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Prescribing patterns and clinical outcomes of biological disease-modifying anti-rheumatic drugs for rheumatoid arthritis in Spain

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Abstract. – OBJECTIVE: New treatments in rheumatoid arthritis (RA) have been developed to improve patient outcomes, raise their quality of life, and reduce joint damage, but long-term responses and remission remain low. This study aimed to analyse the Spanish prescribing patterns and the effectiveness of biological (b) disease-modifying anti-rheumatic drugs (DMARDs) available for RA in clinical practice.

PATIENTS AND METHODS: An observational retrospective study was performed in a teaching hospital, analysing the different combinations of drugs prescribed, real-life effectiveness and reasons for withdrawal.

RESULTS: In total, 210 patients were included, with 19 different patterns (pharmacological groups alone or in combination) of treatment prescribed. Most patients started their treatment with a conventional synthetic (cs) DMARD alone or in combination with a glucocorticosteroid. Among the initial patterns, treatment with only one csDMARD showed a longer duration. The time to first bDMARD was 6 years. TNF-α inhibitors are the most commonly prescribed drugs as initial biological treatments. The highest percentages of good responses and remissions were achieved with tocilizumab, etanercept and infliximab. The time to remission was also lower with tocilizumab. Lack of response, adverse effects and remission were the main causes of bDMARD withdrawal. The duration of treatments until withdrawal was similar among bDMARDs, except for rituximab, for which the duration was slightly shorter.

CONCLUSIONS: Prescribing pattern analysis showed the highest responses and remission rates with tocilizumab and TNF-α inhibitors. The main reasons for withdrawal were lack of response and adverse effects. Further research is needed to improve pharmacological RA management in real-life settings.

Key Words:

Rheumatoid arthritis, Biologic agents, Disease modifying anti-rheumatic drug, Prescribing patterns.

Introduction

Rheumatoid arthritis (RA) is a chronic, systemic and autoimmune disease that affects 0.5-1% of adults in industrialized countries[1]. In 2002, the EPISER study estimated a cumulative prevalence for RA of 0.5 (0.2-0.8) in the Spanish population[2]. RA is a progressive disease characterized by persistent joint inflammation that can produce a loss of functionality, reduce quality of life and enhance morbidity and mortality. The goals of its treatment are to minimize the activity of the disease, preventing joint damage and therefore improving quality of life[3].

In the last 30 years, new treatment paradigms in RA have been developed, including early diagnosis, intensive management and new drugs. These new paradigms have significantly improved patient outcomes, raising the quality of life and reducing joint damage[3-5]. Currently, the management of RA combines non-pharmacological therapies, such as physical and occupational therapy, lifestyle changes and surgical approaches, and pharmacological treatments, including non-steroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, conventional synthetic (cs) disease-modifying anti-rheumatic drugs (DMARDs) (e.g., methotrexate, sulfasalazine, hydroxychloroquine, leflunomide and cyclosporine), biological (b) DMARDs (e.g., infliximab, etanercept, adalimumab, rituximab, abatacept, anakinra, certolizumab, golimumab and tocilizumab) and targeted synthetic (ts) DMARDs (e.g., tofacitinib and baricitinib)[6].

Today, one key recommendation in the treatment of RA to control the progression of the disease is an early diagnosis followed by an effective pharmacological treatment, especially in the first 3-6 months after diagnosis. The 2016 European League Against Rheumatism (EULAR)

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recommendations[7] established the convenience of starting treatment with DMARD drugs as soon as possible after diagnosis. However, despite the growing number of drugs available to treat RA, the management of this disease could often be complex, and the effectiveness of some drugs could be reduced in the long-term treatment; furthermore, remission or low-activity disease are not always achievable[8]. Therefore, the analysis of the outcomes in clinical practice of different pharmacological prescribing patterns in the treatment of RA could be useful to improve the control of this disease. The aim of our study was to analyse the Spanish prescribing patterns and clinical outcomes in the effectiveness of bDMARDs available for RA.

Patients and Methods

An observational retrospective study was performed in a teaching hospital with approximately 1,000 beds in Asturias, Spain, in patients 18 years of age or older, who had been diagnosed with RA and started treatment with at least one bDMARD drug from 1 January 2000 to 31 December 2013. Information was obtained from the records of digitized medical histories. Personal information of the patients was anonymized and coded according to the Spanish law on personal data protection.

In the sample of patients, the demographic and health data analysed were (a) age at the date of diagnosis; (b) sex; (c) disease characteristics [Rheumatoid Factor (RF), Anti-cyclic Citrullinated Protein Antibody (ACPA), erosive, nodular]; (d) severity of the disease measured by the DAS28 index (28-joint Disease Activity Score) and classification as low (DAS28 <3.6), moderate (DAS28 ≥3.6 and <5.5), high (DAS28 ≥5.5) and unknown; (e) clinical evolution of the disease, measured as the total number of hospitalizations per patient and the number of outbreaks per patient and year; f) patterns and lines of pharmacological treatment prescribed; g) time of evolution of the disease when the first DMARDs (cs or b) were prescribed; and h) comorbidities. We used the terms "lines of pharmacological treatment" to define drugs or combinations of drugs concomitantly used and "patterns of pharmacological treatment" to design pharmacological groups used alone or in combinations with other pharmacological groups simultaneously prescribed.

Regarding the different patterns of pharmacological treatment, we studied the (a) frequency, (b) level of inflammatory disease activity and (c) duration of the treatments. With respect to the treatments with bDMARDs, we also analyzed (a) the order in which bDMARDs were prescribed, (b) the frequency of prescription of each bDMARD, (c) the effectiveness, evaluated as the number of good responses and remissions, (d) the duration of treatment until remission, and (e) the causes of withdrawal of each bDMARD, classified as lack of response, adverse effects, remission, losses to follow-up or other causes, as well as the duration of treatment until withdrawal. According to the criteria of the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR)[9], responses to pharmacological treatments were considered "good" when the reduction of DAS28 was ≥ 1.2 or DAS28 was ≥ 3.2, and "clinical remission" was defined when DAS28 was ≤ 2.4.

To record the information extracted from the digitized clinical histories, a data matrix was created using the program Microsoft Excel 2010. In this data matrix, the study variables were defined. Age was treated as a discrete and metric variable and is presented as the median [Quartile 1 - Quartile 3; Q1-Q3]. Other metric variables were expressed as the mean ± standard error of the mean [SEM], and categorical variables were expressed as frequencies and percentages. Statistical analysis was performed with the program IBM SPSS Statistics 24.0 (IBM Corp., Armonk, NY, USA). Pearson's chi-squared (x^2) test was used to compare proportions for categorical variables, and a *t*-test was used to compare means with metric variables. The level of statistical significance was set at $p \leq 0.05$.

Results

Of a total of 235 patients initially selected, 25 were excluded because 11 were in a clinical trial, 10 received a unique dose of a bDMARD and 4 did not have a digitized medical history available. Therefore, a sample of 210 patients was studied. The demographic and health characteristics of the study population are summarized in Table I. At the date of diagnosis, the median [Q1-Q3] age of the sample was 47.3 [36.6-55.6] years, with 73% women. At the beginning of the pharmacological treatment, the mean inflammatory activity of the disease was moderate (initial DAS28: 5.0 ± 0.2). The mean time elapsed until the first treatment

Table I. Characteristics of the study population (n =210)

Characteristic	Value
Age, years [median (Q1-Q3)]	47.3 (36.6-55.6)
Sex [n (%)]	
Female	154 (73)
Male	56 (27)
Disease characteristics [n (%)]	
Seropositive	161 (77)
ACPA+	133 (63)
Erosive	88 (42)
Nodular	20 (10)
DAS28, at the beginning of the biological treatment [n (SEM)]	
< 3.6 – low inflammatory activity	12 (5.7)
< 5.5 – mild inflammatory activity	52 (24.8)
≥ 5.5 – severe inflammatory activity	36 (17.1)
Unknown	110 (52.4)
DAS28 [mean (SEM)]	5.0 (0.2)
Hospitalizations/patient, n [mean (range)]	1 (0-7)
Outbreaks/patient/year, n [mean (SEM)]	0.2 (0.0)
Lines of pharmacological treatment received/patient, n [mean (SEM)]	5.8 (0.2)
Time of evolution of the disease, days [mean (SEM)]	
Wwhen the first DMARD was prescribed	265.4 (64.3)
When the first bDMARD was prescribed	2,075.7 (149.8)
Comorbidities [n (%)]	
Depression	26 (12.4)
Cardiovascular disease	25 (11.9)
Osteoporosis	23 (11)
Gastrointestinal disease	11 (5.2)
Infections	10 (4.8)
Neoplasms	5 (2.4)

ACPA: Anti-cyclic Citrullinated Protein Antibody. DAS28: Disease Activity Score 28. SEM: Standard Error of the Mean. bDMARD: biological Disease Modifying Antirheumatic Drugs.

with csDMARDs or bDMARDs was nearly 9 months (265.4 ± 64.3 days) and that until the first bDMARD treatment was approximately 6 years (2,075.7 ± 149.8 days) of disease evolution.

For the patients studied, 19 different patterns (pharmacological groups alone or in combination) of treatment were prescribed, with a total frequency of 1,209 lines of treatment (drugs alone or in combination). Table II presents the top ten lines of treatment. Methotrexate and prednisone were the most frequently prescribed csDMARDs, and TNF-α inhibitors (etanercept, adalimumab and infliximab) were the most common bDMARDs. The combination of methotrexate plus prednisone was the most common combination of drugs.

As an initial treatment, 10 different patterns combining pharmacological groups were used (Table III). The majority of patients started their treatment with csDMARDs alone or in combination with a glucocorticosteroid (GCS). Initial

Table II. The top 10 drugs or combinations of drugs prescribed (n=1,209).

Order	Drugs	Frequency	Percentage
1	Methotrexate + Prednisone	165	13.6
2	Methotrexate	95	7.9
3	Prednisone	74	6.1
4	Etanercept + Methotrexate + Prednisone	47	3.9
5	Adalimumab + Methotrexate + Prednisone	46	3.8
6	Methotrexate + Deflazacort	38	3.1
7	Leflunomide + Prednisone	38	3.1
8	Leflunomide	33	2.7
9	Infliximab + Methotrexate + Prednisone	33	2.7
10	Deflazacort	28	2.3

Table III. First patterns of treatment depending on DAS28.

Pharmacological group (n)	Total n	DAS28				Duration of the treatment		
		Low	Moderate	High	Unknown	Days	SEM	*p* (*t*-test)*
csDMARDs (1)	81	8	17	11	45	1,118.7	169.4	< 0.01
csDMARDs (1) + GCS (1)	76	1	26	17	32	647.9	81.8	0.19
GCS (1)	32	1	5	5	21	337.4	110.8	< 0.05
bDMARDs (1)	5	0	2	0	3	475.4	242.6	0.54
csDMARDs (2)	5	1	1	1	2	637	371.7	0.77
csDMARDs (2) + GCS (1)	2	0	1	0	1	783.5	141.5	n.a.
bDMARDs (1) + csDMARDs (1) + GCS (1)	3	1	0	1	1	873.7	698.3	n.a.
bDMARDs (1) + csDMARDs (1)	4	0	0	1	3	850	146.5	n.a.
bDMARDs (1) + GCS (1)	1	0	0	0	1	207	–	n.a.
csDMARDs (3) + GCS (1)	1	0	0	0	1	177	–	n.a.
Total	210	12	52	36	110	781.9	77.2	–

csDMARDs: conventional synthetic Disease Modifying AntiRheumatic Drugs. bDMARDs: biologic Disease Modifying AntiRheumatic Drugs. GCS: GlucoCorticoSteroids. SEM: Standard Error of the Mean. (*) each group vs. others; statistical analysis was only performed when n was ≥ 5. n.a.: not applicable.

treatment included one bDMARD in only 13 (6.2%) patients. Among the initial patterns, the duration of the treatment with only one csDMARD compared with other patterns showed a longer duration ($p<0.01$), and a shorter duration of treatment was observed with one GCS compared with other patterns ($p<0.05$). It was not possible to analyse the association between the severity of the inflammatory activity of RA and the type of pattern prescribed as initial treatment because the level of inflammatory disease activity was unknown in more than a half of patients (n=110; 52.3%).

In a total of 405 lines of treatment prescribed, 7 bDMARDs were included: abatacept (n=18), adalimumab (n=111), etanercept (n=101), golimumab (n=6), infliximab (n=76), rituximab (n=38) and tocilizumab (n=55). Table IV shows the order in which bDMARDs were prescribed. As first lines of bDMARD treatment, TNF-α inhibitors were the most commonly prescribed drugs, with the following order of frequency: adalimumab > etanercept > infliximab > golimumab. In the second line of treatment, adalimumab and etanercept were the most frequent, followed by tocilizumab. This drug was also the most frequently prescribed drug in the third line of treatment with bDMARDs, followed by rituximab and etanercept. In the fourth line of treatment, abatacept, rituximab and tocilizumab were the most prescribed and in the fifth line, tocilizumab and adalimumab. Few patients received a sixth (n=3) or a seventh (n=2) line of bDMARDs.

Table V summarizes favourable responses to bDMARDs. The highest percentages of good responses and remissions were observed with tocilizumab (50.9% and 23.6%, respectively), etanercept (42.6% and 19.8%) and infliximab

Table IV. Order of prescription of bDMARDs.

bDMARDs	Lines of treatment															
	Total		1st		2nd		3rd		4th		5th		6th		7th	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Adalimumab	111	27.4	74	35.2	25	23.3	6	12.0	2	8.0	2	25.0	1	33.3	1	50
Etanercept	101	24.9	65	30.9	23	21.5	10	20.0	1	4.0	1	12.5	1	33.3	0	0
Infliximab	76	18.8	56	26.7	18	16.8	1	2.0	0	0	1	12.5	0	0	0	0
Tocilizumab	55	13.6	7	3.3	20	18.7	18	36.0	5	20.0	3	37.5	1	33.3	1	50
Rituximab	38	9.4	6	2.8	15	14.0	11	22.0	6	24.0	0	0	0	0	0	0
Abatacept	18	4.4	0	0	3	2.8	3	6.0	11	44.0	1	12.5	0	0	0	0
Golimumab	6	1.5	2	0.1	3	2.8	1	2.0	0	0	0	0	0	0	0	0
Total	405	100	210	100	107	100	50	100	25	100	8	100	3	100	2	100

(38.2% and 23.7%), although the duration of treatment until remission was significantly lower with tocilizumab ($p<0.05$) and adalimumab ($p<0.05$) and higher with infliximab ($p<0.01$) than with other bDMARDs. The treatment with rituximab was associated with a significantly ($p<0.05$) lower number of good responses than other bDMARDs. No differences among bDMARDs in the percentages of remissions were found. Globally considered, the duration of the treatment with bDMARDs until remission was approximately 2 years (763.3 ± 84.2 days). A shortening in the average duration of the sequential treatments with bDMARDs was observed.

Lack of response, adverse effects and remission were the main causes of withdrawal of bDMARDs (Table VI). The global percentage of withdrawal with these drugs was 62.7%, which was significantly higher (73.7%; $p<0.05$) with infliximab and lower with tocilizumab (36.3%; $p<0.01$) and abatacept (38.9%; $p<0.05$). Lack of response was the main reason for withdrawal in the 35.5% of bDMARD treatments, being more common with etanercept (49.5%; $p<0.01$) and less frequent with tocilizumab (18.2%; $p<0.05$). However, the percentage of withdrawal due to adverse effects related to etanercept was significantly ($p<0.05$) lower than that with other drugs. On the other hand, adalimumab showed higher percentages than other bDMARDs in withdrawals due to adverse effects ($p<0.01$) and remission ($p<0.0.5$). In relation to the duration of treatments until withdrawal, no statistically significant differences were observed among bDMARDs, apart from rituximab, which showed a duration of treatment slightly lower ($p<0.05$) than that with other bDMARDs.

Discussion

Our study presents the prescribing patterns of bDMARDs in the treatment of RA and some of their effects on efficacy and safety. The demographic characteristics of the patients analysed are in line with those of other previously published cohorts of patients with RA, including an initial severe-to-moderate inflammatory activity[10-14].

In the sample analysed in this study, pharmacological treatment for RA started on average one year after diagnosis with the prescription of csDMARDs or GCSs in most cases. Methotrexate and prednisone, alone or in combination, were the most common drugs selected for the initial treatment. The role of methotrexate in the treatment of initial and established RA is well recognized[15,16]. Furthermore, according to the observations of the BeSt study[17] and the current EULAR recommendations[18], the combination of a GCS with methotrexate improves early RA and its long-term evolution. On the other hand, due to current guidelines[15,16,18] for early RA establishing different recommendations depending on the degree of inflammatory activity of the disease, we tried to analyse the patterns of initial treatment in relation to the value of DAS28 in each case; however, the lack of information of this measure in many of the clinical histories does not allow this analysis.

In our study, the mean time until the first prescription of a bDMARD was close to 6 years, lower than that found in a similar cohort of British patients by Hyrich et al[19]. Furthermore, in a chart review study[10] of treatment patterns on RA, the prescription of bDMARDs as the first line of treatment was more frequent in Spain and Germany than in the United Kingdom. Globally considered, in our study, TNF-α inhibitors (adalimumab, etanercept and infliximab) were the bDMARDs most prescribed as first and second lines of treatment. Among TNF-α inhibitors, adalimumab and etanercept were the most consumed, perhaps due to their subcutaneous administration *vs.* the intravenous administration of infliximab. As a third line of treatment, tocilizumab and rituximab were the most commonly prescribed bDMARDs and, as a fourth line, abatacept, following these patterns of prescription, the current guidelines for the treatment of RA and the new evidence on the effectiveness of these drugs.

In the analysis of the effectiveness of TNF-α inhibitors, no differences were found in the percentages of good responses and remissions among adalimumab, etanercept and infliximab. Regarding golimumab, the scarce number of lines of treatment did not allow comparisons to be made. Previously, in a Cochrane review, Singh et al[20] did not find differences in efficacy among adalimumab, etanercept, infliximab, rituximab and abatacept and underlined the need for comparative clinical trials ("head-to head") between these biologic agents. Afterwards, Malottki et al[21] performed a systematic review to compare adalimumab, etanercept, infliximab, rituximab and abatacept after the failure of a TNF-α inhibitor and did not find statistically significant differences in effectiveness among drugs. However, we observed the differences in the duration of treatment until remission, which was approximately 4

Table V. Effectiveness of the different lines of treatment (LT) with bDMARDs.

bDMARD	LT, total		Good responses*			Other responses			Unknown**			Remissions***			Duration of treatment until remission		
	N	%	N	%	*p* (χ^2)	N	%	*p* (χ^2)	N	%	*p* (χ^2)	N	%	*p* (χ^2)	Days	SEM	*p* (*t*-test)
Adalimumab	111	100	38	34.2	0.07	13	11.7	0.13	60	54.0	0.03	13	11.7	0.06	393.3	122.6	< 0.05
Etanercept	101	100	43	42.6	0.11	21	20.8	0.16	37	36.6	< 0.05	20	19.8	0.49	578.2	122.1	0.16
Infliximab	76	100	29	38.2	0.85	14	18.4	0.58	33	43.4	0.73	18	23.7	0.12	1,448	194.7	< 0.01
Tocilizumab	55	100	28	50.9	0.13	7	12.7	0.44	20	36.4	0.15	13	23.6	0.20	372.5	64.4	< 0.05
Rituximab	38	100	12	31.6	< 0.05	2	5.3	n.a.	24	63.2	< 0.05	5	13.2	n.a.	994.2	112.2	0.45
Abatacept	18	100	5	27.8	n.a.	8	44.4	< 0.01	5	27.8	n.a.	1	5.6	n.a.	509.0	–	n.a.
Golimumab	6	100	1	16.7	n.a.	1	16.7	n.a.	4	66.6	n.a.	0	0	n.a.	–	–	n.a.
Total	405	100	156	38.5	–	66	16.3	–	183	45.2	–	71	17.5	–	763.3	84.2	–

(*) Good response: DAS28 reduction >1.2 and/or DAS28 <3.2. (**) unknown: DAS28 value was not available. (***) Remission: DAS28 <2.4. Statistical analysis was performed only when n was ≥ 5. bDMARD: biological Disease Modifying Antirheumatic Drugs. LT: Lines of Treatment. n.a.: Not applicable. SEM: standard error of the mean.

Table VI. Effectiveness of the different lines of treatment (LT) with bDMARDs.

bDMARD	Lack of response			Adverse effects			Remission			Losses to follow up		Other causes*		Withdrawals, total			Duration of treatment until remission		
	N	%	*p* (χ^2)	N	%	*p* (χ^2)	N	%	*p* (χ^2)	N	%	N	%	N	%	*p* (χ^2)	Days	SEM	*p* (*t*-test)
Adalimumab	38	34.2	0.73	33	29.7	< 0.01	9	8.1	< 0.05	0	0	1	0.9	81	73.0	0.09	650.2	75.6	0.64
Etanercept	50	49.5	< 0.01	13	12.9	< 0.05	2	2.0	n.a.	1	1.0	0	0	66	65.3	0.53	673.2	101.5	0.50
Infliximab	31	40.8	0.29	18	23.7	0.34	2	2.6	n.a.	1	1.3	4	5.3	56	73.7	< 0.05	771.0	133.9	0.09
Tocilizumab	10	18.2	< 0.05	6	10.9	0.08	1	1.8	n.a.	1	1.8	2	3.6	20	36.3	< 0.01	328.4	45.3	0.08
Rituximab	10	26.3	0.21	7	18.4	0.83	2	5.3	n.a.	1	2.6	2	5.3	22	57.9	0.52	304.9	83.0	< 0.05
Abatacept	4	22.2	n.a.	3	16.7	n.a.	0	0	n.a.	0	0	0	0	7	38.9	< 0.05	438.3	66.8	0.53
Golimumab	1	16.7	n.a.	0	0	n.a.	1	16.7	n.a.	0	0	0	0	2	33.3	n.a.	207.5	112.5	n.a.
Total	144	35.5	–	80	19.7	–	17	4.2	–	4	1.0	9	2.2	254	62.7	–	618.2	47.8	–

(*) Other causes: pregnancy + surgery + improvement in 2 cases with infliximab. Statistical analysis was performed only when the total number of withdrawals was ≥ 5. n.a.: not applicable. For each biological Disease Modifying AntiRheumatic Drug (bDMARD), the total number of lines of treatment and 100% are the same as in Table V (columns 2 and 3).

years with infliximab and 1 year with adalimumab. In our opinion, in the evaluation of this difference, we should keep in mind that infliximab was the first TNF-α inhibitor marketed in Spain and that it is administered intravenously. Therefore, patients who are taking this drug could have severe-to-moderate RA and, for this reason, require a long time to achieve remission.

The highest percentages of good responses and remissions were observed with tocilizumab, and this drug also showed the lowest duration of treatment until remission. These observations are in line with clinical trials showing that, after 6 months of treatment, in patients taking concomitant methotrexate, compared to placebo, tocilizumab-treated patients were 11 times more likely to achieve Disease Activity Score (DAS) remission[22]. Extensive experience in randomized clinical trials and real-world settings over the last decade has established the short- and long-term efficacy of tocilizumab in adults with moderate-to-severe RA who failed cs or bDMARDs[23]. Apparently, treatment with rituximab was associated with fewer good responses, but this result should be read with caution due to the small size of the sample and the high percentage of "unknown" effectiveness to this drug.

The analysis of the bDMARD withdrawals revealed that more than half of the treatments with bDMARDs were withdrawn, with a lack of response being the most frequent reason for the withdrawal, in agreement with previous observations[13,24]. The percentage of withdrawals of the treatments with infliximab was higher than with the other bDMARDs analysed. However, no differences in the percentage of withdrawals were observed among infliximab, etanercept and adalimumab. These results are in line with the previous report of Flendrie et al[25] but differ from the observations of Arora et al[26], which in a systematic review of European National Dug Registers found lower drug discontinuation rates with etanercept than adalimumab, whereas infliximab had the highest rate. In relation to the duration of treatments until withdrawal, our study did not find differences among TNF-α inhibitors, while in a Spanish previous study, Martínez-Santana et al[27i] observed a lower duration of treatment until withdrawal with infliximab than with etanercept or adalimumab. In our opinion, differences in the design of the studies, as well as in the period of time the drugs have been in the market are factors to consider in the comparative analysis of the results of the mentioned studies.

López-Longo et al[28] found great variability among Spanish centres in the prescription of bDMARDs to treat RA. The main limitation of our study is its observational retrospective nature with a small sample size. Furthermore, the data analysed are limited to the information recorded in the clinical history and the period of time analysed in which bDMARDs were prescribed was 13 years, a wide period that could include prescribing patterns differing according to the date of diagnosis or the duration of RA.

Conclusions

Prescribing pattern analysis showed the highest responses and remission rates with tocilizumab and TNF-α inhibitors. The main reasons for withdrawal were lack of response and adverse effects. Further studies are needed to improve pharmacological RA management in real-life settings.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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