Patient Preference and Adherence

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ORIGINAL RESEARCH

Impact of Adherence to Golimumab on Disease Flares in Rheumatoid Arthritis: Results from a Canadian Observational Study

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Objective: To assess the association between adherence to golimumab treatment and the incidence of disease flares in patients with rheumatoid arthritis (RA) in routine clinical practice.

Methods: A 12-month (M) prospective observational study conducted across 27 Canadian centers, involving patients with RA receiving golimumab as part of routine clinical care. Treatment adherence was assessed with the Compliance Questionnaire in Rheumatology (CQR); non-adherence was defined as a weighted baseline score predictive of ≤80% compliance. Secondary definitions involved the CQR score at M6 and M12. Disease flaring was assessed with the RA-Flare Questionnaire (RA-FQ); flare was defined as a positive response to question 7 ("Are you having a flare?"). The association between adherence and disease flares was analyzed by comparing RA-FQ scores and the proportion of patients reporting flares between the high and low adherence groups. The association between adherence and glucocorticoid use or adverse event (AE) incidence was similarly assessed.

Results: Of 215 patients enrolled, 169 (78.6%) completed the study. No significant difference in mean RA-FQ scores was observed between low and high adherence groups at M6 (22.5 vs 23.8; p=0.56) and M12 (20.8 vs 19.9; p=0.70); disease flares were reported by 35.7% of low adherence patients, compared to 28.2% in the high adherence group (p=0.34). At M12, these rates were 30% vs 24.7%, respectively (p=0.49). Glucocorticoid use was comparable between baseline adherence groups, although a higher rate was observed in the low visit-predicted adherence group based on the M6 CQR score (30.5% vs 16.3%; p=0.04). No significant differences were observed in AE incidence.

Conclusion: In this study, no significant differences in RA-FQ scores and the proportions of patients reporting disease flares or AEs were observed between patients with RA with low and high predicted adherence to golimumab. The increased glucocorticoid use in patients with low adherence merits further investigation.

Trial Registration: ClinicalTrials.gov identifier, NCT03729349.

Keywords: biological disease-modifying antirheumatic drugs, TNF inhibitor, adherence, rheumatoid arthritis, flares

Introduction

Rheumatoid Arthritis (RA) is a chronic inflammatory autoimmune disorder that primarily affects the joints symmetrically, causing pain, swelling, and stiffness.[1,2] It is characterized by progressive inflammation and hyperplasia of the synovial tissue, leading to cartilage and bone damage, as well as the production of rheumatoid factor and anti-citrullinated protein antibodies.[3,4] These symptoms limit physical function and significantly reduce patients' quality of life.[3]

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Initial RA treatment typically includes conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) such as methotrexate and leflunomide, used alone or in combination. For patients who do not respond to first-line treatments, biologic DMARDs (bDMARDs) including tumor necrosis factor inhibitors (TNFi), interleukin-6 inhibitors (IL-6i), T-cell costimulation modulators, or targeted synthetic DMARDs (tsDMARDs) like Janus kinase inhibitors (JAKi), may be prescribed.[3,5,6]

Therapeutic adherence, defined as the extent to which a patient's medication-taking matches their prescribed regimen, is essential for achieving maximum drug effectiveness and optimal treatment outcomes.[7] Previous studies have shown that consistent adherence allows for sustained control of disease activity, lower rates of disease flares, reduced progression of joint damage, and improved quality of life in patients with RA.[8–12] Conversely, non-adherence or low adherence can compromise treatment efficacy, leading to inadequate therapeutic response, increased disease activity, and greater risk of flare-ups.[9,13,14] RA flares are defined as periodic, significant worsening of disease activity, characterized by severe and prolonged symptoms that may necessitate treatment adjustments or new therapies.[15–17] These flare-ups can result in intensified pain, increased joint damage and radiographic progression, stiffness, reduced mobility, and general malaise.[18–20]

Previous research has shown that treatment adherence often decreases over time,[21,22] with non-adherence rates ranging from 9.6% to 55% in patients with RA.[23–26] Although adherence varies by treatment class and route of administration,[27,28] non-adherence to bDMARDs remains a common issue in RA. Understanding real-world patterns and impact of non-adherence can help inform strategies to improve patient outcomes.

Golimumab is a tumor necrosis factor-alpha (TNF-α) inhibitor often used in a monthly dosing regimen in combination with methotrexate for RA treatment.[29] Studies have shown that golimumab can slow disease progression and alleviate associated symptoms, and it has been reported to have a higher adherence rate compared with other bDMARDs.[30–33] This study aimed to assess adherence rates to golimumab treatment among Canadian patients with RA followed in routine clinical care, and to evaluate the association between non-adherence and the incidence of disease flares.

Methods

Study Design and Population

GO FAR (NCT03729349) was a prospective, multi-center, non-interventional real-world study that was carried out in 27 centres across Canada between January 2019 and August 2023. Eligible patients were adults with confirmed RA diagnosed by the treating physician, for whom the treating rheumatologist decided to initiate golimumab treatment prior to and independently of participating in the study. Patients were excluded if they (1) had a diagnosis of axial spondyloarthritis, ankylosing spondylitis or psoriatic arthritis; (2) had received any investigational product in the last 3 months prior to study initiation; or (3) were currently participating in another clinical trial, either investigational or observational.

Baseline demographics, disease characteristics and concomitant rheumatologic medication use were gathered at the initial visit. Clinical disease assessments, patient assessments of adherence and disease flares, and adverse events (AEs) were recorded twice in 6-month intervals during the 12-month observational period.

Ethics approval for the study was obtained from each participating site's independent ethics committee or institutional review board and all study participants provided written informed consent prior to enrollment.

Outcome Measures

Adherence with treatment was assessed with the Compliance Questionnaire in Rheumatology (CQR).[34] CQR is a patient reported compliance/adherence measure designed to assess patient's compliance/adherence with anti-rheumatic treatments. It contains 19 items scored on a 4-point Likert scale, where a total score of 0 indicates no adherence and 100 indicates complete adherence. In a previous study, multiple linear regression analysis generated a weighted CQR score, which showed good validity in detecting satisfactory (>80%) compliance/adherence and correct dosing.[35] Using the previously identified optimal threshold score (Z_k of –0.58489) for the discrimination of satisfactory adherence, patients were classified as having high or low predicted adherence at baseline, 6 and 12 months.

Disease flaring was assessed by using Rheumatoid Arthritis – Flare Questionnaire (RA-FQ) mean score and a flare was defined as a positive response to question 7 (Are you having a Flare?) of the RA-FQ.[36] RA-FQ is a patient reported

flare questionnaire with 7 items that measures 5 components including (a) pain, physical activity, fatigue, stiffness, participation in daily activities over the past week using a numeric rating scale of 0–10, where a score of 0 indicates none and a score of 10 indicates severe symptoms; and (b) self-reporting of symptoms duration >7 days and self-reporting of a flare. A higher score in the first 5 questions and a positive response to questions 6 and 7 indicated worsening flare.

Both questionnaires were completed by the patient in his or her local language (English or French).

Statistical Analysis

The analysis population (effectiveness analysis set; EAS) included patients who received at least 1 dose of golimumab and had both a baseline and at least 1 post-baseline assessment (6- or 12-month visit) within the specified 1-year visit window. Summary statistics were produced for all study variables, including the mean (standard deviation [SD]) or the median (interquartile range [IQR]) for continuous variables, depending on data distribution, and frequency distributions for categorical variables. The efficacy data were summarized by level of adherence, categorized as high or low based on baseline or visit adherence.

The impact of treatment adherence on flares was analyzed by comparing (a) the mean RA-FQ scores and (b) the proportions of patients with a positive answer to question 7 of the RA-FQ between the baseline predicted low and high adherence groups using the differences in means/proportions along with the corresponding 95% confidence interval (CI). Additionally, a secondary analysis was conducted to assess the impact of treatment adherence on flares using visit-predicted adherence instead of baseline-predicted adherence.

Similar methods were used to assess the association between treatment adherence and (a) disease activity, measured with the Clinical Disease Activity Index (CDAI), Physician Global Assessment (MDGA), and Patient Global Assessment (PtGA); (b) glucocorticoids use, and; (c) incidence of AEs and serious AEs (SAEs).

All analyses were performed using SAS software, version 9.4 (SAS Institute, North Carolina, US).

Results

Baseline Patient Characteristics

A total of 215 patients were enrolled, of whom 78.6% completed the study. Primary reasons for study discontinuation included withdrawal by the subject (5.1%), physician decision (4.2%), and loss to follow up (3.3%). The EAS included 180 patients, the majority of whom were female (66.7%) and white (84.7%), with a mean (SD) age of 58 (11.8) years, a BMI of 30.0 (7.2) kg/m^2, and median (IQR) time since RA diagnosis of 4.0 (0, 45.7) years. Mean (SD) CDAI levels of 29.1 (12.3) were indicative of high disease activity at baseline. Most (77.2%) patients at baseline were biologic-naive; 40.0%, 36.7% and 16.1% had received prior methotrexate, csDMARDs and glucocorticoid medication, respectively (Table 1).

Table 1 Baseline demographics and disease characteristics of patients in the effectiveness analysis set and the high and low baseline adherence groups

	Effectiveness Analysis Set (N=180)	High Baseline Adherence (N=88)	Low Baseline Adherence (N=80)
Demographics			
Age, years, mean (SD)	58.1 (11.8)	59.3 (12.1)	55.8 (11.5)
Female gender, %	66.7	69.3	62.5
White, %	84.7[a]	78.5[b]	90.5[c]
BMI, kg/m^2, mean (SD)	30.0 (7.2)[d]	30.2 (7.6)[e]	29.5 (6.7)[f]
RA characteristics			
Time since RA diagnosis, years, median (IQR)	4.0 (0, 45.7)	3.3 (0.3, 45.7)	4.6 (0, 36.2)
Time since first RA symptom, years, mean (SD)	10.2 (9.8)[g]	9.7 (10.3)	10.3 (9.0)[h]

(*Continued*)

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Table 1 (Continued).

	Effectiveness Analysis Set (N=180)	High Baseline Adherence (N=88)	Low Baseline Adherence (N=80)
Disease Activity			
CDAI, mean (SD)	29.1 (12.3)[g]	30.3 (12.8)[i]	27.7 (11.9)
MDGA (0–10 cm), mean (SD)	6.1 (2.4)[g]	6.3 (2.4)[i]	5.9 (2.5)
PtGA (0–10 cm), mean (SD)	6.2 (2.0)[g]	6.4 (2.0)[i]	6.0 (1.9)
Medications, %			
Bionaive	77.2	80.7	75.0
csDMARDs[j]	55.6	59.1	57.5
Methotrexate	40.0	40.9	43.8
Glucocorticoids	16.1	17.0	12.5

Notes: [a]N=163; [b]N=79; [c]N=74; [d]N=136; [e]N=67; [f]N=60; [g]N=179; [h]N=79; [i]N=87; [j]csDMARDs include aminoquinolines, other anti-inflammatory and antirheumatic agents (hydroxychloroquine, sulfasalazine), other immunosuppressants (methotrexate) and leflunomide.

Abbreviations: BMI, body mass index; CDAI, clinical disease activity index; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; EAS, effectiveness analysis set; MDGA, physician global assessment of disease activity; PtGA, patient global assessment of disease activity; RA, rheumatoid arthritis; SD, standard deviation.

Treatment Adherence

Based on the CQR score at baseline, 88 (52.4%) patients were classified as having high adherence. Baseline demographics and disease characteristics were generally comparable between patients in the high and low adherence groups, although the patients with high adherence were older and exhibited slightly higher disease activity (Table 1). Over time, the proportion of patients in the high adherence group increased to 60.9% at 6 months and 67.4% at 12 months (Figure 1).

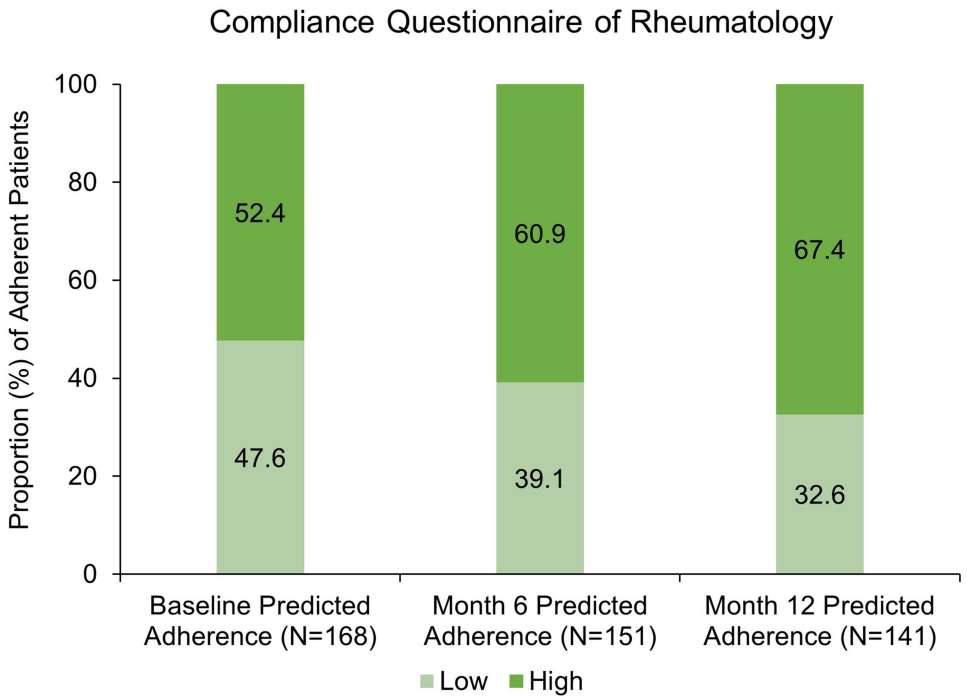

Figure 1 Proportion of patients with high and low predicted adherence in the effectiveness analysis set based on CQR response at baseline, month 6 and 12.
Abbreviations: CQR, Compliance Questionnaire in Rheumatology; High, high predicted adherence; Low, low predicted adherence.

Impact on RA Flares

At 6 months, the mean (SD) RA-FQ score was 23.8 (13.2) in the high baseline adherence group and 22.5 (13.1) in the low baseline adherence group (p=0.56); at 12 months, the corresponding mean (SD) scores were 19.9 (13.5) and 20.8 (12.9) (p=0.70), respectively (Figure 2A). RA flares were reported in 31.8% of patients at month 6 and 26.2% at month 12, with a numerically lower incidence observed in the high adherence group compared to the low adherence group. Specifically, at 6 months, 28.2% of patients in the high adherence group reported flares, versus 35.7% in the low adherence group; at 12 months, these rates were 24.7% and 30%, respectively (Figure 2B).

Similar to the primary analysis using baseline-predicted adherence, no meaningful differences in the mean (SD) RA-FQ scores were observed in the high vs low visit-predicted adherence groups at 6 months (24.3 [12.8] vs 20.9 [12.9]; p=0.12], and at 12 months [20.6 (13.5) vs 19.7 (12.7); p=0.71; Figure S1A]. In terms of disease flaring, 31.8% of patients reported a flare at month 6 and 26.2% at month 12, with slight numerical but not statistical differences observed between the high and low visit-predicted adherence groups at both time points: 32.6% vs 28.6% at month 6, and 28.7% vs 23.9% at month 12 (Figure S1B).

Impact on Disease Activity

Disease activity levels at 6 months were comparable in the high and low baseline-predicted adherence groups based on CDAI [13.8 (10.8) vs 12.9 (10.5)], MDGA [4.5 (2.7) vs 4.3 (2.7)], and PtGA [2.9 (2.6) vs 2.6 (2.4)] (Figure 3). At 12 months, patients in the high baseline-predicted adherence group had significantly lower CDAI (8.4 [7.3] vs 11.9 [10.2]; Δmeans [95% CI]: −3.5 [−6.9, −0.1]) and numerically lower levels of MDGA (3.3 [2.5] vs 3.7 [2.74]) and PtGA (1.8 [1.9] vs 2.2 [2.5]).

No differences at either 6 or 12 months were observed in the high vs low adherence group when using the visit-predicted adherence (Figure S2).

Impact on Glucocorticoid Use

Comparable rates of glucocorticoid use were observed in the high vs low baseline-predicted adherence groups at month 6 (18.2% vs 20%; p=0.76) and month 12 (15.9% vs 18.8%; p=0.63; Figure 4A). However, a lower mean (SD) dose of oral glucocorticoids was used in high vs low baseline-predicted adherence patients in the first 6 months (6.4 [4.2] vs 12.6 [16.0] mg prednisone equivalent), as well as between months 6 and 12 (6.0 [3.8] vs 9.5 [11.9] mg prednisone equivalent).

In the visit-predicted adherence groups, a lower rate of glucocorticoid use was observed in the high vs low adherence groups at 6 months (16.3% vs 30.5%; p=0.04) but not at 12 months (23.2% vs 21.7%; p=0.85; Figure 4B).

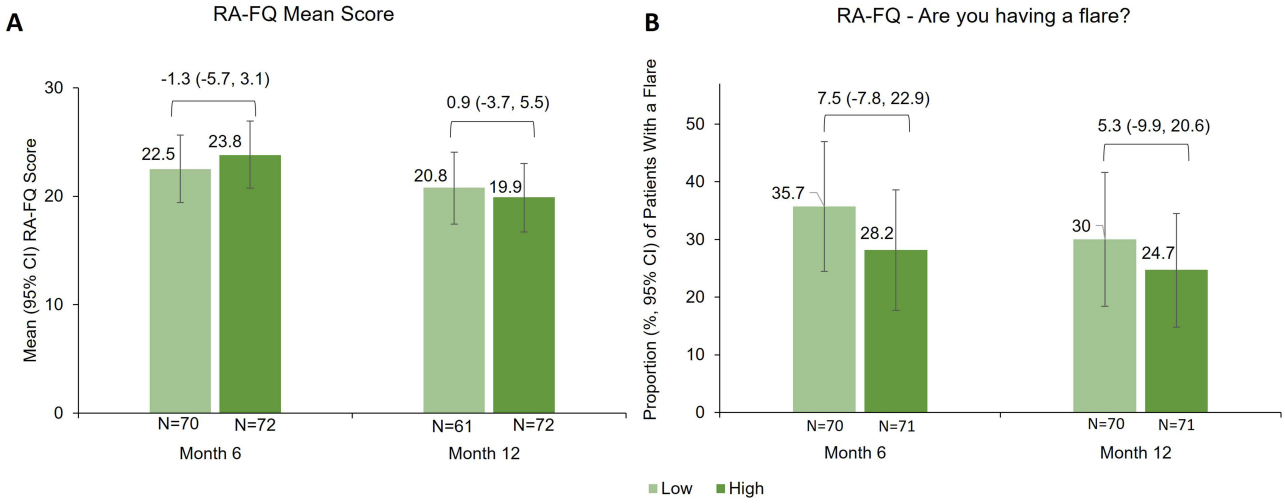

Figure 2 Disease flaring by baseline predicted adherence in low and high adherence groups by (**A**) RA-FQ mean score and (**B**) proportion of patients reporting flare. Values above bars are mean differences between low and high (95% CI).

Abbreviations: CI, confidence interval; High, high predicted adherence; Low, low predicted adherence; RA-FQ, Rheumatoid Arthritis Flare Questionnaire.

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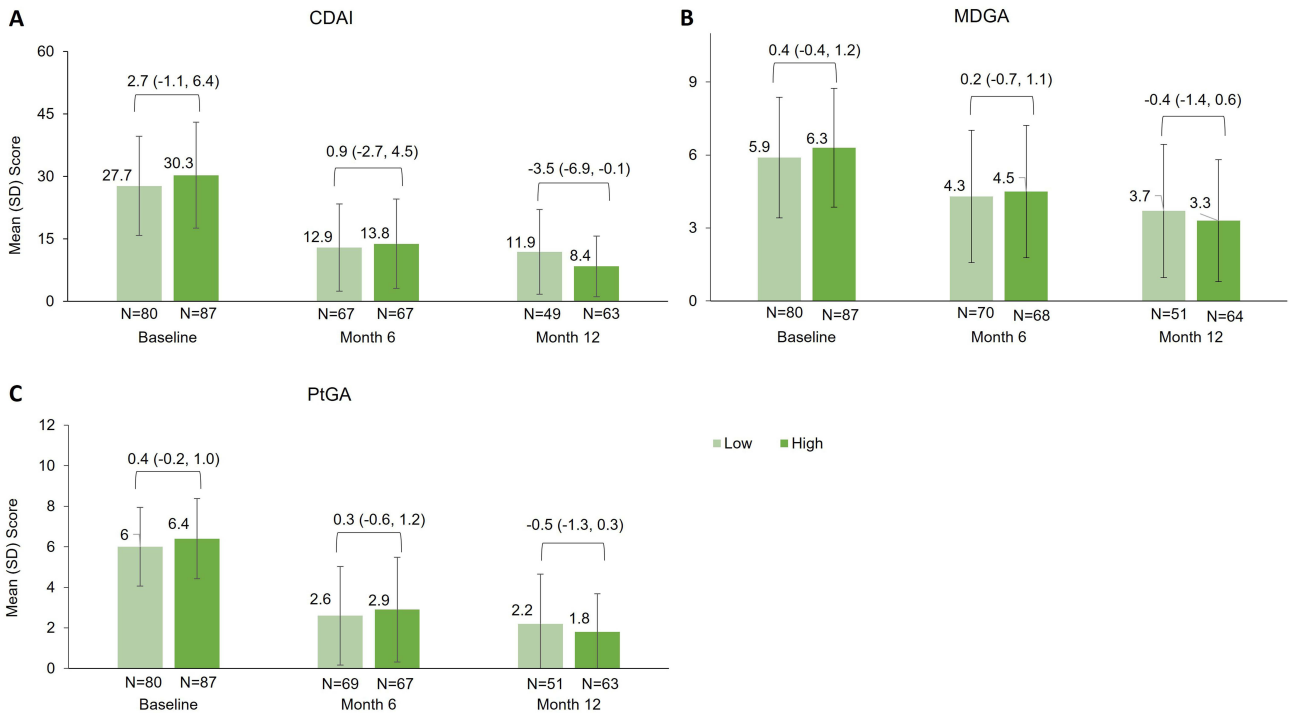

Figure 3 Clinical disease activity by baseline predicted adherence in low and high adherence groups measured with (**A**) CDAI, (**B**) MDGA, and (**C**) PtGA. Values above bars are mean differences between low and high (95% CI).
Abbreviations: CDAI, clinical disease activity index; High, high predicted adherence; Low, low predicted adherence; MDGA, physician global assessment; PtGA, patient global assessment; SD, standard deviation.

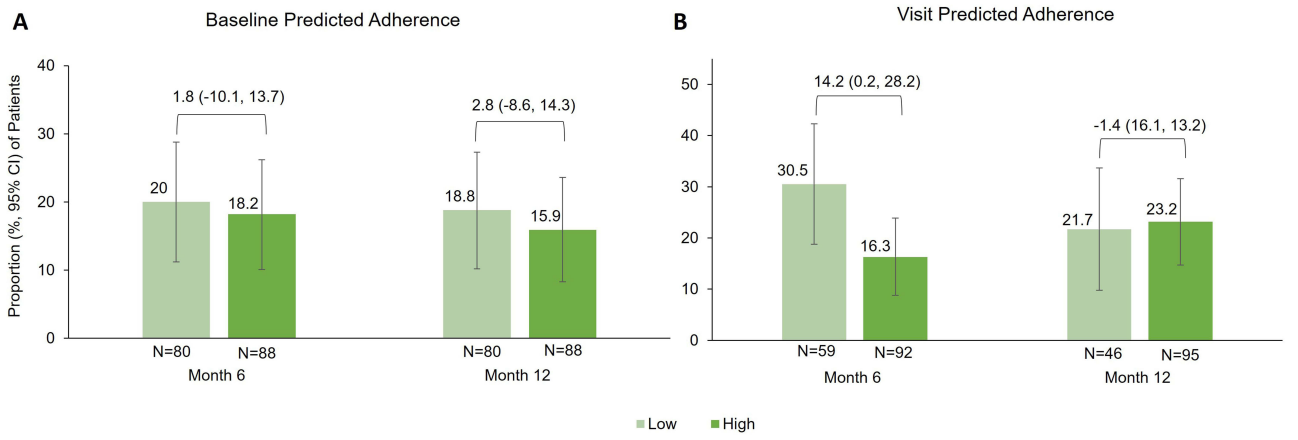

Figure 4 Proportion of patients using glucocorticoids in low and high adherence groups by (**A**) baseline predicted and (**B**) visit predicted adherence. Values above bars are differences in proportions between low and high (95% CI).
Abbreviations: CI, confidence interval; High, high predicted adherence; Low, low predicted adherence.

Impact on AEs

A small numerical difference in reported AEs was observed between baseline-predicted adherence groups, with AEs reported for 44.3% of patients in the high adherence group and 53.8% in the low adherence group (Figure 5A). No differences in AE incidence were observed in high vs low predicted adherence at 6 and 12 months (Figure 5B and C).

The most commonly reported AEs by preferred term were drug ineffective (12.6% of patients), rheumatoid arthritis (8.8% of patients), and arthralgia (4.7% patients), while the most common serious AEs were appendicitis and pneumonia, each occurring in 0.9% of patients (Table S1).

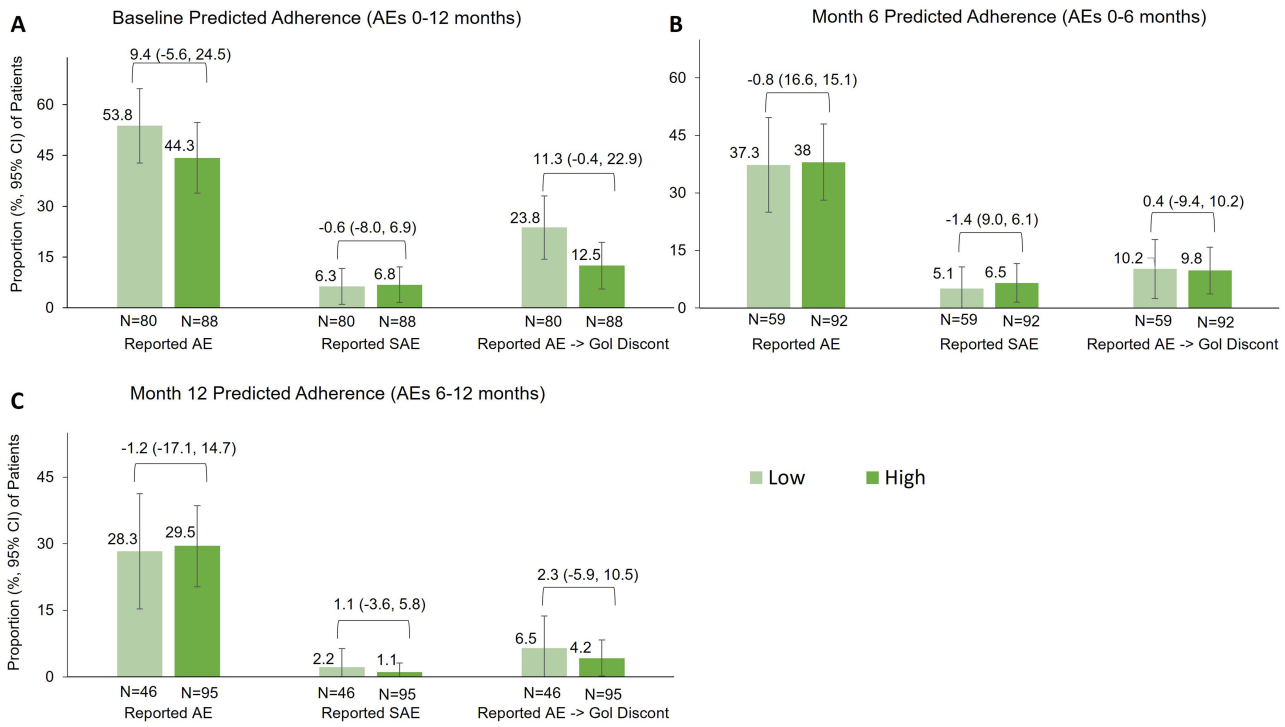

Figure 5 Proportion of patients reporting treatment emergent adverse events in low and high adherence group (**A**) by baseline predicted adherence (**B**) from baseline to the first 6 months by month 6 predicted adherence (**C**) from month 6 to month 12 by month 12 predicted adherence. Values above bars are differences in proportions between low and high (95% CI).

Abbreviations: AE, adverse event; CI, confidence interval; Discont, discontinuation; GoI, golimumab; High, high predicted adherence; Low, low predicted adherence; SAE, serious adverse event.

Discussion

In this prospective, multicentric, non-interventional study of patients with RA treated with golimumab in routine care across Canada, 52% to 67% of patients were classified in the high predicted adherence group during the 12 month period of the study. These results align with previous studies showing similar adherence rates to golimumab in real-world settings.[37–39] Higher RA-FQ scores were observed at baseline compared with the 6 month and 12 month visits, irrespective of adherence group, consistent with prior findings that disease flares are more common at the beginning of biologic treatment. The decline in RA-FQ scores over 12 months was numerically greater among patients in the high predicted adherence group, suggesting that timely adherence to biologic therapy may reduce flare incidence and, consequently, the need for glucocorticoids. Patient support programs (PSPs) have been developed to educate patients on the importance of adherence, address concerns about treatment that could act as a barrier to uptake, and provide reminders to improve medication-taking behavior. Our findings underscore the importance of PSPs in improving patient outcomes, particularly during the early stages of treatment.

Disease flare-ups, as measured by the RA-FQ questionnaire, were comparable between patients in the low and high baseline adherence groups. These results suggest that variations in the adherence to golimumab treatment may not have significant impact on disease control. Notably, a greater proportion of patients in the low adherence group used glucocorticoids, which may have contributed to the comparable rate of flares between adherence groups. Furthermore, some differences in CDAI levels but not MDGA or PtGA were observed at 12 months in patients with high vs low baseline-predicted adherence. Physicians may have used glucocorticoids as a compensatory mechanism to manage disease activity in patients with lower adherence to golimumab and/or early symptoms of disease flares. Previous studies have shown an association between adherence to biologic therapy and steroid use.[40] However, long-term glucocorticoid use is not a sustainable treatment strategy, due to the risk of severe and potentially irreversible adverse effects. Thus, high adherence to bDMARDs can effectively control inflammation, reducing the need for glucocorticoids and mitigating their

associated risks. Alternatively, the observed association between low adherence and glucocorticoid use may be influenced by adverse reactions associated with glucocorticoids or by the effects of polypharmacy. Further studies are needed to confirm this relationship and explore strategies to enhance adherence to biologic therapies, thereby reducing reliance on glucocorticoids and improving long-term disease outcomes.

No differences were observed in the incidence of treatment-emergent AEs/SAEs between low and high adherence groups, which aligns with the comparable rates of flare-ups. Approximately 68% of patients receiving golimumab have previously reported at least one AE, and 4.4% have reported at least one SAE, which is consistent with the safety profile of other TNF-α inhibitors.[41]

Real-world studies such as GO FAR provide valuable insights that complement data from clinical trials, offering a more comprehensive understanding of RA treatment effectiveness. Adherence rates and patient behavior in the real-world may differ significantly from clinical trials due to the inclusion of more diverse patient populations and the absence of strict visit schedules, and understanding these differences is essential for optimizing treatment strategies. The GO FAR study, thus critically contributes to the understanding of golimumab effectiveness in real-world practice.

The GO FAR study did not assess reasons for low adherence such as comorbid conditions, concomitant medication use, access to healthcare services, mental health, patient education, disease activity, complex treatment regimens, incidence of AEs, and other lifestyle factors, and did not account for potential confounding variables that could influence the incidence of disease flares such as rheumatoid factor and anti-citrullinated potein positivity. Furthermore, actual adherence to treatment was not measured; only predicted adherence was reported, which may not fully reflect real-world adherence behavior or its variability over time. Similarly, given that disease flaring was assessed by the patient, misclassification bias of the outcome due to co-occurring conditions such as osteoarthritis and fibromyalgia, cannot be excluded. The study was not powered for inferential hypothesis testing and conclusions were constrained by the limited sample size and the short timeline of the study; it is possible that a larger and/or longer study would have allowed the detection of a significant difference between the high and low adherence groups. Finally, despite reasonable efforts to contact patients, approximately 20% did not have follow-up assessments, which may have introduced selection bias.

Conclusion

In this real-world study, no significant differences were observed in RA-FQ score, the proportion of patients reporting disease flares, or AE rates between patients with RA with low vs high predicted adherence to golimumab treatment. The more frequent use of glucocorticoids within the first 6 months in patients with low predicted adherence warrants further investigation to better understand this association. These findings underscore the importance of identifying barriers to adherence and implementing strategies, such as PSPs, to improve adherence to bDMARDs, particularly in the early stages of treatment. Enhancing adherence could ultimately help to reduce glucocorticoid dependence and improve long-term outcomes in RA management.

Data Sharing Statement

The data sharing policy of Johnson & Johnson is available at https://www.janssen.com/clinical-trials/transparency. As noted on this site, requests for access to the study data can be submitted through Yale Open Data Access [YODA] Project site at http://yoda.yale.edu.

Ethics Approval

The GO FAR study was conducted in accordance with the principles stated in the Declaration of Helsinki and Good Clinical Practice guidelines. Ethics approvals were obtained from Advarra, the Sunnybrook Research Ethics Board (Toronto, Canada), the Newfoundland and Labrador Health Research Ethics Authority, the Comité d'éthique à la recherche du CIUSSS de l'Estrie (Sherbrooke, Quebec), and the Health Research Ethics Board of Alberta. All study patients provided written informed consent prior to data collection.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

LB: Speaker, consultant, and research: Amgen, BMS, Johnson & Johnson, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Gilead, Sandoz, Fresenius Kabi, Teva. PB: Speaker, consultant, and research: AbbVie, BMS, Fresenius Kabi, Johnson & Johnson, Lilly, Novartis, Pfizer, Sandoz, UCB. RA: has not declared any conflicts of interest relevant to this study. PR: Consulting fees from Abbott, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Johnson & Johnson, Novartis, UCB, and Pfizer, and has also received research grants from Johnson & Johnson and Novartis. SA: has not declared any conflicts of interest relevant to this study. TR: Speaker, consultant, and advisory board: AbbVie, Amgen, BioJamp, Celltrion, GSK, Johnson & Johnson, Lilly, Medexus, Nordic Pharma, Novartis, Otsuka, Pfizer, Sandoz, Sanofi Genzyme, UCB, and Viatris, and has also received research grants from AbbVie, Pfizer, and UCB. MR: Employee of Johnson & Johnson. FN: Retiree from Johnson & Johnson, Owner of Johnson & Johnson stock. AC: Employee of Johnson & Johnson. OAM: Employee of Johnson & Johnson, Owner of Johnson & Johnson stock. DH: Consulting fees from AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Johnson & Johnson, Merck, Novartis, Pfizer, Roche, Sanofi Genzyme, Takeda, and UCB, and has also received research grants from AbbVie, Adiga Life-Sciences, Amgen, AstraZeneca, Bristol-Myers Squibb, Can-Fite Biopharma, Celgene, Eli-Lilly, Gilead, GlaxoSmithKline, Johnson & Johnson, Novartis, Pfizer, Regeneron, Sanofi-Genzyme, UCB; Speaker and advisory board: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Elli-Lilly, GlaxoSmithKline, Johnson & Johnson, Novartis, Pfizer, Roche, Sanofi Genzyme, Takeda. The authors report no other conflicts of interest in this work.

References

1. Sparks JA. Rheumatoid Arthritis. *Ann Intern Med*. 2019;170(1):ITC1–ITC16. doi:10.7326/AITC201901010
2. Lin YJ, Anzaghe M, Schulke S. Update on the Pathomechanism, Diagnosis, and Treatment Options for Rheumatoid Arthritis. *Cells*. 2020;9(4):880. doi:10.3390/cells9040880
3. Bessette L, Haraoui B, Rampakakis E, Dembowy J, Trepanier MO, Pope J. Effectiveness of a treat-to-target strategy in patients with moderate to severely active rheumatoid arthritis treated with Abatacept. *Arthritis Res Ther*. 2023;25(1):183. doi:10.1186/s13075-023-03151-2
4. McInnes IB, Schett G. The pathogenesis of rheumatoid arthritis. *N Engl J Med*. 2011;365(23):2205–2219. doi:10.1056/NEJMra1004965
5. Drosos AA, Pelechas E, Kaltsonoudis E, Voulgari PV. Therapeutic Options and Cost-Effectiveness for Rheumatoid Arthritis Treatment. *Curr Rheumatol Rep*. 2020;22(8):44. doi:10.1007/s11926-020-00921-8
6. Smolen JS, Landewe RBM, Bijlsma JWJ, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. *Ann Rheum Dis*. 2020;79(6):685–699. doi:10.1136/annrheumdis-2019-216655
7. Dobbels F, Van Damme-Lombaert R, Vanhaecke J, De Geest S. Growing pains: non-adherence with the immunosuppressive regimen in adolescent transplant recipients. *Pediatr Transplant*. 2005;9(3):381–390. doi:10.1111/j.1399-3046.2005.00356.x
8. Curtis JR, Bykerk VP, Aassi M, Schiff M. Adherence and Persistence with Methotrexate in Rheumatoid Arthritis: a Systematic Review. *J Rheumatol*. 2016;43(11):1997–2009. doi:10.3899/jrheum.151212
9. Waimann CA, Marengo MF, de Achaval S, et al. Electronic monitoring of oral therapies in ethnically diverse and economically disadvantaged patients with rheumatoid arthritis: consequences of low adherence. *Arthritis Rheum*. 2013;65(6):1421–1429. doi:10.1002/art.37917
10. Yoon-Jeong O, Bumhee P, Ki Won M. Effect of Drug Adherence on Treatment Outcome in Rheumatoid Arthritis. *J Rheum Dis*. 2019;26(4):264–272. doi:10.4078/jrd.2019.26.4.264
11. Li L, Cui Y, Yin R, et al. Medication adherence has an impact on disease activity in rheumatoid arthritis: a systematic review and meta-analysis. *Patient Prefer Adherence*. 2017;11:1343–1356. doi:10.2147/PPA.S140457
12. Nakagawa S, Nakaishi M, Hashimoto M, et al. Effect of medication adherence on disease activity among Japanese patients with rheumatoid arthritis. *PLoS One*. 2018;13(11):e0206943. doi:10.1371/journal.pone.0206943
13. Marengo MF, Suarez-Almazor ME. Improving treatment adherence in patients with rheumatoid arthritis: what are the options? *Int J Clin Rheumtol*. 2015;10(5):345–356. doi:10.2217/ijr.15.39
14. Stolshek BS, Wade S, Mutebi A, De AP, Wade RL, Yeaw J. Two-year adherence and costs for biologic therapy for rheumatoid arthritis. *Am J Manag Care*. 2018;24(8):SP315–SP321.

15. Bingham III CO, Alten R, Bartlett SJ, et al. Identifying preliminary domains to detect and measure rheumatoid arthritis flares: report of the OMERACT 10 RA Flare Workshop. *J Rheumatol*. 2011;38(8):1751–1758. doi:10.3899/jrheum.110401
16. Bingham III CO, Pohl C, Woodworth TG, et al. Developing a standardized definition for disease flare in rheumatoid arthritis (OMERACT 9 Special Interest Group). *J Rheumatol*. 2009;36(10):2335–2341. doi:10.3899/jrheum.090369
17. Alten R, Pohl C, Choy EH, et al. Developing a construct to evaluate flares in rheumatoid arthritis: a conceptual report of the OMERACT RA Flare Definition Working Group. *J Rheumatol*. 2011;38(8):1745–1750. doi:10.3899/jrheum.110400
18. Bozzalla-Cassione E, Grignaschi S, Xoxi B, et al. Insights Into the Concept of Rheumatoid Arthritis Flare. *Front Med*. 2022;9:852220. doi:10.3389/fmed.2022.852220
19. Markusse IM, Dirven L, Gerards AH, et al. Disease flares in rheumatoid arthritis are associated with joint damage progression and disability: 10-year results from the BeSt study. *Arthritis Res Ther*. 2015;17(1):232. doi:10.1186/s13075-015-0730-2
20. Bykerk VP, Shadick N, Frits M, et al. Flares in rheumatoid arthritis: frequency and management. A report from the BRASS registry. *J Rheumatol*. 2014;41(2):227–234. doi:10.3899/jrheum.121521
21. Pombo-Suarez M, Maneiro Fernandez JR, Gomez-Reino JJ. Adherence to Treatment in Patients with Rheumatoid Arthritis from Spain. *Patient Prefer Adherence*. 2021;15:111–117. doi:10.2147/PPA.S291983
22. Harrold LR, Andrade SE. Medication adherence of patients with selected rheumatic conditions: a systematic review of the literature. *Semin Arthritis Rheum*. 2009;38(5):396–402. doi:10.1016/j.semarthrit.2008.01.011
23. Dam K, Ji-Young C, Soo-Kyung C, et al. Prevalence and Associated Factors for Non-adherence in Patients with Rheumatoid Arthritis. *J Rheum Dis*. 2018;25(1):47–57. doi:10.4078/jrd.2018.25.1.47
24. Balsa A, Garcia de Yebenes MJ, Carmona L, Group AS. Multilevel factors predict medication adherence in rheumatoid arthritis: a 6-month cohort study. *Ann Rheum Dis*. 2022;81(3):327–334. doi:10.1136/annrheumdis-2021-221163
25. Hopson S, Saverno K, Liu LZ, et al. Impact of Out-of-Pocket Costs on Prescription Fills Among New Initiators of Biologic Therapies for Rheumatoid Arthritis. *J Manag Care Spec Pharm*. 2016;22(2):122–130. doi:10.18553/jmcp.2016.14261
26. Harnett J, Wiederkehr D, Gerber R, Gruben D, Bourret J, Koenig A. Primary Nonadherence, Associated Clinical Outcomes, and Health Care Resource Use Among Patients with Rheumatoid Arthritis Prescribed Treatment with Injectable Biologic Disease-Modifying Antirheumatic Drugs. *J Manag Care Spec Pharm*. 2016;22(3):209–218.
27. Pasma A, Van't Spijker A, Hazes JM, Busschbach JJ, Luime JJ. Factors associated with adherence to pharmaceutical treatment for rheumatoid arthritis patients: a systematic review. *Semin Arthritis Rheum*. 2013;43(1):18–28. doi:10.1016/j.semarthrit.2012.12.001
28. Machado-Alba JE, Machado-Duque ME, Gaviria-Mendoza A, Reyes JM, Gamboa NC. Use of healthcare resources in a cohort of rheumatoid arthritis patients treated with biological disease-modifying antirheumatic drugs or tofacitinib. *Clin Rheumatol*. 2021;40(4):1273–1281. doi:10.1007/s10067-020-05432-6
29. Simponi Aria. Highlights of prescribing information. 2021, Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125433s032lbl.pdf. Accessed September 30, 2024.
30. Rosenberg V, Chodick G, Xue Z, Faccin F, Amital H. Real-World Data of Adherence and Drug Survival of Biologics in Treatment-Naive and Treatment-experienced Adult Patients with Rheumatoid Arthritis. *Adv Ther*. 2023;40(10):4504–4522. doi:10.1007/s12325-023-02607-w
31. Santos-Moreno P, Sanchez-Vanegas G, Monterrosa-Blanco A, et al. Adherence to Subcutaneous Anti-Tumour Necrosis Factor Treatment in a Cohort of Patients with Rheumatoid Arthritis Before and After the Implementation of a Comprehensive Care Model. *Biologics*. 2022;16:199–209. doi:10.2147/BTT.S385422
32. Svedbom A, Storck C, Kachroo S, Govoni M, Khalifa A. Persistence with golimumab in immune-mediated rheumatic diseases: a systematic review of real-world evidence in rheumatoid arthritis, axial spondyloarthritis, and psoriatic arthritis. *Patient Prefer Adherence*. 2017;11:719–729. doi:10.2147/PPA.S128665
33. Amiri F, Mahmoud I, Bouden S, et al. AB0435 Adherence to Biologic Therapies in Inflammatory Rheumatic Diseases: influence of Route of Administration. *Ann Rheumatic Dis*. 2023;82:1406.1401–1406. doi:10.1136/annrheumdis-2023-eular.6143
34. de Klerk E, van der Heijde D, van der Tempel H, van der Linden S. Development of a questionnaire to investigate patient compliance with antirheumatic drug therapy. *J Rheumatol*. 1999;26(12):2635–2641.
35. de Klerk E, van der Heijde D, Landewe R, van der Tempel H, van der Linden S. The compliance-questionnaire-rheumatology compared with electronic medication event monitoring: a validation study. *J Rheumatol*. 2003;30(11):2469–2475.
36. Bartlett SJ, Barbic SP, Bykerk VP, et al. Content and Construct Validity, Reliability, and Responsiveness of the Rheumatoid Arthritis Flare Questionnaire: OMERACT 2016 Workshop Report. *J Rheumatol*. 2017;44(10):1536–1543. doi:10.3899/jrheum.161145
37. Flipo RM, Tubach F, Goupille P, et al. Real-life persistence of golimumab in patients with chronic inflammatory rheumatic diseases: results of the 2-year observational GO-PRACTICE study. *Clin Exp Rheumatol*. 2021;39(3):537–545. doi:10.55563/clinexprheumatol/zizo0l
38. Nantel F, Ling J, Rachich M, et al. Usage and Adherence of Seven Advanced Therapies with Differing Mechanisms of Action for Inflammatory Arthritis in Canada. *Rheumatol Ther*. 2022;9(5):1399–1420. doi:10.1007/s40744-022-00485-2
39. Bhoi P, Bessette L, Bell MJ, Tkaczyk C, Nantel F, Maslova K. Adherence and dosing interval of subcutaneous antitumour necrosis factor biologics among patients with inflammatory arthritis: analysis from a Canadian administrative database. *BMJ Open*. 2017;7(9):e015872. doi:10.1136/bmjopen-2017-015872
40. Lathia U, Ewara EM, Nantel F. Impact of adherence to biological agents on health care resource utilization for patients over the age of 65 years with rheumatoid arthritis. *Patient Prefer Adherence*. 2017;11:1133–1142. doi:10.2147/PPA.S137206
41. Kay J, Fleischmann R, Keystone E, et al. Golimumab 3-year safety update: an analysis of pooled data from the long-term extensions of randomised, double-blind, placebo-controlled trials conducted in patients with rheumatoid arthritis, psoriatic arthritis or ankylosing spondylitis. *Ann Rheum Dis*. 2015;74(3):538–546. doi:10.1136/annrheumdis-2013-204195