Real-life effectiveness of Golimumab in biologic-naïve patients with rheumatoid arthritis – data from the Rheumatic Diseases Portuguese Register (Reuma.pt)

Mourão AF[1,2,3], Ribeiro C[4], Borges J[5], Gonçalves MJ[2,6], Bernardes M[7], Fernandes S[5], Dezerto R[8], Laires PA[8], Machado P[8], Eusébio M[9], Santos MJ[10,2], Canhão H[11] on behalf of REUMA.PT investigators

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ABSTRACT

Objectives: To assess the effectiveness of subcutaneous golimumab 50 mg/monthly combined with methotrexate (SC GLM + MTX) over 52 weeks of treatment, in biologic-naïve RA patients, in a multicentre nationwide cohort from the Rheumatic Diseases Portuguese Register (Reuma.pt).

Methods: Data for this observational study was collected from March 2011 to August 2015. Disease activity (DAS28), functional capacity (HAQ) and patient global disease assessment (PGDA) were measured at baseline and weeks 12, 24 and 52 of treatment. The primary objective was clinical remission over 52 weeks (1 year) and secondary objectives were: functional response and functional remission over 52 weeks, variation of individual components of DAS over time and treatment persistence at week 52. Comparison between baseline variables of subjects with and without clinical remission was performed. The SC GLM + MTX persistence rate was estimated by the Kaplan-Meier analysis. Cox proportional hazard model approach was used to evaluate predictive factors of persistence, response and remission.

Results: A total of 109 patients were enrolled in the study: 94 (86.2%) female, mean age 55.5±13.2 years, mean age at diagnosis 45.5±13.5 years, mean age at beginning of treatment with biologic agents 53.1±13.1 years; 78.1% positive for serum rheumatoid factor. All patients were biologic-naïve and had active disease, despite previous treatment with conventional disease-modifying antirheumatic drugs (DMARDs). At the time of this analysis, 93 patients had a follow-up time of at least 52 weeks (i.e. started treatment before August 2014). Of this group, 38.3% achieved clinical remission, 91.9% functional response and 35.2% functional remission, over 52 weeks. Treatment persistence was 75.3% at 1 year. Disease activity indices were all statistically significantly lower at 12, 24 and 52 weeks when compared to baseline. Older age at diagnosis was associated to a lower probability of clinical remission (HR= 0.96, p= 0.031) whereas higher C-reactive protein baseline levels were associated with a lower probability of functional response (HR= 0.54; p= 0.026).

Conclusions: Golimumab 50 mg + MTX showed effectiveness in the treatment of patients with active RA, in accordance to what previously observed in clinical trials. A consistent and significant decrease in RA disease activity through 52 weeks of treatment and a significant functional improvement were observed, as well as a high persistence on treatment.

Keywords: Rheumatoid arthritis; Golimumab; Effectiveness; Treatment persistence; Real-life data; Rheumatic Diseases Portuguese Register (Reuma.pt).

1. Hospital Egas Moniz (Centro Hospitalar de Lisboa Ocidental), Lisboa, Portugal
2. Instituto de Medicina Molecular (IMM), Unidade de Investigação em Reumatologia da Faculdade de Medicina de Lisboa, Lisboa, Portugal
3. Centro de Estudos de Doenças Crónicas (CEDOC), Faculdade de Ciências Médicas da Universidade Nova de Lisboa, Lisboa, Portugal
4. Hospital de Faro (Centro Hospitalar do Algarve), Faro, Portugal
5. Instituto Português de Reumatologia, Lisboa, Portugal
6. Hospital de Santa Maria (Centro Hospitalar de Lisboa Norte), Lisboa, Portugal
7. Centro Hospitalar de São João, Porto, Portugal
8. Merck Sharp & Dohme, Departamento Médico, Paço de Arcos, Portugal
9. Sociedade Portuguesa de Reumatologia, Lisboa, Portugal
10. Hospital Garcia de Orta, Almada, Portugal
11. EPIDOC, Nova Medical School, Faculdade de Ciências Médicas da Universidade Nova de Lisboa, Lisboa, Portugal

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory immune-mediated disease that, if inadequately treated, can lead to permanent joint damage and deformity associated with substantial disability and reduced quality of life. The current primary target for treatment of RA should be a state of clinical remission, defined as the absence of signs and symptoms of inflammatory disease activity. While remission should be a clear target, low-disease activity may be an acceptable alternative therapeutic goal, particularly in long-standing disease[1].

Biologic disease-modifying antirheumatic drugs (bDMARDs), and tumour necrosis factor antagonists (anti-TNFs) in particular, have dramatically changed RA treatment. The benefits of using these agents earlier in the disease have been recognized and guidelines as well as clinical practice have been adjusted following emerging evidence[2-4].

Golimumab (GLM) is a fully human anti-TNF monoclonal antibody administered subcutaneously (SC) once a month and is available in Portugal since 2010. The use of GLM combined with methotrexate (MTX) in patients with active RA despite methotrexate therapy was shown to significantly reduce the signs and symptoms of RA and improve physical function[5]. In the clinical trial setting, data has been collected regarding GLM efficacy and safety for the treatment of RA[6-12] but data on its effectiveness in real-life practice is still limited. Therefore, patient registries are becoming an increasingly important source of knowledge, as they provide valuable information to assess routine management of the disease and can be used to validate the results obtained during trials and generate epidemiological data.

In Portugal, it is estimated that 63,198 citizens have a diagnosis of RA[13]. The general objective of this study was to assess the effectiveness of SC GLM 50 mg/monthly combined with MTX through 52 weeks of treatment, in biologic-naïve RA patients, in a multicentre nationwide cohort from the Rheumatic Diseases Portuguese Register (Reuma.pt). The primary objective was to evaluate, over 52 weeks, the proportion of patients achieving clinical remission. The secondary objectives were: a) to estimate treatment persistence at 52 weeks; b) to evaluate the proportion of patients achieving functional response and functional remission over 52 weeks; and c) to calculate the variation of the individual components of DAS 28 [number of swollen joints (SJC), number of tender joints (TJC), Patient Global Disease Activity (PGDA) and erythrocyte sedimentation rate (ESR)] between baseline and week 12, 24 and 52. Predictive factors of clinical remission, functional response, functional remission and treatment persistence were investigated.

METHODS

STUDY DESIGN AND PATIENTS

This was an observational study with a retrospective analysis of data of patients in treatment with SC GLM 50 mg/monthly combined with MTX, listed in Reuma.pt. The Reuma.pt is the nationwide clinical register in Portugal. It was developed by the Portuguese Society of Rheumatology (SPR), established in 2008 and is used in daily clinical practice by almost all Rheumatology centres in Portugal[14]. The ultimate goal is to register all patients in Portugal with rheumatic diseases and to follow them up to determine treatment efficacy and safety and to a better knowledge of long-term co-morbidities.

The Reuma.pt Scientific Board Coordination gave authorization for the data of interest to be used in this study and the study was approved by the Lisbon Academic Medical Centre Ethics Committee.

The study was conducted in a cohort of biologic-naïve patients aged ≥18 years with active RA, despite previous treatment with conventional DMARDs (no limit in the number of previous conventional DMARDs), who started SC GLM 50 mg monthly combined with MTX between March 2011 and August 2015. To be included, each participant must have had a clinical diagnosis of RA according to the Rheumatologist and meet the criteria described in the Portuguese guidelines for the use of biological agents in RA[15]. All patients provided written consent as part of their enrolment in Reuma.pt and all data was anonymized.

EVALUATION OF EFFECTIVENESS AND TREATMENT PERSISTENCE

GLM effectiveness was evaluated through the following parameters: proportion of patients achieving clinical remission over 52 weeks [defined by having the composite disease activity score using the 28 tender and swollen joint counts (DAS28-ESR) < 2.6]; percentage of patients achieving functional response over 52 weeks [delta Health Assessment Questionnaire (ΔHAQ) = HAQbaseline – HAQweek 12, 24 or 52 >

0.22]; percentage of patients achieving functional remission through week 52 (HAQ <0.5 at any point through 52 weeks); difference of the individual components of DAS28-ESR swollen joint counts (SJC), tender joint counts (TJC), PGDA and ESR) between baseline and weeks 12, 24 and 52. For clinical remission, functional response, functional remission over 52 weeks and treatment persistence at week 52, only patients with a follow-up time of at least 52 weeks, i.e., patients who were indexed prior to August 2014, were considered. For comparison with PGDA, physician global disease assessment (PhGDA) was also evaluated.

The window of time allowed for measurements were as follows. Baseline: up to 15 days after starting treatment; 12 weeks: 45 days before and after week 12; 24 weeks: 45 days before and 90 days after week 24; 52 weeks: 90 days before and 90 days after week 52.

The proportion of patients that achieved a specified clinical condition (clinical remission, clinical response, etc.) *at a defined time point* (12, 24 or 52 weeks) was calculated considering the patients who had reached that condition at that time point only (window of time considered for each time point). The proportion *over 52 weeks* includes all the patients who had achieved the specified condition during that period: at one specific time point (at week 12, week 24 or week 52), at two of them; or at the three all-time points.

Treatment persistence was evaluated as the time in treatment with SC GLM in combination with MTX from initiation to discontinuation. By definition, persistence is reported as a continuous variable in terms of days for which therapy was administered[16]. Treatment discontinuation is defined as the first occurrence of either one of the following events: 1) End of treatment - 90-day continuous gap of treatment without a subsequent biological treatment; 2) Switch of treatment - first occurrence of any switch to another biological agent within 90 days of the end of treatment of the index biological (SC GLM in combination with MTX). Temporary stops of < 90 days (which may occur for surgery or certain adverse events), after which the patients restarted the same biological agent, were counted as continuous use of the drug[17]. The 90-day cut-off to define treatment persistence was also used in the methodology applied to other registries, such as the British Society of Rheumatology Biologics Registry[17]. Patients were censored at last data collection date (August 2015) or the last date in current Reuma.pt dataset, whichever came first.

STATISTICAL ANALYSIS

Statistical analyses were performed using the software Stata IC version 12[18]. Significance level for all analyses was set at 0.05.

Descriptive statistics was used for clinical remission, functional remission and response, SJC, TJC, PGDA, PhGDA and ESR. For qualitative data, absolute and relative frequencies are presented. Proportions are based on the total number of subjects with non-missing values unless specified otherwise. Mean values are presented and not median because of the small sample size.

For comparison between baseline characteristics of subjects with and without remission, two-sample test of proportions and Wilcoxon-Mann-Whitney test were used. Comparisons within subjects at baseline and after treatment were performed with Wilcoxon's matched-pairs signed-rank test. Stuart-Maxwell test was used for comparison of DAS28-ESR subgroups. The use of non-parametric tests is justified by the decrease in sample size, due to the comparison within subjects.

The persistence on SC GLM therapy (in combination with MTX) was estimated by Kaplan-Meier analysis. The Cox proportional hazard model was used to evaluate the effect of baseline patient characteristics on treatment persistence. The hazard ratio of a covariate was calculated by the exponential of the respectively estimated Cox proportional hazard regression coefficient. The median time of treatment persistence adjusted by covariates was estimated as the shortest time at which the estimated survival function is less or equal to 0.05. The estimated survival function is defined by the survival function at baseline to the power of the exponential of linear predictor of the Cox proportional hazard model. All the covariates included in the model were time-fixed at baseline. Cox proportional hazard model approach was also used to investigate predictive factors of clinical remission, functional response and functional remission, in order to consider the time until the response or remission. Missing data was never imputed.

RESULTS

PATIENTS

A total of 109 patients were enrolled in the study. Table I shows the baseline characteristics. From these, 93 had a follow-up time of at least 52 weeks (i.e. started treat-

TABLE I. BASELINE PATIENTS CHARACTERISTICS

	Total N	
Female	109	94 (86.2%)
Age mean (sd)	109	55.5 (13.2)
Age of RA diagnosis mean (sd)	103	45.5 (13.5)
Age of starting biologics mean (sd)	109	53.1 (13.1)
Rheumatoid factor positive	96	75 (78.1%)
Anti-CCP positive	96	63 (65.6%)
Body Mass Index (kg/m^2) mean (sd)	49	25.98 (3.8)
Concomitant medication		
Convencional DMARDs	109	109 (100%)
NSAIDs	69	46 (66.7%)
Glucocorticoids	92	85 (92.4%)
Smoking habits	97	
Current smoker		18 (18.6%)
Past smoker		7 (7.2%)
Comorbidities	82	
High blood pressure		25 (30.5%)
Diabetes		8 (9.8%)
Thyroid disease		8 (9.8%)
Sjögren's syndrome		6 (7.3%)
Hyperlipidemia		16 (19.5%)
Cardiovascular diseases		1 (1.2%)
Other		18 (22.0%)

ment before August 2014). At baseline, all patients had a DAS28-ESR ≥ 3.2, except one (DAS-28-ESR of 2.67). The mean DAS28-ESR was 5.41±1.17 and the mean HAQ was 1.43±0.63.

Over 52 weeks of treatment, an overall decrease in RA activity index (DAS28-ESR) was observed, which was particularly marked during the first 12 weeks of treatment. Mean DAS28-ESR decreased from 5.4 (high activity) at baseline to 3.2 (low activity) at week 52 of treatment, and mean HAQ decreased from 1.43 (moderate disability) to 0.91 (mild disability). A statistically significant decrease was observed in all common RA indices from baseline to week 12, week 24 and week 52 (Table II).

CLINICAL REMISSION

Of the 60 subjects with at least 52 weeks of treatment and with information regarding DAS28, 23 (38.3%) achieved clinical remission, at least in a single time point over 52 weeks. The proportion of patients in remission increased over time: 20% of patients at 12 weeks, 25.8% of patients at week 24 and 30.4% of patients at week 52. Conversely, the percentage of patients with moderate and high activity disease declined (Figure 1). Comparison of baseline characteristics between patients with and without remission at 52 weeks of treatment did not show any statistically significant difference (data not shown).

FUNCTIONAL RESPONSE AND FUNCTIONAL REMISSION

Of the 37 subjects with at least 52 weeks of follow-up and with information regarding HAQ, 34 (91.9%) achieved functional response (ΔHAQ >0.22). Functional remission (HAQ<0.5) was achieved by 19 (35.2%) of the 54 subjects with a follow-up of at least 52 weeks and HAQ information.

VARIATION OF THE INDIVIDUAL COMPONENTS OF DAS28

Regarding the components of DAS28 (SJC, TJC, PGDA and ESR), the values decreased over time and at weeks 12, 24 and 52 were all statistical significantly lower than at baseline (Table II). PGDA was always higher than PhGDA, although a similar decreasing trend was observed.

TREATMENT PERSISTENCE

Treatment persistence was 75.3% for individuals with at least 52 weeks of follow-up (Figure 2). In the first year of treatment, 23 patients stopped treatment or were lost to follow-up. For the first 12 weeks, 3 patients stopped treatment or were lost to follow-up, and for the first 24 weeks of treatment, 12 patients stopped treatment or were lost to follow-up. Discontinuation (23/96 patients) was due to: inefficacy (15 patients), serious adverse events (2), surgery (1), and other reasons (5).

PREDICTIVE FACTORS

Cox regression revealed age at diagnosis as an important factor for clinical remission: an increase of 1 year in age at diagnosis will decrease by 4% the rate of clinical remission (HR=0.96, p=0.031). For functional remission, CRP levels seem to have a relevant role (HR=0.54; p=0.026): an increase in one unit of CRP will decrease by 46% the rate of functional remission. For treatment persistence no variables were identified since the model was considered not statistically significant (p>0.05) (Table III).

TABLE II. DISEASE INDICES: COMPARISON WITHIN SUBJECTS. BASELINE AND AFTER 12 WEEKS OF TREATMENT, BASELINE AND AFTER 24 WEEKS OF TREATMENT, BASELINE AND AFTER 52 WEEKS OF TREATMENT

	Baseline	Week 12	p-value	Baseline	Week 24	p-value	Baseline	Week 52	p-value
DAS28-ESR mean (sd)	5.6 (1.15)	3.7 (1.17)	0.0000	5.4 (1.08)	3.4 (1.17)	0.0000	5.4 (1.02)	3.3 (1.25)	0.0000
DAS28-ESR<2.6*	0 (0.0%)	9 (19.6%)		0 (0.0%)	13 (25.5%)		0 (0.0%)	9 (30.0%)	
DAS28-ESR ≥2.6 and ≤3.2*	0 (0.0%)	9 (19.6%)	0.0001	0 (0.0%)	8 (15.7%)	0.0000	0 (0.0%)	7 (23.3%)	0.0001
DAS28-ESR>3.2*	46 (100%)	28 (60.9%)		51 (100%)	30 (58.8%)		30 (100%)	14 (46.7%)	
DAS3V mean (sd)	5.1 (1.14)	3.4 (1.07)	0.0000	5.01 (1.06)	3.3 (1.08)	0.0000	5.2 (1.10)	3.1 (1.16)	0.0000
Tender joints 28 mean (sd)	10.6 (8.70)	4.8 (5.90)	0.0000	10.2 (7.90)	3.6 (4.80)	0.0000	10.8 (8.50)	2.6 (4.50)	0.0000
Swollen joints 28 mean (sd)	7.5 (4.60)	2.1 (2.60)	0.0000	7.0 (4.30)	2.0 (2.70)	0.0000	7.5 (4.80)	1.3 (2.30)	0.0000
ESR mean (sd)	30.2 (20.00)	17.4 (14.10)	0.0000	29.9 (18.90)	16.6 (12.20)	0.0000	32.0 (20.50)	22.1 (19.60)	0.0024
CRP mean (sd)	2.0 (2.20)	0.7 (1.10)	0.0000	1.8 (1.88)	1.34 (5.75)	0.0000	2.0 (2.03)	0.7 (0.84)	0.0000
Patient's VAS mean (sd)	65.7 (22.60)	43.3 (24.10)	0.0000	60.2 (24.10)	34.3 (23.60)	0.0000	61.1 (24.10)	33.0 (24.20)	0.0000
Physician's VAS mean (sd)	53.5 (17.30)	28.2 (18.60)	0.0000	53.2 (19.10)	22.9 (14.70)	0.0000	53.0 (22.00)	20.0 (14.70)	0.0000
HAQ mean (sd)	1.40 (0.62)	1.05 (0.63)	0.0000	1.35 (0.65)	0.98 (0.64)	0.0002	1.41 (0.64)	1.01 (0.64)	0.0007

All comparisons were performed with Wilcoxon's matched-pairs signed-rank test except DAS28-ESR subgroups*, where Stuart-Maxwell test was used. Sample size is not constant due to (12 weeks): DAS28-ER (n=46), DAS 3V (n=52), Tender joints 28 (n=56), Swollen joints 28 (n=56), ESR (n=52), CRP (n=51), Patient's VAS (n=50), Physician's VAS (n=42), HAQ (n=39). Sample size is not constant due to (24 weeks): DAS28-ER (n=51), DAS 3V (n=58), Tender joints 28 (n=62), Swollen joints 28 (n=62), ESR (n=58), CRP (n=58), Patient's VAS (n=54), Physician's VAS (n=48), HAQ (n=41). Sample size is not constant due to (52 weeks): DAS28-ER (n=30DAS 3V (n=30), Tender joints 28 (n=44), Swollen joints 28 (n=44), ESR (n=40), CRP (n=38), Patient's VAS (n=32), Physician's VAS (n=28), HAQ (n=32).

DISCUSSION

The baseline characteristics of this RA cohort are similar to those reported in other national European biologics registries, namely the Spanish registry Biobadaser[19], the Swedish Biologics Registry[20] and the Danish Danbio registry[21].

The proportion of patients achieving clinical remission over 52 weeks was 38.3% and at week 52 was 30.4%. These values are similar to the one observed in the Golimumab clinical trial GO-FORWARD: 36.8% for the 50 mg+MTX group at week 52[5]. Similar values were found in the Danbio registry for clinical remission with other anti-TNFs: 27% for infliximab, 33% for etanercept and 39% for adalimumab[22]. In the British registry BSRBR[23] 17.4% and 23.5% were described for 2008 and 2007, respectively (pooled data of patients in infliximab, adalimumab and etanercept), however, in this registry, mean DAS28 at baseline was above 6, meaning that patients had a more active disease before initiating treatment with anti-TNFs. Also in the GO-FORWARD study[5], 48.5% of patients receiving GLM 50 mg + MTX achieved low disease activity (DAS28 ≤3.2) at week 52. In this study, a similar value was obtained: 52.1% at week 52. These data show good agreement between clinical trial and clinical practice settings.

Consistent with DAS28 improvement, all the individual components of DAS28 also improved, as expected. A clear difference between PGDA and PhGDA was observed. The trend of disease assessment over time was the same, but patient values were always higher than physician's. This discrepancy has been previously reported in several studies and pathologies[24-26] and may be due to different drivers of assessment: the drivers of patients are the pain and functional incapacity, whereas the drivers of physicians are joint counts and acute phase reactants[26].

The decrease of disease activity was followed by an important functional improvement: over 52 weeks, 91.9% of patients achieved functional response and 35.2% achieved functional remission, suggesting that a relevant number of patients hardly had any difficulties in daily activities at week 52 of treatment with GLM+MTX.

Regarding physical function, it is now in-

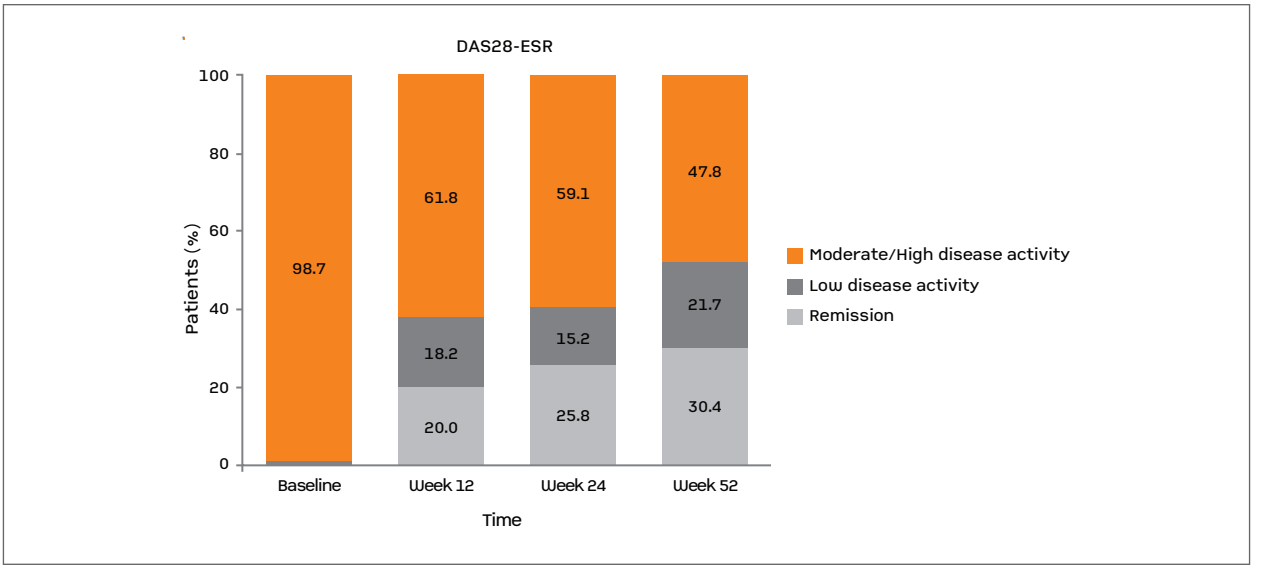

FIGURE 1. Proportion of patients achieving clinical remission (DAS28-ESR <2.6), low disease activity (DAS28-ESR ≥2.6 and ≤3.2) and moderate/high disease activity (>3.2) over time. Number of patients with DAS28-ESR information at baseline, week 12, week 24 and week 52, respectively: n=74, n=55, n=66, n=46

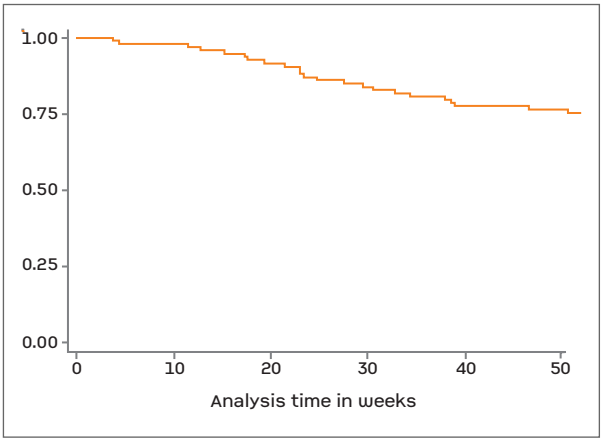

FIGURE 2. Kaplan-Meier survival curve for patients in treatment with golimumab with a follow-up time of ≥ 52 weeks (n= 93)

creasingly accepted that functional remission may not be an achievable target for many patients, as only part of their disability is reversible. The probability of response in functional scores decreases from ~60% in early disease to ~30% in established disease reflecting chronic damage[27]. Distinction was beyond the scope of our study.

Age at diagnosis was identified as an important factor for clinical remission in this cohort, suggesting that the earlier the diagnosis, the better the prognosis, with higher probability of clinical remission. This can be explained by the fact that an early diagnosis allows an early disease control, preventing the progression of the disease. Moreover, the inflammation biomarker CRP was associated to functional remission: an increase in baseline CRP levels seems to decrease the probability of functional remission.

In a recent study about prediction of remission and low disease activity in conventional DMARD-refractory patients with RA treated with GLM[28], a greater likelihood of low disease activity and remission was associated with being male; younger age; lower HAQ, ESR (or CRP) and TJC (or SJC) scores; and absence of comorbidities. Age at diagnosis was not considered in this study[28]. In a different study, from the Danish Registry, older age, low functional status, and concomitant prednisolone treatment were negative predictors of a clinical response and remission[22]. However, predictive factors are far from being consensual: younger patients, for instance, were found to have better clinical outcomes in several studies[29-31] but, conversely, no association with age and clinical response was found in other studies[32,33]. Golimumab SC 50 mg + MTX persistence rate was 75.3% at week 52. This value is in accordance with a recent systematic review and meta-analysis of drug registries and health care databases that showed a discontinuation rate of TNF inhibitors at 1 year between 18% and 27%[34] but is numerically higher than the persistence described in other studies of GLM: in a study

TABLE III. COX REGRESSION FOR CLINICAL REMISSION, FUNCTIONAL REMISSION AND TREATMENT PERSISTENCE, WITH EFRON METHOD FOR TIES WITH ROBUST ESTIMATES OF VARIANCE

	Variable	Hazard ratio	p-value	95% CI	Model p-value
Clinical remission	Age at diagnosis	**0.96**	**0.031**	[0.93; 1.00]	
	CRP	0.96	0.764	[0.76; 1.22]	
	Rheumatoid factor	0.68	0.479	[0.27; 1.72]	**0.0173**
Functional remission	Female	0.82	0.845	[0.13; 5.48]	
	Age at diagnosis	0.99	0.577	[0.94; 1.04]	
	CRP	**0.54**	**0.026**	[0.32; 0.93]	
	ESR	1.00	0.917	[0.97; 1.03]	**0.0363**
Treatment persistence	Female	0.34	0.021	[0.13; 0.85]	
	Age of beginning treatment with biologics (golimumab)	0.98	0.355	[0.95; 1.02]	
	Years of disease until treatment with biologics (golimumab)	1.00	0.977	[0.93; 1.08]	0.0950

Only patients with a follow-up ≥ 52 weeks and available data were considered. CRP, C reactive protein; ESR, erythrocyte sedimentation rate.

using Canadian claims data, the 12-month GLM survival rate was 66% in biologic naïve RA patients[35] and in an Italian multicentre observational cohort, the persistence rate in RA patients through 1 year was 63%[36]. Among RA patients newly initiating subcutaneous biologic agents in Germany (Disease Analyzer Patient Database), persistence at 12 months was 51.9%[37]. Data from a Swedish registry[38] with patients with immune-mediated rheumatic diseases (ankylosing spondylitis, psoriatic arthritis and RA, total N= 4903) newly treated with anti-TNFs showed a survival probability of 58% (95%CI: 55-62%) at 1 year. In this last study, pairwise comparisons revealed that, after one year of treatment, GLM had significantly higher persistence than Adalimumab and Etanercept. The variable results in GLM persistence rates previously mentioned may be justified by differences in measures of persistence and/or data sources: in administrative databases, persistence is defined in terms of prescription refills, whereas the data from clinical registries rely on physician-reported data.

The length of time that patients remain on anti-rheumatic therapy is an important measure of effectiveness since length of time on therapy is a composite measure that accounts for sustained, positive therapeutic benefit as well as negative therapeutic benefit (e.g. adverse reactions, unacceptable costs and loss of efficacy)[39]. A high persistence rate can thus be indirectly linked to a favourable benefit/risk profile. In the reference clinical trial GO-FORWARD, to week 52, only 5.6% discontinued treatment. This difference is expected since in clinical trials there is a tight control of the patient and the medication and trials mostly exclude patients with a long duration of disease, very severe and very mild disease, multiple previous conventional DMARDs, high doses of corticosteroids, problems with compliance and co-morbidities[39].

The limitations of this work include the small sample size of the overall cohort and comparison groups and, also, the substantial missing data that limited the use of multivariate models and stratified analyses. Cox regression analysis for hazard ratios, for instance, was only performed for a very limited number of variables. Another drawback was that information concerning corticosteroid and other concomitant medication was only available at baseline, meaning that conclusions on concomitant medication tapering and discontinuation over GLM treatment could not be drawn. Another limitation concerns the decision to report an adverse event, which is up to the treating physician, and not controlled as in a clinical trial. Still, registries provide crucial information about effectiveness of therapies administered in daily routine conditions and may support the results from clinical trials, where patients are treated in highly specialized centres per protocol.

CONCLUSION

To conclude, the results obtained support that goli-

mumab is effective: a consistent and significant decrease in RA disease activity through 52 weeks of treatment and a significant functional improvement were observed, as well as a high persistence on treatment. In terms of efficacy, these results, from clinical practice, are very similar to what has been previously established in clinical trials. Undoubtedly, Reuma.pt is a remarkable epidemiological tool, and due to the continuous enrolment of new patients, more powerful and accurate measurements will be possible in the near future.

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CORRESPONDENCE TO

Ana Filipa Mourão
Serviço de Reumatologia, Hospital Egas Moniz,
Centro Hospitalar de Lisboa Ocidental
Rua da Junqueira 126,
1349-019 Lisboa, Portugal.
E-mail: afilipamourao@gmail.com

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