

1.1 Supplementary Material

List of ICD-9CM codes and exemption codes (EC) for comorbidities considered in the study.

Diabetes, ICD-9CM codes: 25002501, 2502, 2503, 2507, 2504, 2505, 2506. EC: "013.250".

Malignancies, ICD-9CM codes: 14, 15, 16, 18, 170, 171, 172, 174, 175, 176, 179, 190, 191, 192, 193, 194, 1950, 1951, 1952, 1953, 1954, 1955, 1958, 200, 201, 202, 203, 204, 205, 206, 207, 208, 196, 197, 198, 1990, 1991. EC: "048".

Chronic obstructive pulmonary disease (COPD), ICD-9CM codes: 490, 491, 492, 493, 494, 495, 496, 500, 501, 502, 503, 504, 505. EC: "024.518.81".

Acquired immune deficiency syndrome (AIDS), ICD-9CM codes: 042, 043, 044. EC: "020".

Liver disease, ICD-9CM codes: 5712, 5714, 5715, 5716, 5722, 5723, 5724, 5728. EC: "008.571.2", "008.571.5", "008.571.6", "016"

Chronic kidney disease, ICD-9CM codes: 582, 5830, 5831, 5832, 5833, 5835, 5836, 5837, 5834, 585586588. EC: "031.403", "031.404", "D31.403", "D31.404", "023"

Congestive heart failure (HF), ICD-9CM code: 428. EC: "021.428".

Acute myocardial infarction (AMI), ICD-9CM codes: 410, 412. EC: "002.414"

Peripheral vascular disease, ICD-9CM codes: 441, 4439, 7854, V434. EC: "002.441.2", "002.441.7", "002.441.9", "002.442", "002.444", "002.447.1"

Cerebrovascular accident, ICD-9CM codes: 430–438. EC: "002.433", "002.434", "002.437"

Dementia, ICD-9CM code: 290. EC: "011.290.0", "011.290.1", "011.290.2", "011.290.4", "011.291.1", "011.294.0", "029.331.0".

Haemiplegia, ICD-9CM codes: 342, 3441.

Connective tissue diseases, ICD-9CM codes: 7100, 7101, 7104, 7140, 7141, 7142, 71481(5171), 725.

Peptic ulcer disease, ICD-9CM codes: 531, 532, 533, 534.

Supplementary table S1. Duration of drug exposure and prevalence of comorbidities for each bDMARD considered in final analysis.

bDMARD	Number of treatment courses (first-line)	Mean (SD) days of drug exposure in first-line treatment strategy	Comorbidities, N (%)	Number of treatment courses (subsequent lines of treatment)	Mean (SD) days of drug exposure in subsequent lines of treatment	Comorbidities, N (%)
ABA	189	648.41 (470.09)	37 (19.58)	562	724.7 (583.85)	61 (10.85)
ADA	1,143	1,220.12 (1,036.12)	122 (10.67)	556	741.73 (716.29)	62 (11.15)
CTZ	156	520.13 (327.40)	12 (7.69)	155	451.43 (326.20)	14 (9.03)
ETA	1,787	1,349.28 (1,064.98)	238 (13.32)	691	972.45 (903.12)	81 (11.72)
GOL	151	551.76 (334.13)	17 (11.26)	178	480.75 (350.77)	23 (12.92)
IFX	861	1,234.07 (1,075.78)	88 (10.22)	188	647.86 (668.08)	21 (11.17)
RTX	179	633.63 (575.83)	111 (62.01)	338	776.86 (618.17)	43 (12.72)
TCZ	191	681.32 (427.51)	23 (12.04)	368	586.41 (417.70)	43 (11.68)

List of abbreviations: bDMARDs – biological disease-modifying antirheumatic drugs; SD – standard deviation; ABA – abatacept; ADA – adalimumab; CTZ – certolizumab pegol; ETA – etanercept; GOL – golimumab; IFX – infliximab; RTX – rituximab; TCZ – tocilizumab.

Supplementary table S2. Univariate analysis of bDMARDs prescription relative risk in the subsequent lines of treatment (following first one), related to each comorbidity.

bDMARD subsequent lines	Comorbidities								
	OR (95%CI)	1 comorbidity	≥ 2 comorbidities	AMI	COPD	Mild liver disease	Diabetes mellitus	Solid tumour	Infections
ABA		0.99	0.37	1.23	1.23	0.65	1.08	0.49	1.41
		(0.69-1.43)	(0.10-1.33)	(0.40-3.84)	(0.35-4.28)	(0.27-1.55)	(0.67-1.73)	(0.19-1.26)	(1.04-1.89)
ADA		0.92	1.11	1.67	1.75	0.83	0.99	0.74	1.11
		(0.63-1.34)	(0.45-2.76)	(0.57-4.83)	(0.55-5.54)	(0.37-1.85)	(0.61-1.60)	(0.32-1.71)	(0.82-1.52)
CTZ		0.85	N.A.	N.A.	0.89	N.A.	1.15	0.59	1.23
		(0.47-1.56)			(0.10-7.68)		(0.56-2.36)	(1.33-2.60)	(0.77-1.96)
ETA		1	1	1	1	1	1	1	1
GOL		1.11	1.18	3.30	2.35	0.77	0.89	1.30	1.48
		(0.65-1.88)	(0.32-4.34)	(0.99-10.94)	(0.56-9.94)	(0.22-2.70)	(0.42-1.87)	(0.47-3.63)	(0.97-2.26)
IFX		0.98	0.73	1.23	0.73	0.24	1.45	0.98	1.48
		(0.57-1.67)	(0.16-3.37)	(0.25-6.13)	(0.09-6.32)	(0.03-1.84)	(0.78-2.69)	(0.32-2.99)	(0.98-2.24)
RTX		1.14	0.83	2.06	0.82	1.37	1.05	0.81	1.24
		(0.75-1.72)	(0.26-2.66)	(0.66-6.45)	(0.16-4.23)	(0.61-3.09)	(0.60-1.83)	(0.31-2.12)	(0.87-1.76)
TCZ		1.08	0.38	1.25	1.89	0.37	1.17	0.62	1.05
		(0.72-1.63)	(0.08-1.72)	(0.35-4.47)	(0.54-6.57)	(0.11-1.29)	(0.69-1.97)	(0.22-1.72)	(0.74-1.49)

List of abbreviations: bDMARDs – biologic disease-modifying anti-rheumatic drugs; OR – odds ratio; AMI – acute myocardial infarction; COPD – chronic obstructive pulmonary disease; ABA – abatacept; ADA – adalimumab; CTZ – certolizumab; ETA – etanercept; GOL – golimumab; IFX – infliximab; RTX – rituximab; TCZ – tocilizumab; N.A. – not applicable.