Only one disease		
Rheumatoid arthritis	26	15
Psoriatic arthritis	16	10
Ankylosing spondylitis	32	14
Ulcerative colitis	41	29
Crohn's disease	34	27
Psoriasis	14	7
Two diseases		
Two gastroenterological	31	21
Two rheumatologic	15	10
Gastroenterological and dermatological	4	2
Rheumatologic and dermatological	21	15
Rheumatologic and gastroenterological	17	9
Three or more	14	10

[§]Patients were matched for gender, age, disease, and duration of infliximab treatment in years.
[¶]The originator cohort included patients treated with infliximab-originator on January 1st, 2013 and the biosimilar cohort included those treated with infliximab-biosimilar on January 1st, 2016.

Supplementary Table S7. Minimum detectable odds-ratio with 80% power; the second analysis.

	Originator[¶]			Biosimilar[¶]					
	Overall[§] n (%)	Naïve n (%)	Prevalent n (%)	Overall[§,a] n (%)	Minimum detectable OR[C]	Naïve[b] n (%)	Minimum detectable OR[C]	Switchers[c] n (%)	Minimum detectable OR[C]
All patients	265	85	180	169		78		91	
Persistent patients	145 (54.7)	27 (31.8)	118 (65.6)	78 (46.2)	0.62 / 1.64	26 (33.2)	0.34 / 2.47	52 (57.1)	0.48 / 2.24
Patients with at least one ED admission or hospitalisation	153 (57.7)	49 (57.6)	104 (57.8)	94 (55.6)	0.63 / 1.64	51 (65.4)	0.41 / 2.62	43 (47.3)	0.48 / 2.13
Patients with at least one hospitalisation	106 (40.0)	40 (47.1)	66 (37.6)	63 (37.3)	0.59 / 1.64	45 (57.7)	0.39 / 2.47	18 (19.8)	0.45 / 2.08
Patients with at least one ED admission	102 (38.5)	35 (41.2)	67 (37.2)	72 (42.6)	0.59 / 1.67	32 (41.0)	0.38 / 2.44	40 (44.0)	0.46 / 2.08
Patients with at least one specialist visit	191 (72.1)	75 (88.2)	116 (64.4)	134 (79.3)	0.59 / 1.67	63 (80.8)	0.32 / 11.48	71 (78.0)	0.48 / 2.22
Patients with at least one rheumatologic vis≠it	92 (34.7)	20 (23.5)	72 (40.0)	56 (33.1)	0.63 / 1.69	29 (37.2)	0.27 / 2.60	27 (29.7)	0.46 / 2.07
Patients with at least one gastroenterological visit	85 (32.1)	61 (71.8)	24 (13.3)	77 (45.6)	0.57 / 1.69	37 (47.4)	0.40 / 3.21	40 (44.0)	0.27 / 2.60
Patients with at least one dermatological visit	68 (25.7)	16 (18.8)	52 (28.9)	53 (31.4)	0.56 / 1.71	17 (21.8)	0.22 / 2.73	36 (39.6)	0.42 / 2.15

[¶]The originator cohort included patients treated with infliximab-originator on January 1st, 2013 and the biosimilar cohort included those treated with infliximab-biosimilar on January 1st, 2016.

[§]Patients were matched for gender, age, disease, and duration of infliximab treatment in years.

[a]comparison between the overall biosimilar cohort and the overall originator cohort; [b]comparison between the naïve biosimilar cohort and the naïve originator cohort; [c]comparison between the switcher biosimilar cohort and the prevalent originator cohort.

[C] Using a one-sided test at the alpha = 5% level.

ED: Emergency Department; n: number; OR: odds ratio.