Real-life persistence of golimumab in patients with chronic inflammatory rheumatic diseases: results of the 2-year observational GO-PRACTICE study

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Abstract

Objective

GO-PRACTICE aimed to evaluate the persistence, clinical response and safety of golimumab in adult patients with chronic inflammatory rheumatic disease.

Methods

Prospective observational study with 24 months of follow-up, involving 134 rheumatologists from public or private health establishments in France. The primary outcome was the persistence of golimumab 24 months after initial prescription. Cumulative persistence probabilities were determined from Kaplan-Meier estimates. Secondary outcomes included an evaluation of disease activity and golimumab safety profile.

Results

Of 754 consecutively recruited patients, 170 had rheumatoid arthritis (RA) (54.3 years, 74.1% female, 64.7% biologics-naïve), 106 had psoriatic arthritis (PsA) (48.1 years, 70% female, 66.0% biologics-naïve) and 478 had axial spondyloarthritis (axSpA) (42.8 years, 54.6% female, 60.9% biologics-naïve). Golimumab persistence at 2 years was 56.5%, 45.1% and 52.6%, respectively, in RA, PsA and axSpA groups. Persistence was higher in biologics-naïve (58.3%) than in biologics pre-treated patients (42.7%, p<0.01). For 362 patients continuing golimumab at 2 years, disease activity improved significantly from baseline to 2 years: mean 28-joint disease activity score for RA and PsA was lowered by 2.06 and 1.89 points, and mean ankylosing spondylitis disease activity score was lowered by 3.11 points (p<0.0001) for axSpA. Patient appreciation of disease activity also improved; 8.9% of discontinuations were due to intolerance.

Conclusion

Golimumab persistence was satisfactory at 2 years and accompanied by improvements in clinical effectiveness in 362 patients continuing golimumab at 2 years. Golimumab was well tolerated and its safety profile was consistent with those reported in previous studies.

Key words

golimumab, rheumatoid arthritis, spondyloarthritis, biological therapy, clinical study

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Introduction

Rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) are the three most prevalent chronic inflammatory rheumatic diseases. They are all immune-mediated progressive disorders that cause severe pain, joint damage and loss of function. They negatively impact patient quality of life (QoL) and result in considerable economic burden (1, 2). Despite varying symptoms, RA, PsA and axSpA have key pathophysiological features in common. They can therefore be managed with similar anti-rheumatic medications, such as disease modifying anti-rheumatic drugs (DMARDs), glucocorticoids, and biologics, among which tumour necrosis factor antagonists (anti-TNF-α) are the most used (3, 4). Non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics are also frequently employed for pain management, and are the first-line therapy for axSpA (5).

Biologic therapy has revolutionised the treatment of chronic inflammatory rheumatic diseases, and anti-TNF-α are the most frequently prescribed class. Currently, 5 anti-TNF-α therapies are available: the intravenous infliximab, and the subcutaneous etanercept, adalimumab, certolizumab pegol, and golimumab (GOL). GOL was the latest anti-TNF-α treatment to be approved by the European Medicines Agency for RA, PsA and axSpA, (2009). It is a human immunoglobulin G1κ (IgG1κ) monoclonal antibody that binds with high affinity and specificity to soluble and transmembrane forms of TNF-α, thereby neutralising its biological activity (6). GOL is meant to be administered subcutaneously as 50 mg injection once a month (7, 8).

Over the past decade the efficacy and safety of GOL in patients with RA, PsA and axSpA have been demonstrated in several phase III, randomised controlled trials (RCTs) and their open-label extensions, that selected patients based on varying disease characteristics, comorbidities and treatment histories. These include the GO-FORWARD (9), GO-RAISE (10), GO-REVEAL (11), GO-BEFORE (12), GO-FURTHER (13) and GO-AHEAD (14) trials. GOL'S safety profile has also been shown to be similar to that of other anti-TNF-α (15). Studies evaluating GOL's effectiveness and persistence in real-world cohorts of RA, PsA or axSpA patients are also available (16), however all but one (17) are retrospective.

The GO-PRACTICE study was designed to comply with a request by the French Health Authorities (Haute Autorité de Santé - HAS) for long-term data in RA, PsA and axSpA patients in the context of a post-marketing study, for the re-evaluation of GOL. Persistence is defined as "the duration of time from initiation to discontinuation of therapy" (18), and can be used as a surrogate measure of long-term treatment success, as it reflects the effectiveness, safety and satisfaction associated with a given treatment (19). The aim of this prospective cohort study was to evaluate the persistence of GOL in RA, PsA and axSpA patients who had never received GOL, over a period of 2 years and under real-life conditions in France.

Methods

Study design

GO-PRACTICE, an observational, open-label, prospective cohort study, involving 134 centres in France, was performed according to the Declaration of Helsinki and Good Clinical Practice. The study protocol was approved by the national ethics board. All patients were informed verbally and in writing about the treatment and the study, and they provided their consent prior to enrolment.

Participants

Patients 18 years or older with a confirmed diagnosis of RA, PsA and axSpA were consecutively included upon initial GOL prescription. The decision to prescribe GOL to patients was independent of their willingness to participate. Patients were not eligible if they had prior or ongoing treatment with GOL, including participation in previous clinical trials evaluating GOL.

Patients were assessed prior to initial GOL administration, as per routine practice, and every 12 months thereafter for 2 years (a total of 3 planned visits over 24 months). Intermediate visits were possible, as needed, where the patient's private rheumatologist

completed a brief questionnaire detailing the visit. Monthly 50 mg subcutaneous GOL injections were administered as per the product label. Intermediate study evaluations were also carried out upon treatment modification or discontinuation.

Instruments and assessments

The primary objective was to evaluate the persistence of GOL in RA, PsA and axSpA patients at 2 years. This was estimated with the Kaplan-Meier method for the total cohort, for each of the 3 indications and by biologics treatment history (biologics-naïve patients *vs*. biologics-pretreated patients). Patients were considered persistent at 2 years if they had confirmed to their investigating physician that they were continuing treatment at the 24-month study visit. All permanent discontinuations of GOL were confirmed by the physician via a treatment discontinuation form.

Baseline sociodemographic and medical characteristics were reported descriptively. Disease activity was evaluated at baseline, 12 and 24 months, and upon treatment discontinuation. RA and PsA disease activity assessments were performed using the 28-joint Disease Activity Score (DAS28) (20) based on C-reactive protein (CRP). AxSpA Disease activity was evaluated with the Ankylosing Spondylitis Disease Activity Score (ASDAS) (21) based on CRP. Patient-reported disease activity scores were recorded at baseline, then every 3 months up to 24 months, and at treatment discontinuation. RA and PsA patients reported disease activity via the Routine Assessment of Patient Index Data 3 (RAPID3) instrument (22). AxSpA patients used the 10-point Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) (23). Adverse events (AEs) were reported by type, seriousness, timing and outcomes.

Data management and statistics

Assuming 40% of patients would continue GOL after 24 months, a sample size of 576 patients was needed to obtain a precision of 4% and a 95% confidence level. Accounting for a lost-to-follow-up rate of 30% at 24 months, we planned to include 750 patients.

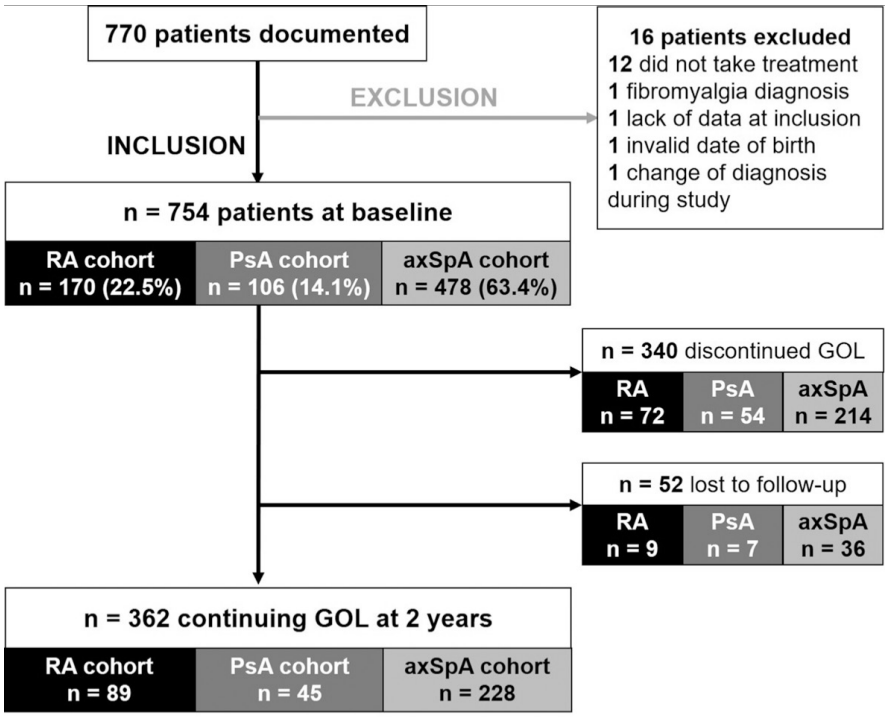


Fig. 1. Patient flow in the study, from enrolment up to 2 years of follow-up.

Rheumatologists recorded data for each patient in paper case report forms (CRFs). RAPID3 and BASDAI questionnaires were recorded by patients in a paper Patient Diary. A quality control was performed in 10% of active participating centres. For continuous variables, the number of patients with non-missing data, mean, standard deviation (SD), median and range were calculated. For ordinal and categorical variables, frequencies were reported as percentages. Planned multiple imputation techniques were not implemented, as missing data was not frequent; incomplete observations were included in the analysis.

All statistical analyses were performed using version 9.2 of the SAS® software. Cumulative persistence probabilities of GOL in different subgroups were estimated with the Kaplan-Meier (KM) method and compared using the log-rank test. Patients with a confirmed discontinuation of GOL or who were lost-to-follow-up without confirmation of their persistence status were censored from the KM analysis. Groups were compared using the Student's *t*-test or Wilcoxon test for continuous variables, and the χ^2 or Fisher's exact test for categorical variables. Changes over time from baseline were analysed using repeated measures (ANOVA). Factors associated with GOL discontinuation were identified, using a Cox Proportional-Hazards Model with variables from demographic characteristics, comorbidities, disease history and treatment history at baseline.

The safety population included all patients who received at least one dose of GOL. All AEs were coded using the Medical Dictionary for Regulatory Activities (MedDRA). The incidence of AEs and serious adverse events (SAE) by MedDRA System Organ Class (SOC) were calculated (number, frequency) for the total population and by indication.

Results

Baseline characteristics of the evaluable population

Between 15/01/2015 and 29/03/2016, 770 patients were enrolled, of which 16 were excluded from the baseline analysis, for reasons detailed in the patient flow diagram (Fig. 1). Of 754 participants included in the analysis, 170 had RA (22.5%), 106 had PsA (14.1%) and 478 had axSpA (63.4%).

Baseline patient characteristics are presented in Table I. Mean age was lowest in the axSpA cohort (42.8±12.1 years)

compared to the PsA and RA groups (48.1±12.9 and 54.3±12.3 years). The proportion of females was highest in RA (74.1%), followed by PsA (66.0%) and axSpA (54.6%). A higher percentage of PsA patients were obese (36.2%) compared to axSpA (17.8%) and RA (15.5%) patients. In line with the mean ages observed in the 3 groups, full-time employment was highest in axSpA patients followed by PsA and RA patients (48.7%, 35.8% and 34.7%, respectively).

Baseline disease characteristics

Mean duration since rheumatic disease diagnosis was highest for RA (8.6±9.9 years), compared to axSpA (7.6±9.2 years) and PsA patients (6.1±7.0 years); Table I. For RA patients, rheumatoid factors were detected in 122 (71.8%) patients; extra-articular manifestations were observed in 21 patients (12.4%), including 7 with pleuro-pulmonary complications, 2 with cardiac complications, and 1 each with vascular complications, hepatic complications, haematological manifestations and Felty's syndrome; the mean DAS28 (CRP) was 4.34±1.11. Cutaneous psoriasis was present in most PsA patients (n=88, 83.0%) and extra-articular manifestations were reported in 6 patients (5.7%), of whom 3 had cardiac complications and 1 reported acute anterior uveitis (AAU). Axial joints were affected in 56 patients (52.8%), peripheral joints in 96 (90.6%), and 47 (44.3%) had both axial and peripheral joint involvement. Mean DAS28 (CRP) was 3.89±1.00.

Human leukocyte antigen-B27 was detected in 66.3% of axSpA patients. Extra-articular manifestations were observed in 129 participants (27.0%), including 85 (17.8%) with AAU and 33 (6.9%) with inflammatory bowel disease. Axial and peripheral joints were affected in 457 (95.6%) and 271 (56.7%) patients, respectively. Both axial and peripheral involvement were observed in 252 patients (52.7%). Mean ASDAS (CRP) was 3.16±0.79.

Baseline treatment history

At baseline, 282 patients (37.5%) had already been treated with another biologic. Previous DMARD use was more frequent among RA patients (91.8%), followed by PsA (79.2%) and axSpA patients (34.1%). Previous corticosteroid use was also more frequent in RA patients (63.5%), compared to PsA (34.9%) and axSpA patients (16.5%). NSAIDs and analgesics were most frequently prescribed in axSpA (90.0%) and PsA (86.8%) than in RA (71.2%) – Table I.

Initial golimumab prescription and co-treatments

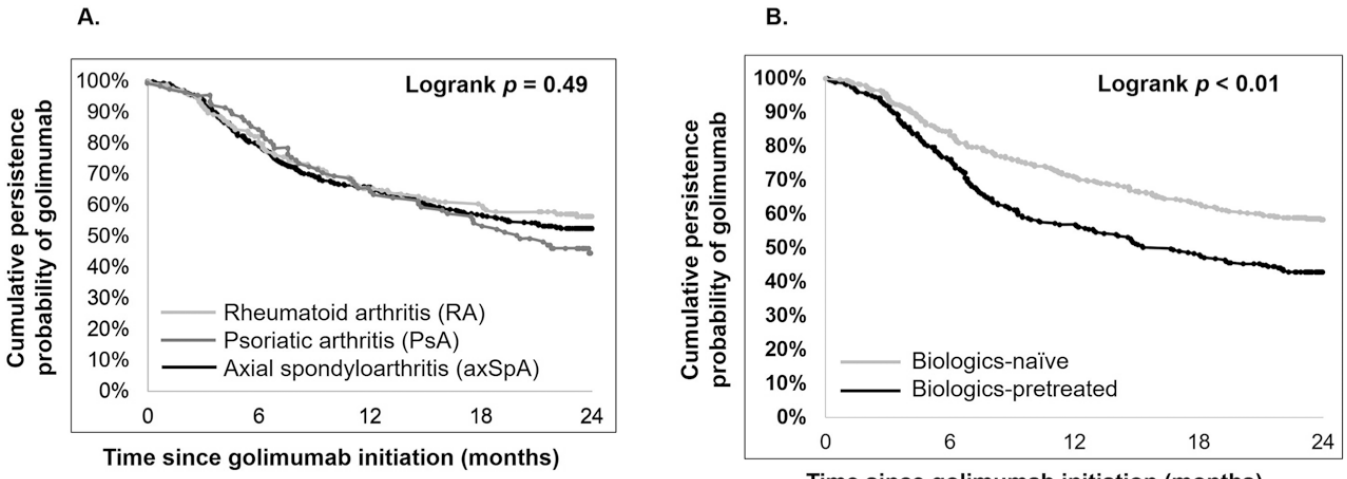
Almost all the patients in the cohort were initially prescribed a monthly dose of 50 mg GOL, for an average duration of 5 months. Most patients were also prescribed at least one concomitant treatment (97.6% of RA, 85.8% of PsA and 78.9% of axSpA patients). A majority of RA patients were co-prescribed DMARDs (n=143, 84.6%) *versus* 56.6% of PsA patients (n=60) and 17.2% of axSpA patients (n=82). Corticosteroids were co-prescribed to 53.3% of RA patients (n=90), 25.5% of PsA patients (n=27) and only 5.9% (n=28) of axSpA patients. NSAIDs and/or analgesics were given to 73.6%

Table I. Baseline characteristics of the RA, PsA and axSpA cohorts, and the total study cohort.

	RA (n=170)	PsA (n=106)	axSpA (n=478)	Total cohort (n=754)
Mean age, y	54.3 ± 12.3	48.1 ± 12.9	42.8 ± 12.1	46.1 ± 13.1
Median (range)	55.0 (22.0-86.0)	48.5 (22.0-77.0)	41.0 (19.0-79.0)	45.0 (19.0-86.0)
Female, n (%)	126 (74.1)	70 (66.0)	261 (54.6)	457 (60.6)
BMI, n (%)				
n	**168**	**105**	**471**	**744**
Underweight (<18.5 kg/m^2)	9 (5.4)	1 (1.0)	19 (4.0)	29 (3.9)
Normal (18.5-24.9 kg/m^2)	71 (42.3)	32 (30.5)	221 (46.9)	324 (43.5)
Overweight (25-29.9 kg/m^2)	62 (36.9)	34 (32.4)	147 (31.2)	243 (32.7)
Obese (>30 kg/m^2)	26 (15.5)	38 (36.2)	84 (17.8)	148 (19.9)
Mean time since diagnosis, y	**8.6 ± 9.9**	**6.1 ± 7.0**	**7.6 ± 9.2**	**7.6 ± 9.1**
Median (range)	5.0 (0.2-63.3)	2.9 (0.1-34.2)	4.2 (0.0-51.8)	4.1 (0.0-63.3)
Mean CRP, mg/L	11.6 ± 16.7	8.5 ± 11.2	11.4 ± 17.9	NC
Mean ESR, mm/h	20.2 ± 16.3	19.9 ± 21.8	16.4 ± 18.0	NC
Biotherapy naïve, n (%)	110 (64.7)	70 (66.0)	291 (60.9)	471 (62.5)
At least 1 co-morbidity, n (%)	149 (87.6)	103 (97.2)	391 (81.8)	643 (85.3)
	n = 170	**n = 106**	**n = 478**	**n = 754**
Prior biologics, n (%) [a]	59 (34.7)	36 (34.0)	187 (39.1)	282 (37.5)
Biologics-naïve	110 (64.7)	70 (66.0)	291 (60.9)	471 (62.5)
1 biologic	23 (13.5)	22 (20.8)	90 (18.8)	135 (17.9)
2 biologics	15 (8.8)	10 (9.4)	59 (12.3)	84 (11.1)
3 biologics	7 (4.1)	4 (3.8)	36 (7.5)	47 (6.2)
4 and more biologics	14 (8.2)	0 (0)	2 (0.4)	16 (2.1)
Prior DMARD, n (%)	156 (91.8)	84 (79.2)	163 (34.1)	403 (53.4)
MTX	146 (85.9)	83 (78.3)	110 (23.0)	339 (45.0)
Ongoing	90 (52.9)	45 (42.5)	46 (9.6)	181 (24.0)
Prior Corticosteroids, n (%)	108 (63.5)	37 (34.9)	79 (16.5)	224 (29.7)
Prior NSAIDs/Analgesics, n (%)	121 (71.2)	92 (86.8)	430 (90.0)	643 (85.3)
Prior surgeries, n **(%)**	66 (38.8)	42 (39.6)	102 (21.3)	210 (27.9)
Employment status, n (%)				
	n = 170	**n = 106**	**n = 478**	**n = 754**
Full-time	59 (34.7)	38 (35.8)	233 (48.7)	330 (43.8)
Part-time	18 (10.6)	19 (17.9)	75 (15.7)	112 (14.9)
Student	1 (0.59)	0 (0)	6 (1.26)	7 (0.93)
Retired	49 (28.8)	21 (19.8)	40 (8.37)	110 (14.6)
Unemployed	16 (9.41)	9 (8.49)	49 (10.3)	74 (9.81)
Homemaker	5 (2.94)	3 (2.83)	12 (2.51)	20 (2.65)
Disability/Unable to work	14 (8.24)	15 (14.2)	49 (10.3)	78 (10.3)
2 statuses provided	8 (4.71)	1 (0.94)	14 (2.93)	23 (3.05)

[a] Prior biologics data missing for 1 patient with rheumatoid arthritis.

axSpA: axial spondyloarthritis; BMI: body mass index; CRP: C-reactive protein; DMARD: disease-modifying anti-rheumatic drug; ESR: erythrocyte sedimentation rate; MTX: methotrexate; n: number of patients; NC: not calculated; NSAID: non-steroidal anti-inflammatory drug; PsA: psoriatic arthritis; RA: rheumatoid arthritis; y: year(s).



GOL Persistence	12 months	24 months
RA	65.4%	56.5%
PsA	66.0%	45.1%
axSpA	65.8%	52.6%
Total	*65.7%*	*52.4%*

GOL Persistence	12 months	24 months
Biologics-naïve	71.2%	58.3%
Biologics-pretreated	56.8%	42.7%
Total	*65.7%*	*52.4%*

Fig. 2. Kaplan-Meier curves showing the cumulative golimumab persistence probabilities over 24 months for: **A**) RA, PsA and axSpA patients, **B**) patients by biologics history.

Table II. Cumulative persistence probabilities of biologics-naïve and pretreated patients continuing GOL therapy at 6, 12, 18 and 24 months in the RA, PsA and axSpA cohorts.

		Cumulative GOL persistence probabilities (%) with 95% confidence intervals (CI)				
	Baseline population	6 months (%)	12 months (%)	18 months (%)	24 months (%)	*Log rank, p*
All patients	**n=754** [a]	**80.6 (77.5 – 83.3)**	**65.7 (62.1 – 69.1)**	**57.5 (53.8 – 61.0)**	**52.4 (48.7 – 56.0)**	
BN	n=471 [a]	83.3 (79.5 – 86.4)	71.2 (66.7 – 75.1)	63.2 (58.5 – 67.5)	58.3 (53.5 – 62.8)	**<0.01**
BP	n=282 [a]	76.1 (70.6 – 80.7)	56.8 (50.7 – 62.4)	48.2 (42.1 – 53.9)	42.7 (36.8 – 48.6)	
RA	**n=170** [a]	**80.4 (73.5 – 85.6)**	**65.4 (57.7 – 72.1)**	**60.4 (52.6 – 67.4)**	**56.5 (48.5 – 63.7)**	
BN	n=110 [a]	85.3 (77.1 – 90.7)	69.6 (60.0 – 77.3)	63.8 (53.9 – 72.1)	60.6 (50.5 – 69.2)	0.06
BP	n=59 [a]	70.7 (57.2 – 80.6)	56.9 (43.2 – 68.4)	53.5 (39.9 – 65.2)	48.2 (34.8 – 60.2)	
PsA	**n=106**	**86.0 (77.5 – 91.5)**	**66.0 (55.8 – 74.4)**	**54.8 (44.5 – 64.0)**	**45.1 (35.0 – 54.7)**	
BN	n=70	87.7 (76.9 – 93.6)	72.3 (59.7 – 81.6)	59.7 (46.7 – 70.5)	51.3 (38.3 – 62.8)	0.06
BP	n=36	82.9 (65.8 – 91.9)	54.3 (36.6 – 69.0)	45.7 (28.9 – 61.0)	34.1 (19.1 – 49.6)	
axSpA	**n=478**	**79.5 (75.5 – 83.0)**	**65.8 (61.3 – 70.0)**	**57.1 (52.4 – 61.5)**	**52.6 (47.9 – 57.1)**	
BN	n=291	81.5 (76.3 – 85.6)	71.5 (65.8 – 76.5)	63.9 (57.8 – 69.3)	59.2 (53.1 – 64.8)	**<0.01**
BP	n=187	76.5 (69.7 – 82.0)	57.2 (49.7 – 64.0)	46.9 (39.4 – 53.9)	42.7 (35.3 – 49.8)	

[a] prior biologics data was missing for 1 patient with rheumatoid arthritis.
axSpA: axial spondyloarthritis; BN: biologics-naïve; BP: biologics-pretreated; GOL: golimumab; PsA: psoriatic arthritis; RA: rheumatoid arthritis.

of PsA (n=78) and axSpA (n=352) patients, and 60.9% RA patients (n=103).

Golimumab persistence at 2 years

The persistence rate of GOL in the total study cohort at 2 years after initial prescription was 52.4% [95% CI 48.7–56.0%] (Table II). The 2-year persistence was highest in RA and lowest in PsA patients (Fig. 2a, Table II). Of 754 participants, 340 patients discontinued (72 RA, 54 PsA and 214 axSpA patients) and 52 patients were lost to follow-up (Fig. 1). Most frequent reason for discontinuation in the cohort was primary non-response (n=129, 17.1%) and secondary failure (n=87, 11.5%); 67 patients (8.9%) discontinued due to intolerance, 43 (12.6%) because they wished to stop GOL treatment. Of 362 patients persisting on GOL at 2 years, prescriptions were renewed for 338 (93.3%). Moreover, GOL persistence at 2 years was noted to be higher in patients who took GOL as their first line of biologic treatment than in those who received GOL as a second or further line of biologic – 58.3% [95% CI 53.5–62.8%] *vs*. 42.7% [95% CI 36.8–48.6%], $p<0.01$ (Fig. 2b, Table II). While a similar trend was noted for all indications, this difference was statistically significant only in the axSpA cohort (Table II).

Having gastrointestinal disease at baseline was associated with a higher risk of treatment discontinuation in RA patients (HR 3.85, 95%CI [1.97–7.55]) but a lower risk of discontinuation in

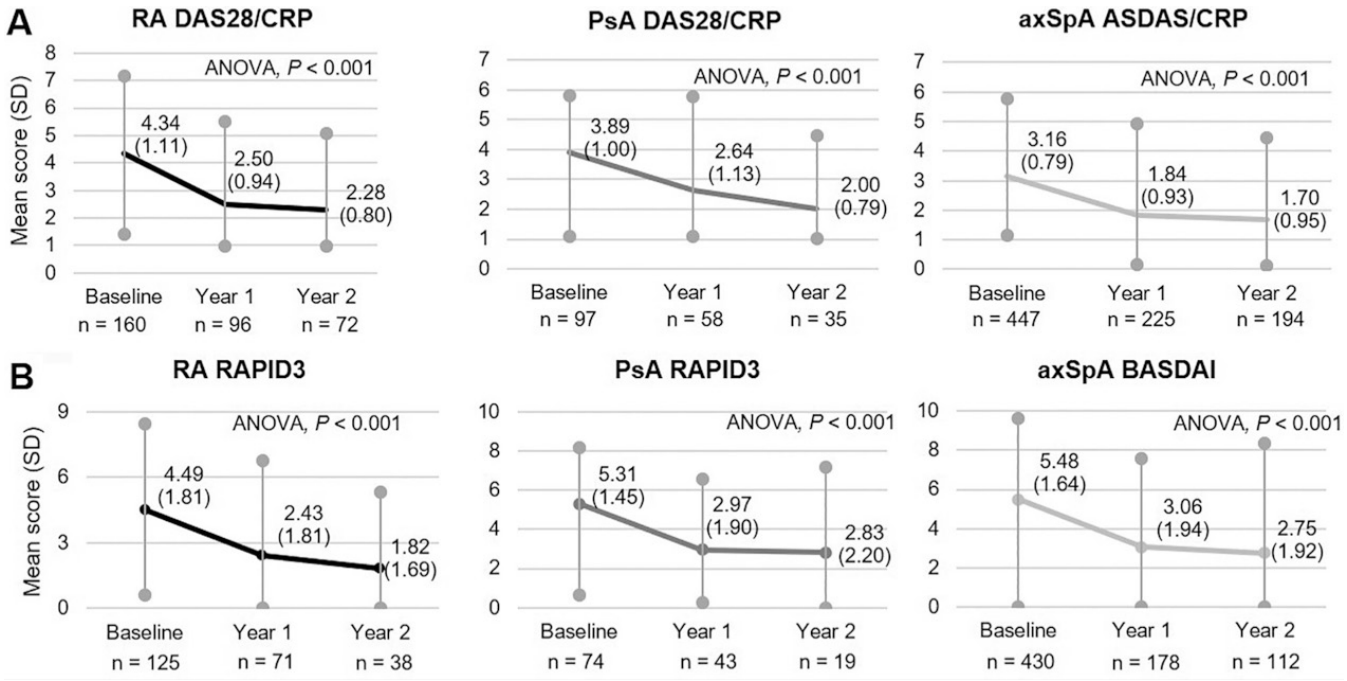


Fig. 3. A: Evolution of the Disease activity in patients persisting on GOL at 2 years as assessed by the physician for RA and PsA patients (DAS28/CRP) and for axSpA patients (ASDAS/CRP), at baseline, 1 year and 2 years; **B**: Evolution of the Disease activity as reported by the patient persisting on GOL at 2 years for RA and PsA (RAPID3) and for axSpA (BASDAI), at baseline, 1 year and 2 years.
Mean (SD) disease activity scores are reported at each time point together with the maximum and minimum range values. The number of patients for whom data was available at each timepoint is also indicated.

PsA patients (HR 0.04, 95%CI [0.003–0.52]). Among axSpA patients, the risk of discontinuing GOL was twice lower in males than in females: HR 0.52, 95%IC [0.39–0.70].

Disease activity evolution for patients persisting on golimumab for 2 years

RA: mean baseline DAS28 (CRP) decreased to 2.28 ± 0.80 at year 2 (p<0.0001) for those continuing GOL, as shown in Figure 3a. Baseline RA activity was low (≤3.20), moderate (≤ 5.10) and high (>5.10) in 13.9%, 57.6% and 28.5% of patients with available data (n=160). RA activity was low and moderate in 86.1% and 13.9% of patients continuing GOL at 2 years (n=72); 71.8% of these patients demonstrated a clinically significant improvement of disease activity (equivalent to a score decrease of ≥1.2). Mean DAS28 (n=40) was 4.09±1.21 at discontinuation for those who stopped GOL before 2 years. The mean RAPID3 score also dropped significantly through 2 years (Fig. 3b); mean RAPID3 at GOL discontinuation was 5.09±1.44 for those who stopped GOL before 2 years.

PsA: mean baseline DAS28 (CRP) decreased to 2.00±0.79 at year 2 (p<0.0001) for PsA patients persisting on GOL (Fig. 3a). Baseline PsA activity was low, moderate and high in 22.7%, 66.0% and 11.3% of patients (n=97). At year 2, 91.4% and 8.6% of patients had low and moderate PsA activity (n=35) and PsA activity was clinically improved in 72.7% of these patients. For those who discontinued GOL, mean DAS28 (CRP) was 3.78 ± 1.06 at discontinuation. Mean RAPID3 scores decreased significantly from baseline to 2 year for those continuing GOL (p<0.0001) (Fig. 3b), and mean RAPID3 at discontinuation was 6.27±1.07 for those who stopped GOL before 2 years.

axSpA: mean baseline ASDAS (CRP) scores for patients continuing GOL improved to 1.70±0.95 at year 2 (p<0.0001) (Fig. 3a). At baseline (n=447), 91.9% of patients had high or very high disease activity (ASDAS ≥2.1) and 7.8% had moderate disease activity (ASDAS 1.3 to 2.1). At 2 years (n=194), clinically significant improvement (score decrease of ≥1.1) was observed in 59.8% of axSpA patients; 38.1% were in remission (ASDAS <1.3), 34.0% had moderate and 27.8% had high or very high disease activity. For those who discontinued GOL, mean ASDAS (CRP) was 2.96±0.88 at discontinuation. Mean BASDAI (Fig. 3b) also showed significant improvements from baseline to 2 years. Mean BASDAI at discontinuation (5.72±2.00) was comparable to the baseline score.

Safety

Overall, 46.7% of patients who received GOL reported at least one AE. AEs were reported for 47.5% of axSpA patients (689 events), 46.5% of RA patients (220 events) and 43.4% of PsA patients (146 events) (Table III). SAEs were reported in 17.0% of PsA patients (30 events), 11.2% of RA patients (43 events) and 8.8% of axSpA patients (116 events).

Overall, 61 SAEs were assessed as possibly related to GOL, which were most frequently general disorders and administration site conditions (27 of 61, 44.3%) and infections and infestations (10 of 61, 16.4%). Other possibly related SAEs included 1 case each of blood and lymphatic system disorder (preferred term

Table III. All AEs in the total cohort, with classification by SOC.

	RA (n=170)	PsA (n=106)	axSpA (n=478)	Total (n=754)
Number of AEs, n	220	146	689	1055
Number of SAEs, n (% of AEs)	43 (19.5)	30 (20.5)	116 (16.8)	189 (17.9)
Patients with AEs, n (%)	79 (46.5)	46 (43.4)	227 (47.5)	352 (46.7)
Patients with SAEs, n (%)	19 (11.2)	18 (17.0)	42 (8.8)	79 (10.5)
AEs by SOC	n=220	n=146	n=689	n=1055
General disorders and administration site conditions	82 (37.3)	58 (39.7)	243 (35.3)	**383 (36.3)**
Infections and infestations	51 (23.2)	26 (17.8)	144 (20.9)	**221 (20.9)**
Injury, poisoning and procedural complications	8 (3.6)	9 (6.2)	55 (8.0)	**72 (6.8)**
Skin and subcutaneous tissue disorders	8 (3.6)	10 (6.8)	42 (6.1)	**60 (5.7)**
Gastrointestinal disorders	7 (3.2)	4 (2.7)	44 (6.4)	**55 (5.2)**
Nervous system disorders	5 (2.3)	6 (4.1)	31 (4.5)	**42 (4.0)**
Musculoskeletal and connective tissue disorders	14 (6.4)	5 (3.4)	16 (2.3)	**35 (3.3)**
Surgical and medical procedures	7 (3.2)	7 (4.8)	16 (2.3)	**30 (2.8)**
Respiratory, thoracic and mediastinal disorders	5 (2.3)	4 (2.7)	17 (2.5)	**26 (2.5)**
Psychiatric disorders	7 (3.2)	3 (2.1)	13 (1.9)	**23 (2.2)**
Investigations	1 (0.5)	3 (2.1)	9 (1.3)	**13 (1.2)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	3 (1.4)	2 (1.4)	7 (1.0)	**12 (1.1)**
Vascular disorders	4 (1.8)	0 (0)	8 (1.2)	**12 (1.1)**
Eye disorders	1 (0.5)	0 (0)	9 (1.3)	**10 (10.0)**
Hepatobiliary disorders	6 (2.7)	2 (1.4)	2 (0.3)	**10 (10.0)**
Reproductive system and breast disorders	2 (0.9)	1 (0.7)	7 (1.0)	**10 (10.0)**
Blood and lymphatic system disorders	2 (0.9)	1 (0.7)	5 (0.7)	**8 (0.8)**
Cardiac disorders	3 (1.4)	0 (0)	5 (0.7)	**8 (0.8)**
Metabolism and nutrition disorders	0 (0)	2 (1.4)	5 (0.7)	**7 (0.7)**
Renal and urinary disorders	0 (0)	2 (1.4)	4 (0.6)	**6 (0.7)**
Immune system disorders	1 (0.5)	1 (0.7)	2 (0.3)	**4 (0.4)**
Endocrine disorders	1 (0.5)	0 (0)	2 (0.3)	**3 (0.3)**
Ear and labyrinth disorders	1 (0.5)	0 (0)	1 (0.1)	**2 (0.2)**
Social circumstances	1 (0.5)	0 (0)	1 (0.1)	**2 (0.2)**
Pregnancy, puerperium and perinatal conditions	0 (0)	0 (0)	1 (0.1)	**1 (0.1)**

AE: adverse event; axSpA: axal spondyloarthritis; PsA: psoriatic arthritis; RA: rheumatoid arthritis; SAE: serious adverse event; SOC: System Organ Class.

(PT) thrombocytopenia), cardiac disorder (PT pericarditis), nervous system disorder (PT brain lesion), reproductive system and breast disorder (PT cervical dysplasia) and surgical and medical procedure (PT cervical conisation).

Two patients died (0.3% of 754): one committed suicide and the cause of death could not be obtained for the other.

Discussion

The prospective cohort in GO-PRACTICE is the second-largest of its kind, after the GO-NICE study (17), to present data concerning GOL use in all three indications under real-life clinical practice. It is also the first prospective cohort to evaluate GOL persistence in RA, PsA and axSpA. Subcutaneous GOL administered monthly in a 50 mg dose was effective in real-life RA, PsA and axSpA patients who persisted on the treatment, which complements the findings of the afore-mentioned RCTs.

Golimumab persistence at 2 years

The two-year persistence of GOL in RA, PsA, axSpA patients of this study was as expected for an anti-TNF therapy, at 56.5%, 45.1% and 52.6%, respectively, and much better for biologics-naïve than biologics-pretreated patients. The GOL persistence observed in this study was within the range of GOL persistence estimates observed in most retrospective registry studies with larger sample sizes. In a systematic review of real-world GOL persistence in RA, PsA and axSpA from up to 12 cohorts (16), the reported persistence estimates at 6 months, 1 year and 2 years ranged from 63% to 90% (24-27), 47% to 80% (24-26, 28-31) and 32% to 77% (24-27, 29, 32-34), respectively. In a retrospective analysis of the French Health Insurance Database, evaluating the impact of anti-TNF-α non-persistence on healthcare costs, the one-year persistence of subcutaneous anti-TNF-α therapies (including GOL) was found to be at 56.1% (2133 of 3804 patients who initiated any subcutaneous anti-TNF-α therapy between July and December 2012) (35). In a multicentre Greek study involving 166, 82 and 80 patients with RA PsA and AS, respectively, the 2- and 3-year drug survival was highest in AS patients (79% and 76%), compared to RA (69% and 60%) and PsA patients (58% and 53%) (36).

Persistence can depend on factors other than safety and effectiveness. We found that gastrointestinal disease was positively and negatively associated with GOL discontinuation in RA and PsA patients, respectively. In axSpA, females were at a greater risk for discontinuation.

Differences between GOL persistence for the three indications was not shown to be significant in our study, which was also the case in the retrospective GOL persistence studies (16). Four of these studies stratified persistence by indication, and showed that GOL persistence was higher in axSpA patients compared to RA or PsA patients, however not statistically significant (25, 26, 33, 34). A recent retrospective analysis of the Spanish registry of patients with rheumatic disorders receiving biological

drugs (BIOBADASER) revealed similar 5-year GOL persistence rates in RA, PsA and axSpA (37).

In line with our findings, Saevarsdottir *et al*. (Sweden, 2,106 patients) (26) and Hernandez *et al*. (Spain, 353 patients) (37) demonstrated that GOL persistence was significantly higher in biologics-naïve patients compared to those previously treated with biologics, across all three indications. Favalli *et al*. (Italy, 136 patient cohort) (32) reported 2-year GOL persistence in RA patients at 61% and 57%, for biologics-naïve and pretreated patients, respectively. Conversely, Manara *et al*. (33) (Italy, 180 patients) and Rotar and Tomsic (25) (Slovenia, 103 patients) did not find such a difference in patients treated with GOL.

In five retrospective studies assessing GOL persistence for up to 3 years compared to other anti-TNF-α therapies, GOL persistence was generally found to be significantly greater than for etanercept, adalimumab, certolizumab, infliximab (24, 30, 32, 38, 39). However, in the ANSWER study (40), GOL's 3-year persistence (61.3%) was reported to be lower than for abatacept, tocilizumab, etanercept and infliximab (and slightly higher than for adalimumab and certolizumab).

Clinical response and safety

Clinically significant improvements in disease activity were observed for RA, PsA and axSpA patients who persisted on GOL. Similar trends of overall clinical improvement are also observed in the GO-NICE study (17, 41), in a prospective observational study involving participants with AS (42), and in phase III trials of GOL (9-14). Nevertheless, upon GOL discontinuation, Nevertheless, RA, PsA and axSpA patients who withdrew from GOL treatment were found to have disease activity scores at discontinuation that were comparable to the baseline scores, denoting unchanged outcomes.

GOL treatment was well tolerated in our study, similar to the safety findings of GO-NICE (17) and prior RCTs (9-15) and observational studies (42,43). AE frequencies were similar in RA, PsA and axSpA patients, but SAEs were most frequent in PsA patients.

Study strengths and limitations

A strength of this study is the relatively large cohort of RA, PsA and axSpA patients who were prospectively and consecutively enrolled, to reflect real-life conditions. This cohort also allowed for the analysis of the persistence and treatment effects of GOL in biologics-naïve and biologics-pretreated patients.

One of the main limitations of this study, as is the case with most observational studies, is the high rate of missing data, especially for the patient-reported disease activity assessments. This cohort was relatively homogenous, given that it included patients only from France – this aspect could limit the generalisability of the study outcomes to other healthcare settings. Treatment compliance was not evaluated as part of this study, which may thus provide a partial understanding of overall GOL dosing and its influence on treatment success. However, persistence alone, as defined by the continuity of GOL treatment at 2-years, is considered a clinically pertinent outcome as it reflects that the treatment was sufficiently successful and well tolerated to be continued.

A selection bias may exist, concerning the physicians or patients, as it depends on their motivation to participate in this study. Generally, the responses to GOL as well as overall outcomes of patients in this cohort correspond to the effects observed in previous published pivotal trials and another prospective cohort study on golimumab (GO-NICE), which externally validates the findings of GO-PRACTICE.

Conclusions

GOL persistence at 2 years in RA, PsA and axSpA patients was as expected, and accompanied by significant improvements in disease activity in those who persisted on the treatment. Biologics naïve patients demonstrated better GOL persistence compared to biologics pretreated patients, coupled with much improved clinical outcomes across all three indications. Subcutaneous GOL 50 mg once monthly was thus an effective treatment in RA, PsA and axSpA patients who continued GOL in real-life settings in France. GOL was well tolerated and no new safety signals were observed.

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