Safety and Efficacy of Golimumab Administered Intravenously in Adults with Ankylosing Spondylitis: Results through Week 28 of the GO-ALIVE Study

Atul Deodhar, John D. Reveille, Diane D. Harrison, Lilianne Kim, Kim Hung Lo, Jocelyn H. Leu, and Elizabeth C. Hsia

ABSTRACT. ***Objective.*** To evaluate the safety and efficacy of intravenous golimumab (GOL) in patients with active ankylosing spondylitis (AS).

Methods. In a phase III, randomized, double-blind, placebo (PBO)-controlled trial, 208 patients were randomized (1:1) to intravenous (IV) infusions of GOL 2 mg/kg (n = 105) at weeks 0, 4, 12, and every 8 weeks, or PBO (n = 103) at weeks 0, 4, and 12, with crossover to GOL at Week 16. The primary endpoint was ≥ 20% improvement from baseline in the Assessment of Spondyloarthritis International Society Criteria (ASAS20) at Week 16. Secondary endpoints included ASAS40, ≥ 50% improvement in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI50), and change in the Bath Ankylosing Spondylitis Functional Index (BASFI) at Week 16. Safety was monitored through Week 28.

Results. Significantly greater proportions of GOL-treated patients had ASAS20 response at Week 2 (37.1% vs 19.4%; p = 0.005) and at Week 16 (73.3% vs 26.2%; p < 0.001). At Week 16, 41.0% of those receiving GOL achieved BASDAI50 compared with 14.6% of those taking PBO (p < 0.001), and the GOL group had greater mean improvement in BASFI (–2.4 vs –0.5; p < 0.001). Through Week 16, 23.3% of patients in the PBO group and 32.4% of patients in the GOL group had ≥ 1 adverse event (AE); infections being the commonest type of AE. Through Week 28, two GOL-treated patients had a serious AE.

Conclusion. GOL 2 mg/kg administered IV at weeks 0, 4, and every 8 weeks significantly reduced the signs and symptoms of AS in adults. AE were consistent with other antitumor necrosis factor therapies, with no new safety signals (Clinicaltrials.gov: NCT02186873). (First Release December 15 2017; J Rheumatol 2018;45:341–8; doi:10.3899/jrheum.170487)

Key Indexing Terms:
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The American College of Rheumatology, the Spondylitis Association of America, and the Spondyloarthritis Research and Treatment Network (SPARTAN) treatment recommendations suggest the use of antitumor necrosis factor (TNF) therapy for patients with active ankylosing spondylitis (AS) despite therapy with nonsteroidal antiinflammatory drugs (NSAID)[1]. Golimumab (GOL), a fully human monoclonal anti-TNF-α therapy, is currently approved for use as a subcutaneous (SC) injection for adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and AS[2], and also as an intravenous (IV) infusion for adults with RA[3]. In the phase III GO-FURTHER trial of patients with active RA despite methotrexate (MTX) therapy, IV GOL 2 mg/kg plus MTX demonstrated robust efficacy[4] and a safety profile consistent with that of SC GOL in patients with RA[5,6], PsA[7], and AS[8].

Given the various biologic treatment options available for AS[1], patient preferences for some factors, such as route of administration and treatment setting, should be considered. Some patients are unable or unwilling to self-administer SC biologics at home and may prefer IV biologics. In a previous study, patients with RA receiving IV therapy generally preferred to receive their medication in a medical facility[9], and in 1 study, patients cited "safety of the hospital administration" and "reassuring effect of the doctor's presence" as

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reasons for preferring to receive their medication in a healthcare facility[10]. Some patients also prefer the less frequent dosing interval for IV therapies compared with SC therapies[10]. The approved dosing frequency for IV GOL in patients with RA is every 8 weeks after an induction regimen of 2 doses 4 weeks apart[3] compared with monthly injections for SC GOL[2] and more frequent administrations (weekly or biweekly) for other SC anti-TNF therapies[11,12]. In the GO-ALIVE study, the safety and efficacy of IV GOL were evaluated in patients with AS, and results through Week 28 are reported herein.

MATERIALS AND METHODS

Patients. Those eligible were adults (aged ≥ 18 yrs) with a diagnosis of AS (defined by the modified New York criteria[13]) for at least 3 months, having symptoms of active disease [Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)[14] ≥ 4, a visual analog scale (0–10 cm) score for total back pain of ≥ 4] at screening and at baseline, a high-sensitivity C-reactive protein level of ≥ 0.3 mg/dl, and either an inadequate response or intolerance to NSAID. Patients with complete ankylosis of the spine were eligible, but were limited to 10% of the study population. Concomitant use of MTX (≤ 25 mg/week), sulfasalazine (SSZ), hydroxychloroquine (HCQ), NSAID, other analgesics, and low-dose oral corticosteroids (dose equivalent to ≤ 10 mg prednisone/day) was permitted at stable doses; patients were excluded if they had received systemic disease-modifying antirheumatic drugs other than MTX, SSZ, or HCQ within 4 weeks of the first study agent administration. A maximum of 20% of the study population could have received prior treatment with 1 anti-TNF other than GOL. These patients could not have experienced primary failure (defined as lack of response or discontinuation due to lack of efficacy within the first 16 weeks of treatment) to the anti-TNF therapy and could not have received the anti-TNF therapy within 3 months before the first study agent administration (except etanercept within 6 weeks). Previous treatment with other biologics, tofacitinib, or other Janus kinase inhibitors was not permitted.

Patients were screened for tuberculosis (TB) within 6 weeks before the first administration of study agent. Patients with evidence of active TB were excluded. Patients with latent TB were eligible if they were currently receiving treatment for latent TB.

Study design. GO-ALIVE was a phase III, double-blind, placebo (PBO)-controlled trial. Eligible patients were randomly assigned (1:1) using an interactive Web–response system to receive IV infusions of PBO at weeks 0, 4, and 12 or GOL 2 mg/kg at weeks 0, 4, 12, and every 8 weeks thereafter. Patients in the PBO group crossed over to receive GOL 2 mg/kg at weeks 16 and 20 and every 8 weeks thereafter. Patients randomized to the GOL group received a PBO infusion at Week 16 to maintain the blind. Randomization was stratified by geographic region and prior anti-TNF therapy (yes/no).

This trial was registered with clinicaltrials.gov (NCT02186873) and was conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practices. All patients were required to give written informed consent before any study-related procedures were performed. The protocol was approved by Schulman Associates IRB for 10 sites in Canada (approval number: 201404734) and the United States (approval number: 201404241); the remaining 36 sites received approval from their local ethics committees.

Assessments. The primary endpoint was the proportion of patients who achieved an improvement of ≥ 20% in the Assessment of Spondyloarthritis International Society criteria (ASAS20 response)[15] at Week 16. Other efficacy endpoints included ASAS40 response, ASAS partial remission[15], ASAS 5/6 response[16], Ankylosing Spondylitis Disease Activity Score (ASDAS) inactive disease (< 1.3), ≥ 50% improvement in BASDAI (BASDAI50 response), and changes in the Bath Ankylosing Spondylitis Metrology Index (BASMI)[17]. Enthesitis was assessed using the University of California San Francisco enthesitis index[18]. Improvements in physical function were evaluated using the Bath Ankylosing Spondylitis Functional Index (BASFI)[19]. Health-related quality of life (HRQOL) was evaluated using the physical and mental component summary (PCS/MCS) scores of the Medical Outcomes Study Short Form-36 questionnaire (SF-36) and the Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire[20].

Patients were monitored throughout the study for adverse events (AE), including hematology and chemistry assessments. Serum samples for the determination of GOL concentrations were collected through Week 20. These samples were also used for evaluation of the presence of antibodies to GOL using a recently developed, highly sensitive, drug-tolerant, enzyme immunoassay method in patients who received ≥ 1 administration of GOL and had ≥ 1 postadministration sample available.

Statistical analysis. The primary endpoint was the proportion of patients achieving an ASAS20 response at Week 16. Major secondary endpoints were ASAS40 response, BASDAI50 response, and change from baseline in BASFI, all at Week 16. For composite endpoints, missing components were imputed using last observation carried forward methodology if only some but not all components were missing; if all components were missing, those patients were classified as nonresponders for dichotomous endpoints. Patients who initiated prohibited therapies increased the dose of SSZ, MTX, HCQ, or oral corticosteroids above baseline level, or discontinued study agent owing to lack of efficacy prior to Week 16 were to be classified as nonresponders; no patient met these criteria. A Cochran-Mantel-Haenszel (CMH) test was used to test differences between treatment groups for dichotomous endpoints. Mixed-effect model for repeated measures methodology based on observed data was used to analyze the controlled continuous endpoints. All statistical tests were performed at a 2-sided $\alpha = 0.05$ level. To control for multiplicity, major secondary endpoints were tested sequentially (according to the order listed above) only when the primary endpoint achieved statistical significance. In addition, 5 other controlled secondary endpoints were also tested sequentially in the following order: change from baseline in SF-36 PCS, change from baseline in SF-36 MCS, proportion of patients achieving ASAS partial remission, change from baseline in ASQoL, and change from baseline in BASMI (linear)[21], all at Week 16. For other efficacy endpoints, nominal p values were provided.

It was estimated that 100 patients in each treatment group would provide about 93% power to detect the treatment difference between PBO and GOL for the primary endpoint assuming a PBO response rate of 25% and a GOL response rate of 40% (patients with prior anti-TNF therapy) and 50% (patients with no prior anti-TNF therapy), using a CMH test at $\alpha = 0.05$ (2-sided).

RESULTS

Patient disposition and baseline characteristics. Data for this report were collected from September 2014 to March 2016. There were 312 patients screened from 46 sites; of these, 208 from 40 sites in 8 countries (Canada, Germany, Republic of Korea, Mexico, Poland, Russia, Ukraine, and the United States) were randomized to PBO (n = 103) or GOL (n = 105) and treated. Through Week 16, 4 patients (all in the PBO group) discontinued treatment: 3 withdrew consent and 1 was lost to followup (Figure 1). After Week 16 and through Week 28, 1 additional patient (GOL group) discontinued treatment; this patient discontinued study agent because of AE of increased alanine aminotransferase (ALT) and increased aspartate aminotransferase (AST), neither considered by the investigator to be related to study medication.

Overall, 78% of patients were male, and the mean age was 39 years. Mean time since AS diagnosis was 5.5 years; 89.9%

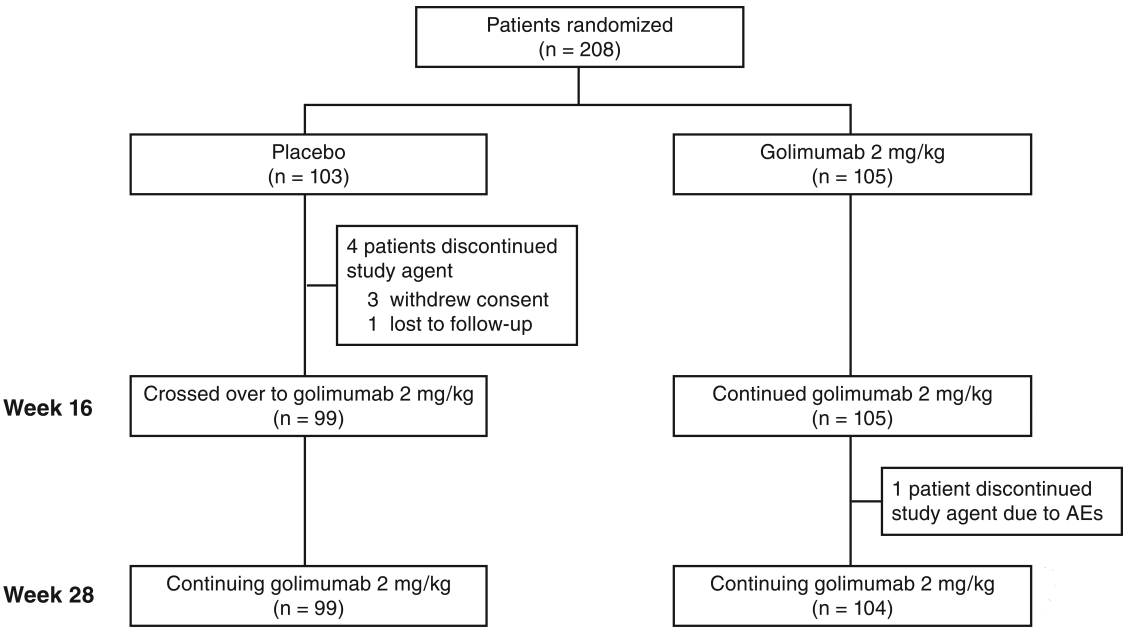

Figure 1. Patient disposition through Week 28. AE: adverse event.

were HLA-B27–positive, and 12 patients (5.8%) had complete ankylosis of the spine (Table 1). Baseline demographic and disease characteristics were generally comparable between the treatment groups. Thirty patients (PBO, n = 14; GOL, n = 16) had received prior therapy with 1 anti-TNF agent.

Clinical efficacy and HRQOL. The primary endpoint was achieved by 73.3% of patients in the GOL group who demonstrated an ASAS20 response compared with 26.2% in the PBO group at Week 16 ($p < 0.001$; Table 2), with a significantly greater proportion of GOL-treated patients having an ASAS20 response at Week 2 compared with PBO (37.1% vs 19.4%; $p = 0.005$). The robustness of the primary endpoint was supported by 8 sensitivity analyses using various data handling and treatment failure rules (data not shown). Greater proportions of patients in the GOL group had ≥ 20% improvement in each of the 4 individual ASAS components (patient's global assessment of disease activity, patient's global assessment of total back pain, BASFI, and inflammation) at Week 16 compared with PBO (Table 2). In addition, significantly greater proportions of patients in the GOL group achieved ASAS40 response, ASAS partial remission, and ASAS 5/6 response at Week 16 compared with PBO (Table 2). After Week 16, the proportions of patients achieving an ASAS20 and ASAS40 response were maintained through Week 28 for patients in the GOL group; among patients who initially received PBO and crossed over to GOL at Week 16, improvements were observed at Week 20 and maintained through Week 28 (Figure 2).

Other measures of disease activity were also evaluated. The proportion of patients with a BASDAI50 response was also significantly greater in the GOL group compared with PBO at Week 16 (Table 2). Additionally, the mean change in ASDAS score from baseline to Week 16 was –0.4 in the PBO group and –2.0 in the GOL group ($p < 0.001$). Response rates for ASDAS inactive disease were also significantly greater in the GOL group compared with PBO at Week 2 (7.6% vs 0%; $p = 0.004$) and Week 16 (20.0% vs 2.9%; $p < 0.001$). For patients randomized to PBO, the proportions of patients achieving BASDAI50 response and ASDAS inactive disease increased at Week 20, following crossover to GOL, and were maintained through Week 28 (Figure 2).

The mean improvement in physical function (BASFI) at Week 16 was also significantly greater in the GOL group compared with PBO (–2.4 vs –0.5; $p < 0.001$). The mean improvement from baseline in BASMI score was also greater in the GOL group compared with PBO at Week 16 (–0.4 vs –0.1; $p = 0.001$). At Week 28, the mean change from baseline in BASMI score for patients in the PBO group (–0.3), who began receiving GOL at Week 16, improved nearly to that for patients in the GOL group (–0.4). Among patients with enthesitis at baseline, those in the GOL group had greater mean changes from baseline in enthesitis score when compared with the PBO group at weeks 2 (–2.3 vs –0.7) and 16 (–3.5 vs –1.2; $p < 0.001$ for both).

Patients in the GOL group also had significantly greater improvements in HRQOL at Week 16 compared with the PBO group, as demonstrated by mean improvements from baseline in SF-36 PCS/MCS and ASQoL scores (Table 3).

Among patients with complete ankylosis of the spine at study enrollment, 0 of 7 in the PBO group and 3 of 5 (60.0%) in the GOL group achieved an ASAS20 response at Week 16 ($p = 0.018$). Additionally, in posthoc analyses in this

Table 1. Baseline demographic and disease characteristics. Data are presented as mean ± SD unless otherwise noted.

Characteristics	Placebo	Golimumab, 2 mg/kg
Patients randomized, n	103	105
Age, yrs	39.2 ± 10.8	38.4 ± 10.1
Male, n (%)	77 (74.8)	86 (81.9)
Time since inflammatory back pain first occurred, yrs	11.6 ± 9.1	10.2 ± 8.9
Time since diagnosis of AS, yrs	5.5 ± 5.9	5.6 ± 6.6
Patients with complete ankylosis of the spine, n (%)	7 (6.8)	5 (4.8)
ASAS components		
Patient's global assessment of disease activity, VAS 0–10 cm	7.1 ± 1.7	7.3 ± 1.3
Patient's assessment of total back pain, VAS 0–10 cm	7.3 ± 1.5	7.2 ± 1.3
BASFI	6.1 ± 2.0	6.3 ± 1.9
Inflammation	7.4 ± 1.6	7.3 ± 1.5
BASDAI	7.1 ± 1.2	7.0 ± 1.2
ASDAS	4.1 ± 0.8	4.2 ± 0.7
BASMI	5.0 ± 0.8	5.0 ± 0.9
CRP, mg/l	19.3 ± 16.7	20.0 ± 18.2
Prior anti-TNF therapy, n		
Adalimumab	0	1
Certolizumab	3	8
Etanercept	2	0
Infliximab	9	7
SF-36 PCS score	32.1 ± 5.9	32.4 ± 5.6
SF-36 MCS score	41.9 ± 10.2	40.0 ± 10.4
ASQoL	12.4 ± 4.1	12.8 ± 4.0
Concomitant medication use		
Oral corticosteroids		
Patients, n (%)	23 (22.3)	32 (30.5)
Dose, mg/day[a]	6.1 ± 2.5	7.8 ± 2.7
MTX		
Patients, n (%)	21 (20.4)	15 (14.3)
Dose, mg/week	13.7 ± 5.0	16.7 ± 4.9
NSAID, n (%)	90 (87.4)	94 (89.5)
Sulfasalazine, n (%)	39 (37.9)	41 (39.0)

[a]Dose equivalent to prednisone/day. AS: ankylosing spondylitis; ASAS: ASsessment in Ankylosing Spondylitis International Working Group criteria; ASDAS: Ankylosing Spondylitis Disease Activity Score; ASQoL: Ankylosing Spondylitis Quality of Life; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; CRP: C-reactive protein; MTX: methotrexate; NSAID: nonsteroidal anti-inflammatory drugs; SF-36 PCS/MCS: physical and mental component summary of the Medical Outcomes Study Short Form-36 questionnaire; TNF: tumor necrosis factor; VAS: visual analog scale.

Table 2. Clinical efficacy at Week 16. Data presented as n (%) unless otherwise noted.

Characteristics	Placebo	Golimumab, 2 mg/kg
Patients randomized, n	103	105
ASAS20	27 (26.2)	77 (73.3)**
ASAS40	9 (8.7)	50 (47.6)**
ASAS partial remission	4 (3.9)	17 (16.2)*
ASAS 5/6 response	12 (11.7)	68 (64.8)**
ASDAS inactive disease	3 (2.9)	21 (20.0)**
BASDAI50	15 (14.6)	43 (41.0)**
Change from baseline in ASDAS, n (mean ± SD)	102 (–0.4 ± 0.8)	104 (–2.0 ± 1.0**)
Change from baseline in BASFI, n (mean ± SD)	98 (–0.5 ± 2.0)	105 (–2.4 ± 2.1**)
Change from baseline in BASMI (linear), n (mean ± SD)	96 (–0.1 ± 0.5)	100 (–0.4 ± 0.6**)
Patients with ≥ 20% improvement in ASAS components		
Patient's global assessment of disease activity	34 (33.0)	86 (81.9)**
Patient's assessment of total back pain	38 (36.9)	74 (70.5)**
BASFI	33 (32.0)	75 (71.4)**
Inflammation	37 (35.9)	83 (79.0)**

* $p < 0.01$. ** $p \leq 0.001$. ASAS20/40: ≥ 20%/40% improvement in ASsessment in Ankylosing Spondylitis (ASAS) International Working Group criteria; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI50: ≥ 50% improvement in Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index.

subgroup, the response rates for ASAS40 and BASDAI50 and mean changes from baseline in BASFI and BASMI scores were numerically greater in the GOL group compared with PBO (Appendix 1).

Analysis of AE. Through Week 16, 23.3% of patients in the PBO group and 32.4% of patients in the GOL group had 1 or more AE (Table 4). Infections were the most common type of AE (PBO, 7.8%; GOL, 11.4%); of these, nasopharyngitis and upper respiratory tract infection were the most frequent. Three patients, all in the GOL group (2.9%), had an infusion reaction (fatigue, dizziness, rash); none was considered serious or severe. Two patients had a serious AE (SAE; pneumonia, n = 1; pancreatitis, n = 1); both occurred in the GOL group. Three patients, all in the PBO group, reported eye disorders through Week 16; 1 patient reported eye pain with no history of other eye symptoms, and 2 patients with a history of uveitis that was not ongoing at the start of the trial reported iritis (n = 1) and uveitis (n = 1) through Week 16.

Through Week 28, 34.8% of all GOL-treated patients (i.e., all patients in the GOL group and all patients in the PBO group who received ≥ 1 infusion of GOL) had ≥ 1 AE (Table 4); infections were the most common type (17.2%). No additional patients experienced an infusion reaction or an SAE between weeks 16 and 28. There were no reports of new or worsening inflammatory bowel disease and no reports of depression, demyelination, opportunistic infection, malignancy, or death through Week 28. There were no cases of anaphylaxis or serum sickness–like reactions.

Through Week 28, 22.1% of all GOL-treated patients had an ALT value in the normal range at baseline and a postbaseline abnormal ALT value. Most of these patients had maximum ALT values of < 2 × the upper limit of normal (ULN). One patient had an increase ≥ 3 to < 5 × ULN; none had an increase ≥ 5 × ULN.

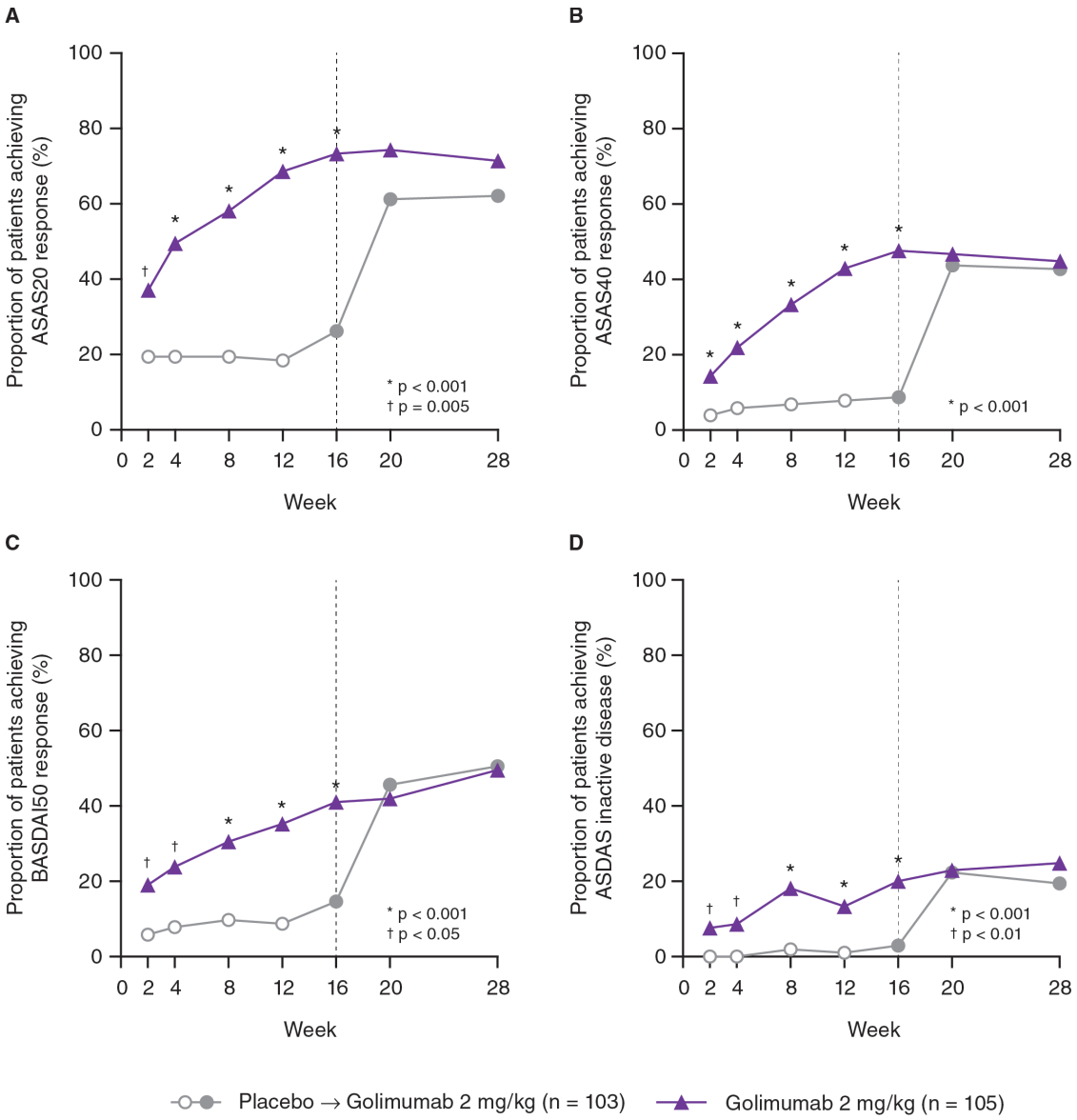

Figure 2. Proportion of patients achieving an ASAS20 response (A), ASAS40 response (B), BASDAI50 response (C), or ASDAS inactive disease (D) through Week 28. Patients randomized to placebo crossed over to golimumab 2 mg/kg at Week 16 (dotted line). ASAS20/40: ≥ 20%/40% improvement in ASsessment in Ankylosing Spondylitis International Working Group criteria; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI50: ≥ 50% improvement in Bath Ankylosing Spondylitis Disease Activity Index.

Among GOL-treated patients, 10.3% had an AST value in the normal range at baseline and a postbaseline abnormal AST value through Week 28. All of these increases were < 2 × ULN.

Twenty-one GOL-treated patients received prophylaxis for latent TB during the study; none developed active TB. One-third had an elevated ALT level through Week 28; all increases were < 3 × ULN. Three patients had an elevated AST level through Week 28; all increases were < 2 × ULN.

Pharmacokinetics and immunogenicity. After administration of IV GOL 2 mg/kg at weeks 0, 4, and every 8 weeks, median trough serum GOL concentration reached steady state by Week 12 and was maintained at Week 20 (0.65 μg/ml). Among GOL-treated patients, 20 (19.0%) tested positive for antibodies to GOL through Week 20 using a highly sensitive, drug-tolerant immunoassay. Among the 20 antibody-positive patients, 6 were positive for neutralizing antibodies. Median trough GOL concentrations tended to be lower in patients who were positive for antibodies to GOL, and GOL concentrations tended to decrease as peak titers increased. At Week 20, 13 (65%) of the 20 antibody-positive patients had an ASAS20 response, and 6 (30%) had an ASAS40 response;

Table 3. Health-related quality of life at Week 16. Data are n (mean ± SD) unless otherwise indicated.

Variables	Placebo	Golimumab, 2 mg/kg
Patients randomized, n	103	105
Change from baseline in SF-36 PCS score	98 (2.9 ± 6.2)	104 (8.5 ± 7.5*)
Change from baseline in SF-36 MCS score	98 (0.8 ± 10.0)	104 (6.5 ± 9.1*)
Change from baseline in ASQoL	98 (–1.8 ± 4.6)	104 (–5.4 ± 5.0*)

*p ≤ 0.001. ASQoL: Ankylosing Spondylitis Qualify of Life; SF-36 PCS/MCS: physical and mental component summary of the Medical Outcomes Study Short Form-36 questionnaire.

among the 84 patients who tested negative for antibodies to GOL, 65 (77%) had an ASAS20 response and 43 (51%) had an ASAS40 response. None of the infusion reactions occurred in patients who tested positive for antibodies to GOL.

DISCUSSION

Through Week 28 of the GO-ALIVE study, the signs and symptoms of AS were significantly improved among patients treated with IV GOL 2 mg/kg compared with those receiving PBO. The primary endpoint was achieved, with 73% of patients in the GOL group achieving an ASAS20 response at Week 16 compared with 26% of patients in the PBO group, and separation between the GOL and the PBO group was observed as early as Week 2. Of note, among the small subgroup of patients who had complete ankylosis of the spine, 3 of the 5 GOL-treated patients achieved an ASAS20 response at Week 16 compared with no patient in the PBO group. Additional data are needed to assess the efficacy of IV GOL in patients with complete ankylosis.

All major secondary endpoints were met, which demonstrated that the response to IV GOL in this population was robust. Mean improvements in clinical efficacy measures and HRQOL were significantly greater in the GOL group compared with PBO. The significantly greater improvements in the SF-36 MCS score with IV GOL compared with PBO are particularly notable in this patient population[8,22,23].

Current treatment recommendations for adults with AS outline various therapy options with the overall treatment goals being to "reduce symptoms, maintain spinal flexibility and normal posture, reduce functional limitations, maintain work ability, and decrease disease complications"[1]. These recommendations support the use of anti-TNF therapy for patients with active AS despite receiving NSAID. The treat-to-target concept is not as well developed for spondyloarthritides as with RA[24]; however, an international task force currently suggests that clinical remission/inactive disease of musculoskeletal symptoms should be a major treatment target[25]. Nearly 30% of patients randomized to GOL in GO-ALIVE achieved ASDAS inactive disease at Week 16.

GOL has demonstrated efficacy in patients with AS by both SC[8] and IV routes of administration. Currently, GOL is the only anti-TNF therapy that can be administered as either an SC injection (monthly) or an IV infusion (over 30 min every 8 weeks). Patients often have preferences for mode and frequency of treatment administration for biologic therapies[9,10]. Patient involvement in determining treatment decisions has been shown to improve treatment satisfaction[26] and also efficacy outcomes[27]. Thus, the international task force treatment recommendations support the consideration of patient preferences as part of the shared decision-making discussion with physicians[25].

There was a higher incidence of AE with GOL than with PBO through Week 16, which is consistent with previous PBO-controlled trials of anti-TNF therapies in AS[8,22,28]. Infections were the most common type of AE; most were not classified by the investigators as serious or severe. Few infusion reactions were reported. Two SAE occurred; both in the GOL group (pneumonia and pancreatitis) and before Week 16, with no additional SAE between weeks 16 and 28. No cases of new or worsening inflammatory bowel disease

Table 4. Adverse events through Week 28. Data presented as n (%) unless otherwise noted.

Variables	Weeks 0–16		Weeks 0–28
	Placebo	GOL, 2 mg/kg	Combined GOL, 2 mg/kg*
Patients, n	103	105	204
Mean duration of followup, weeks	16.0	16.1	20.2
Patients who discontinued because of an AE	0	0	1 (0.5)
Patients with ≥ 1 AE	24 (23.3)	34 (32.4)	71 (34.8)
Patients with ≥ 1 infection	8 (7.8)	12 (11.4)	35 (17.2)
Patients with ≥ 1 infusion reaction	0	3 (2.9)	3 (1.5)
Patients with ≥ 1 SAE	0	2 (1.9)	2 (1.0)
Serious infections	0	1 (1.0)	1 (0.5)
Malignancies	0	0	0
Deaths	0	0	0

* The combined GOL group includes patients randomized to the placebo group who crossed over to GOL at Week 16 and patients randomized to the GOL group at baseline. GOL: golimumab; AE: adverse event; SAE: serious AE.

occurred through Week 28, and there were no reports of depression, demyelination, opportunistic infection, malignancy, or death.

Twenty patients tested positive for antibodies to GOL using a highly sensitive, drug-tolerant assay, which was consistent with other rheumatologic indications tested with the drug-tolerant immunoassay. The higher incidence of antibodies to GOL in comparison with the previous assay[3] was expected from using a more sensitive assay and was mostly due to low titer antibodies, which did not have an apparent effect on drug concentrations or efficacy. Higher titer antibodies, which were mostly neutralizing, appeared to be associated with lower GOL concentrations and diminished efficacy; however, there were too few patients with these high titers to draw any firm conclusions. Overall, development of antibodies to GOL did not preclude clinical response and there did not appear to be an effect of antibodies to GOL on infusion reactions because no infusion reaction occurred in patients who tested positive for antibodies to GOL.

The results through Week 28 of the GO-ALIVE study demonstrated significantly greater clinical response and improvements in HRQOL with GOL compared with PBO in patients with AS. The incidence and type of AE that occurred through Week 28 were consistent with the established safety profile of anti-TNF therapies in patients with AS, and no new safety signals were identified. The safety and efficacy of IV GOL 2 mg/kg in this patient population will be reported through 1 year in a subsequent publication.

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APPENDIX 1. Efficacy at Week 16 for patients with complete ankylosis at baseline. Data presented as n (%) unless otherwise noted.

Variables	Placebo	Golimumab, 2 mg/kg
Patients randomized, n	7	5
ASAS20	0	3 (60.0)*
ASAS40	0	1 (20.0)
BASDAI50	0	1 (20.0)
ASAS partial remission	0	0
ASDAS inactive disease	0	0
Change from baseline in BASFI, mean ± SD	0.7 ± 0.7	–1.1 ± 2.0
Change from baseline in BASMI (linear), mean ± SD	–0.02 ± 0.55	–0.34 ± 0.36

* $p < 0.05$. ASAS20/40: ≥ 20%/40% improvement in ASsessment in Ankylosing Spondylitis (ASAS) International Working Group criteria; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI50: ≥ 50% improvement in Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index.

Correction

Safety and Efficacy of Golimumab Administered Intravenously in Adults with Ankylosing Spondylitis: Results through Week 28 of the GO-ALIVE Study

Deodhar A, Reveille JD, Harrison DD, Kim L, Lo KH, Leu JH, Hsia EC. Safety and efficacy of golimumab administered intravenously in adults with ankylosing spondylitis: results through week 28 of the GO-ALIVE study. J Rheumatol 2017; doi:10.3899/jrheum.170487. In Figure 2 of this article, the legend for Panel C is incorrect. The legend should read, "Placebo → Golimumab 2 mg/kg (n = 103)".

This correction applies only to the December 15 First Release. The correct figure appears online and will appear in the March print edition.

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