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Efficacy and Safety of Intravenous Golimumab in Ankylosing Spondylitis Patients With Early and Late Disease Through One Year of the GO-ALIVE Study

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Background/Objective: This post hoc analysis assessed efficacy and safety of intravenous (IV) golimumab in ankylosing spondylitis (AS) patients with early disease (ED) versus late disease (LD).

Methods: The phase 3, double-blind, GO-ALIVE study randomized patients to IV golimumab 2 mg/kg at weeks 0 and 4 and then every 8 weeks through week 52, or placebo at weeks 0, 4, and 12 with crossover to IV golimumab at week 16. Clinical efficacy was assessed by ≥20% improvement in Assessment of Spondyloarthritis International Society response criteria (ASAS20), ≥50% improvement in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI 50), and Ankylosing Spondylitis Disease Activity Score (ASDAS) <1.3 (inactive disease). Using self-reported duration of inflammatory back pain (IBP), patients were grouped into quartiles: first = ED and fourth = LD. Descriptive statistics summarized efficacy and safety findings through 1 year.

Results: Early disease patients (n = 60) were ~10 years younger and had shorter median AS (IBP) symptom duration (2–3 years) versus LD patients (n = 52; 21–24 years). At week 16, numerically higher proportions of golimumab- than placebo-treated patients achieved ASAS20 (ED: 71% vs. 32%; LD: 67% vs. 21%), BASDAI 50 (ED: 40% vs. 12%; LD: 33% vs. 7%), and ASDAS <1.3 (ED: 17% vs. 4%; LD 8% vs. 0%) regardless of IBP duration. Efficacy was durable through 1 year of treatment; however, response rates were numerically higher in patients with ED versus LD. Through week 60, adverse events and serious adverse events, respectively, were reported by 46% and 3% of ED patients and 61% and 2% of LD patients.

Conclusion: Prompt diagnosis of AS and early treatment with IV golimumab may yield more robust improvements in disease activity.

Key Words: ankylosing spondylitis, efficacy, inflammatory back pain, intravenous golimumab, safety, tumor necrosis factor inhibitor

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Ankylosing spondylitis (AS) is an immune-mediated disease associated with chronic inflammation of the spine that is more prevalent in men than women, with symptoms often appearing before age 40 years.[1,2] Typically, patients experience severe back pain, spinal stiffness, and reduced spinal mobility that may result in deformity and functional disability.[2] Specifically, patients with AS complain of inflammatory back pain (IBP) that has an insidious onset, improves with exercise, and is often nocturnal, as well as progressive spinal stiffness, and approximately 90% are human leukocyte antigen B27 (HLA-B27) positive.[2] Many health care practitioners do not recognize the characteristics of IBP in patients with chronic back pain, and there is an average of 5- to 9-year delay between symptom onset and physician diagnosis of AS.[3,4]

Treatment of patients with AS requires individualization based on clinical presentation (axial, peripheral, and extramusculoskeletal manifestations) and underlying comorbidities.[5] Current treatment guidelines from the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network conditionally recommend continuous use of nonsteroidal anti-inflammatory drugs (NSAIDs) and exercise/physical therapy as first-line treatment and a tumor necrosis factor inhibitor (TNFi) for patients with persistent disease activity despite NSAID treatment.[1,5] Tumor necrosis factor inhibitor treatment in patients with AS is associated with reduced joint pain, reduced functional limitations, induction of partial remission, and reduced disease complications.[1,2,6,7]

Golimumab, a fully human monoclonal antibody targeting TNF-α, is approved to treat adults with rheumatoid arthritis, psoriatic arthritis, and AS when given as a subcutaneous injection[8] or as an intravenous (IV) infusion.[9] The pivotal GO-ALIVE study demonstrated that golimumab administered intravenously was efficacious in treating the signs and symptoms of AS with a safety profile

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consistent with other TNFi.[10,11] Furthermore, IV golimumab–treated patients had meaningful improvements in clinical efficacy and health-related quality of life, as well as enhanced work productivity through 1 year.[10–12] A recent systematic literature review and network meta-analysis of 30 randomized, controlled, phases 2 and 3 trials in 6711 patients with AS found that golimumab 2 mg/kg administered intravenously ranked highly for efficacy (e.g., improvement of ≥20% in the Assessment of Spondyloarthritis International Society [ASAS20] criteria, change from baseline in Bath Ankylosing Spondylitis Functional Index [BASFI], and change from baseline in C-reactive protein levels at weeks 12–16).[13]

Early aggressive treatment of inflammatory arthritis is known to improve physical function and other related symptoms, slow disease progression, and improve quality of life in patients with rheumatoid arthritis[14]; however, information pertaining to the benefits of treating AS patients with symptoms of early disease is limited.[15,16] Initiation of biologic treatment in patients with early disease may improve symptoms and signs and health-related quality of life to a greater extent than in patients with longer disease duration.[17,18] Accordingly, the objective of this post hoc analysis of the GO-ALIVE trial was to compare the efficacy and safety of IV golimumab in AS patients with early versus late disease based on self-reported AS (IBP) symptom duration.

METHODS

Study Design and Patients

GO-ALIVE (ClinicalTrials.gov NCT02186873) was a phase 3, double-blind, placebo-controlled trial. Eligibility criteria and the study design of GO-ALIVE were previously reported.[10,11] Adults with a diagnosis of AS ("definite" using the modified New York criteria) for ≥3 months with signs of active disease and inadequate response or intolerance to NSAIDs were eligible for inclusion in GO-ALIVE. Up to 10% of the study population could have complete ankylosis of the spine. Eligible patients were randomly assigned (1:1) to receive IV infusions of placebo at weeks 0, 4, and 12, followed by crossover to golimumab 2 mg/kg at weeks 16 and 20 and then every 8 weeks through week 52 (placebo→IV golimumab) or IV golimumab 2 mg/kg at weeks 0 and 4 and then every 8 weeks through week 52.

Stable doses of methotrexate (MTX; ≤25 mg/wk), sulfasalazine (SSZ), hydroxychloroquine (HCQ), NSAIDs, other analgesics, and low-dose oral corticosteroids (dose equivalent to ≤10 mg prednisone per day) were permitted for patients who were receiving these medications at baseline. 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. Up to 20% of the study population could have received a prior TNFi other than golimumab; these patients could not have discontinued the prior TNFi because of primary treatment failure. Any prior TNFi therapy had to be discontinued at least 3 months (at least 6 weeks for etanercept) before the first study drug administration.

The GO-ALIVE study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practices. The study protocol was reviewed by an institutional review board or an independent ethics committee at participating sites, and all patients provided written informed consent.

Post Hoc Study Population, Definitions, and Evaluations

Among 208 patients enrolled in GO-ALIVE, quartile cutoffs were used to group patients into categories of self-reported duration of IBP symptoms, which provides a more accurate estimate of disease duration, given that a definitive AS diagnosis is often delayed.[3,4] Accordingly, patients with early disease were defined as those with AS (IBP) symptom duration in the first quartile (i.e., IBP ≤4 years; n = 60), whereas late disease was defined as patients with AS (IBP) symptom duration in the fourth quartile (i.e., IBP ≥15.5 years; n = 52). Post hoc analyses were limited to patients with early and late disease.

The primary endpoint of the GO-ALIVE trial was the proportion of patients with an ASAS20 response at week 16.[10] In the current post hoc analyses, the proportions of patients achieving ASAS20 or ASAS40 response[19] were also evaluated at week 52. Disease activity was assessed at weeks 16 and 52 using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)[20] and the Ankylosing Spondylitis Disease Activity Score (ASDAS; inactive disease, score <1.3; major improvement, decrease ≥2.0; and clinically important improvement, decrease ≥1.1).[21,22] In addition, physical function was assessed using BASFI,[23] improvements in spinal mobility were assessed using the Bath Ankylosing Spondylitis Metrology Index (BASMI),[24] and changes in enthesitis were assessed using the University of California San Francisco enthesitis index[25] among patients with enthesitis at baseline (n = 59 early disease, n = 49 late disease). Health-related quality of life was evaluated using the Ankylosing Spondylitis Quality of Life (ASQoL) score.[26] Patient-reported night back pain and total back pain were also evaluated using the BASFI.

Adverse events (AEs) were monitored throughout the study with the final safety follow-up visit at week 60.

Statistical Methods

Clinical efficacy results at weeks 16 and 52 for the early and late disease groups were summarized using counts and percentages for discrete variables and mean (SD) or median (interquartile range) for continuous variables. No formal comparisons were performed between patients with early versus late disease because of the limited sample size of the cohorts and post hoc nature of the analysis. In the formal analysis plan, treatment failure at week 16 was defined as initiation of new disease-modifying antirheumatic drugs, biologics, or systemic immunosuppressives or oral, IV, or intramuscular corticosteroids; increase in dose of MTX, SSZ, HCQ, or oral corticosteroids above baseline dose; and/or discontinuation of study agent due to lack of efficacy. Through week 16, patients who met treatment failure rules were to be counted as nonresponders; missing composite scores were imputed using last observation carried forward for individual components or nonresponder imputation if all components were missing.[10] At week 52, no treatment failure rules were applied; missing data for categorical variables were imputed as described for week 16,[11] and continuous variables were reported using observed data with no imputation for missing scores. In addition, a sensitivity analysis was performed comparing IBP duration among responders and nonresponders for each efficacy outcome that included data from all randomized patients (quartiles 1–4).

The proportions of patients reporting ≥1 AE, commonly reported AEs (occurring in ≥3 patients), serious AEs (SAEs), AEs leading to study agent discontinuation, and infections were summarized at weeks 16 and 60 by actual treatment received for patients with early versus late disease.

RESULTS

Demographics and Baseline Disease Characteristics

A total of 112 patients were included in this post hoc analysis, including 60 patients with early disease and 52 with late

TABLE 1. Baseline Demographics and Clinical Characteristics[a]

	Early Disease		Late Disease	
	Placebo n = 25	IV Golimumab n = 35	Placebo n = 28	IV Golimumab n = 24
Male, n (%)	16 (64)	28 (80)	21 (75)	19 (79)
White, n (%)	22 (88)	27 (77)	27 (96)	22 (92)
Age, y				
Mean (SD)	33 (8.9)	35 (10.9)	45 (9.4)	45 (10.6)
Median (IQR)	31 (25, 38)	31 (28, 45)	46 (37, 51)	43 (39, 54)
AS (IBP) symptom duration, y				
Mean (SD)	3 (1.5)	2 (1.2)	24 (6.0)	24 (7.6)
Median (IQR)	3 (1, 4)	2 (1, 3)	24 (20, 28)	21 (18, 27)
AS duration since diagnosis, y				
Mean (SD)	3 (4.4)	1 (1.4)	9 (8.1)	12 (9.5)
Median (IQR)	1.3 (0.6, 2.9)	0.8 (0.6, 1.8)	6.8 (1.4, 13.4)	13.0 (2.7, 20.5)
Complete ankylosis, n (%)	1 (4.0)	1 (2.9)	4 (14.3)	2 (8.3)
HLA-B27^{+} status, n (%)	22 (88)	27 (77)	26 (93)	22 (92)
Disease activity				
ASAS components				
PGA (VAS 0–10 cm)[b,c]	6.9 (1.59)	7.2 (1.24)	7.4 (1.18)	7.5 (1.39)
BASFI (VAS 0–10 cm)[b]	5.6 (1.81)	6.0 (1.91)	6.3 (1.75)	7.2 (1.43)
Total back pain (VAS 0–10 cm)	7.4 (1.50)	7.0 (1.24)	7.5 (1.24)	7.7 (1.00)
Inflammation (average of last 2 questions of BASDAI concerning morning stiffness)	7.0 (1.84)	7.1 (1.40)	7.5 (1.27)	7.5 (1.36)
BASDAI (VAS 0–10 cm)	6.9 (1.30)	7.0 (1.14)	7.1 (1.00)	7.5 (1.08)
ASDAS[b,c,e]	4.2 (0.65)	4.2 (0.76)	4.2 (0.77)	4.3 (0.64)
BASMI (VAS 0–10 cm)[b,d]	5.0 (0.62)	5.0 (0.90)	5.1 (0.78)	5.3 (0.90)
ASQoL (0–18)[b,c]	12.9 (4.49)	11.6 (4.32)	12.3 (3.47)	14.7 (3.08)
Night back pain (VAS 0–10 cm)[b,c]	7.2 (1.90)	7.0 (1.48)	7.1 (1.61)	7.6 (1.24)
Enthesitis score, UCSF (0–17)[b,d]	4.9 (4.31)	4.6 (2.89)	5.9 (4.24)	6.5 (4.70)
C-reactive protein, mg/L	21 (16.2)	22 (21.7)	22 (19.7)	17 (13.1)
Prior TNFi treatment	0	0	0	0

[a]Mean (SD) reported unless otherwise stated.

[b]Early disease: placebo, n = 24.

[c]Late disease: IV golimumab, n=23.

[d]Late disease: IV golimumab, n = 21.

[e]<1.3 inactive disease; <2.1 low disease activity, >3.5 very high disease activity.

IQR, interquartile range; PGA, Patient Global Assessment; UCSF, University of California San Francisco; VAS, visual analog scale.

disease. Through week 60, 110 patients remained enrolled in the study (1 placebo patient each in the early and late disease subgroups did not cross over to golimumab at week 16); no patient met the treatment failure criteria.

Most patients were male (64%–80%) and white (≥77%) (Table 1). Baseline data indicated that patients with late disease (i.e., longstanding IBP, median duration of 21–24 years) were approximately 10 years older compared with patients with early disease (i.e., more recent-onset IBP, median duration of 2–3 years). Median times since AS diagnosis by a physician were 0.8 to 1.3 and 6.8 to 13.0 years for patients with early versus late disease, respectively. Among patients with late disease, the median AS duration since diagnosis by a physician was numerically lower in the placebo group than in the golimumab group (6.8 vs. 13.0 years, respectively). At baseline, a higher proportion of patients with late disease had complete ankylosis compared with those with early disease (11.5% vs. 3.3%). Prior TNFi treatment was not reported by any patient included in the early and late disease cohorts.

Disease activity at baseline, as measured by ASAS components, BASDAI, ASDAS, BASMI, ASQoL, and night back pain, was generally balanced between treatment groups for patients with early and late disease (Table 1). Relative to patients with late disease, those with early disease appeared to have less functional impairment (mean BASFI, 6.3–7.2 vs. 5.6–6.0), less severe enthesitis (mean enthesitis score, 5.9–6.5 vs. 4.6–4.9), and lower incidence of HLA-B27 positivity (92%–93% vs. 77%–88%).

Clinical Efficacy by Disease Duration Status

Regardless of duration of IBP, higher proportions of IV golimumab– than placebo-treated patients achieved ASAS20, ASAS40, BASDAI 50, and ASDAS responses at week 16. While response rates for less rigorous response criteria were fairly consistent between early and late disease, more rigorous response criteria were achieved by higher proportions of patients with early disease (Figs. 1-3). Specifically, among IV golimumab–treated

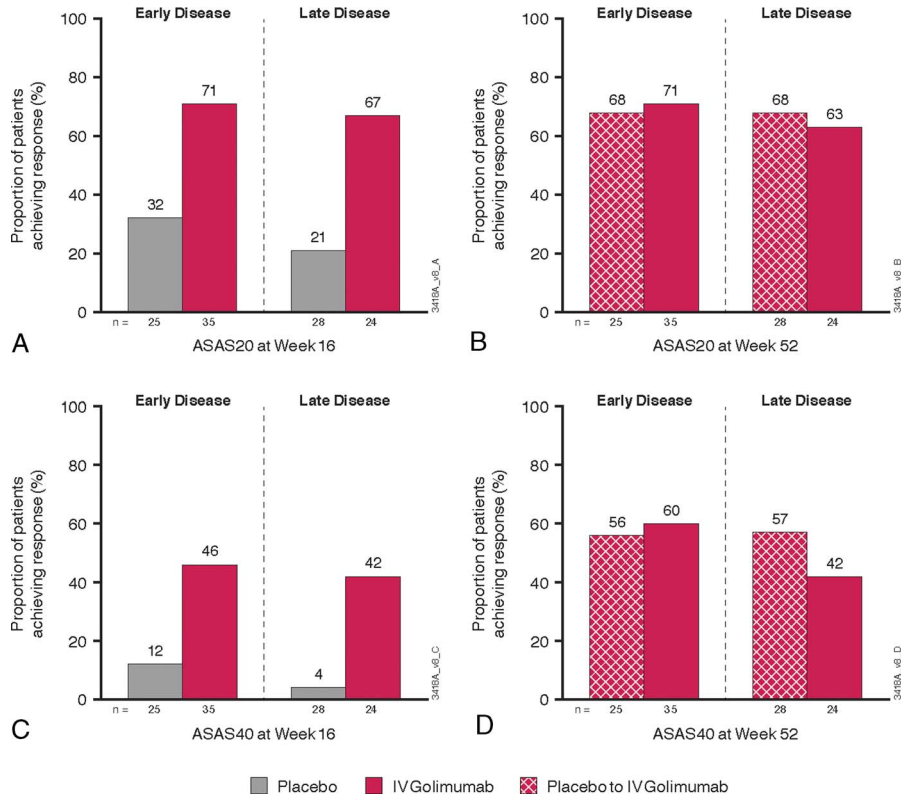

FIGURE 1. The proportions of patients achieving (A) ASAS20 at week 16, (B) ASAS20 at week 52, (C) ASAS40 at week 16, and (D) ASAS40 at week 52 among patients with early and late disease. ASAS20/40 response = improvement of at least 20%/40% from baseline in the ASAS criteria.

patients with early and late disease, respectively, BASDAI 50 response was achieved by 40% versus 33% of patients (Fig. 2), and ASDAS inactive disease was achieved by 17% versus 8% at week 16 (Fig. 3).

The proportions of patients achieving BASDAI 50 response and ASDAS inactive disease increased from weeks 16 to 52 to a greater extent in patients with early disease versus late disease. Among IV golimumab–randomized patients, 40% of those with early disease and 33% with late disease achieved a BASDAI 50 at week 16, and 60% and 42%, respectively, achieved a BASDAI 50 at week 52; in addition, ASDAS inactive disease was achieved by 17% of patients with early disease and 8% with late disease at week 16 and 37% and 4%, respectively, at week 52. Placebo→IV golimumab patients achieved similar response rates at week 52 as patients who received a full year of IV golimumab in both early disease and late disease subgroups.

Regardless of duration of IBP, mean improvements in other measures of disease activity were maintained from week 16 to week 52 (see Table, Supplemental Digital Content 1, http://links.lww.com/RHU/A450, which shows other measures of disease activity). Mean (SD) improvements from baseline to week 16 in BASFI and enthesitis scores were numerically greater with treatment of IV golimumab (−2.3 [2.1] and −2.9 [2.9], respectively) versus placebo (−0.4 [2.0] and 0.1 [3.6], respectively) for patients with early

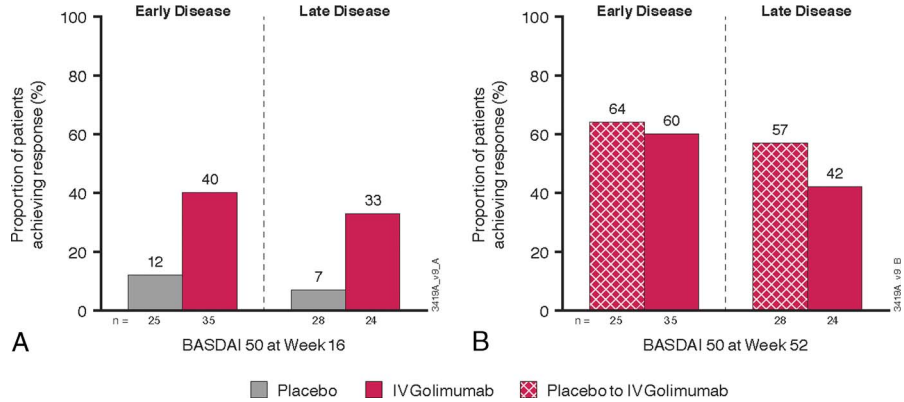

FIGURE 2. The proportions of patients achieving (A) BASDAI 50 at week 16 and (B) BASDAI 50 at week 52 among patients with early and late disease. BASDAI50 response = at least 50% improvement in Bath Ankylosing Spondylitis Disease.

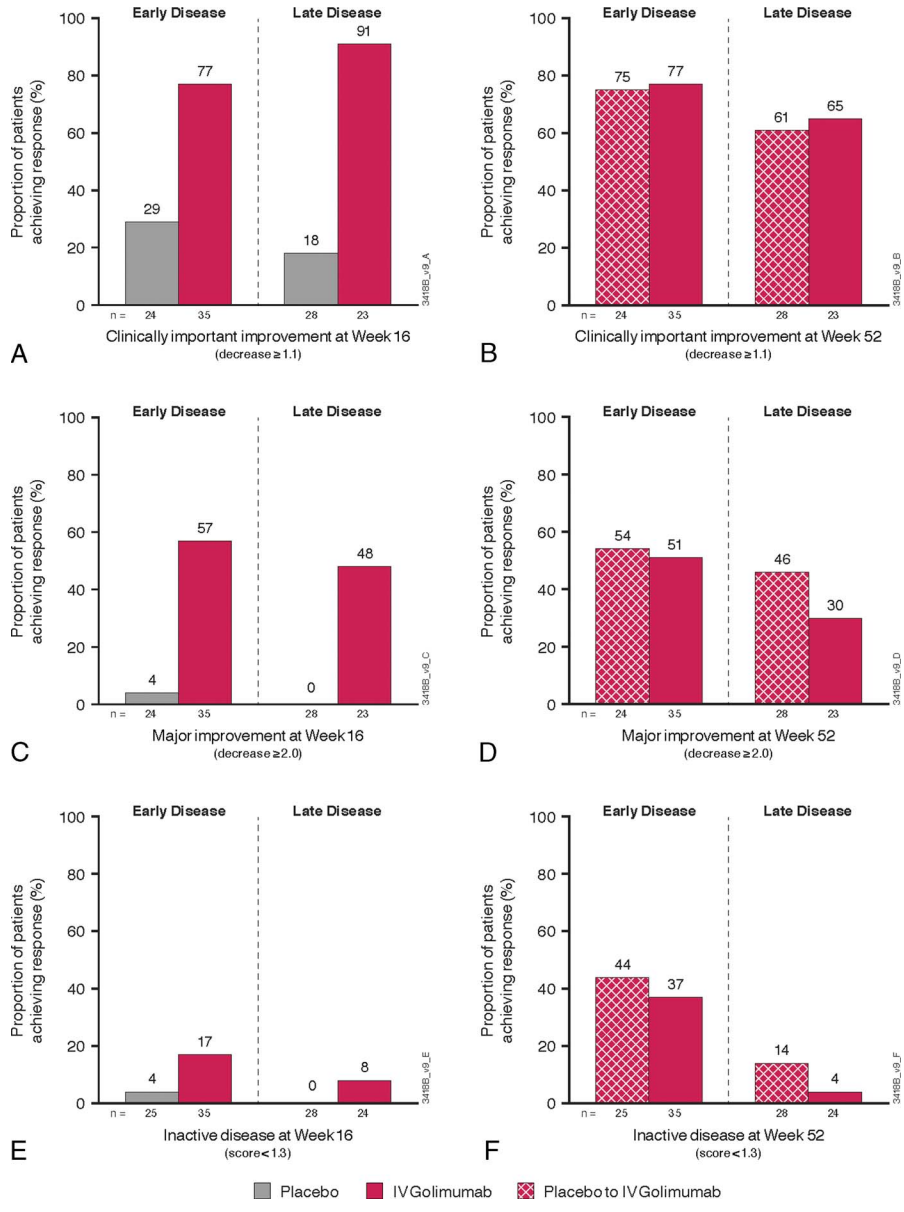

FIGURE 3. The proportions of patients achieving (A) ASDAS clinically important improvement at week 16, (B) ASDAS clinically important improvement at week 52, (C) ASDAS major improvement at week 16, (D) ASDAS major improvement at week 52, (E) ASDAS inactive disease at week 16, and (F) ASDAS inactive disease at week 52 among patients with early and late disease.

disease; similar trends were observed for those with late disease. Further, mean improvements at week 16 in the IV golimumab group were generally maintained at 1 year across the early disease and late disease subgroups. Within each cohort, placebo→IV golimumab patients achieved similar improvements at 1 year as those who received IV golimumab from week 0.

Also in patients with early and late disease, IV golimumab–treated patients reported greater improvements from baseline to week 16 in ASQoL, night back pain, and total back pain than placebo patients (see Figure, Supplemental Digital Content 2, http://links.lww.com/RHU/A451, which shows quality of life assessments). Further improvement or maintenance of these mean improvements was observed for IV golimumab and placebo→IV golimumab groups at week 52 with responses similar for patients with early versus late disease.

Findings from the responder analysis corroborated results of the cohort analysis wherein patients who achieved clinical response at weeks 16 or 52 had numerically shorter AS (IBP) symptom duration on average when compared with nonresponders (Table, Supplemental Digital Content 3, http://links.lww.com/RHU/A452, which shows the responder analysis based on IBP duration).

Safety Through Week 60

During the placebo-controlled period (weeks 0–16), higher proportions of both placebo- and IV golimumab–treated patients with late disease reported at least 1 AE (11 [39%] and 11 [46%], respectively) and infection (3 [11%] and 4 [17%], respectively) versus those with early disease (3 [12%] and 10 [29%] and 0 [0%] and 3 [9%] respectively; Table 2). Through week 60,

TABLE 2. Safety Outcomes

	Through Week 16				Through Week 60	
	Early Disease		Late Disease		Early Disease	Late Disease
	PBO (n = 25)	IV GLM (n = 35)	PBO (n = 28)	IV GLM (n = 24)	Combined IV GLM (n = 59)	Combined IV GLM (n = 51)
Mean duration of follow-up, wk	16	16	16	16	53	51
Patients with ≥1 AE, n (%)	3 (12)	10 (29)	11 (39)	11 (46)	27 (46)	31 (61)
Most common AEs (reported in ≥3 patients), n (%)						
Headache	0	2 (6)	1 (4)	1 (4)	3 (5)	1 (2)
Nasopharyngitis	0	1 (3)	1 (4)	2 (8)	5 (9)	9 (18)
Upper respiratory tract infection	0	1 (3)	1 (4)	1 (4)	3 (5)	5 (10)
Diarrhea	0	0	2 (7)	1 (4)	1 (2)	4 (8)
Alanine aminotransferase increased	0	1 (3)	0	0	2 (3)	4 (8)
Aspartate aminotransferase increased	0	0	0	0	1 (2)	3 (6)
Arthralgia	0	1 (3)	0	0	3 (5)	0
Catarrh	0	0	1 (4)	1 (4)	0	3 (6)
Patients with ≥1 SAE, n (%)	0	1 (3)	0	0	2 (3)	1 (2)
Patients who discontinued due to AE, n (%)[a]	0	0	0	0	1 (2)	1 (2)
Patients with ≥1 infection	0	3 (9)	3 (11)	4 (17)	16 (27)	15 (29)

[a] For week 60, early disease n = 60 PBO → IV GLM and late disease n = 52 PBO → IV GLM.
GLM, golimumab; PBO, placebo.

few patients experienced an SAE. Two patients with early disease, both randomized to IV golimumab, experienced an SAE (sinus tachycardia and pancreatitis), and 1 SAE occurred in a patient with late disease (wrist fracture in an IV golimumab–randomized patient). Discontinuation of study drug due to an AE was infrequent: 1 patient (2%) each in the early and late disease subgroups.

Overall, no new safety signals for IV golimumab were observed through week 60. No patient with early or late disease had an infusion reaction, serious infection, case of active tuberculosis, opportunistic infection, malignancy, or death during the study period.

DISCUSSION

The GO-ALIVE trial previously demonstrated the efficacy of IV golimumab in patients with active AS.[10,11] In this post hoc analysis of data from GO-ALIVE, golimumab was efficacious in improving the signs and symptoms of AS for both patients with early and late disease, with numerically higher mean improvements and response rates (e.g., ASAS20, BASDAI, and ASDAS) in patients with early disease. Efficacy was durable through 1 year of golimumab treatment; however, greater proportions of patients with early disease achieved the "high hurdle" endpoints of BASDAI 50 response and ASDAS inactive disease at 1 year compared with those with late disease. Similar patterns were observed in placebo-treated patients who crossed over to golimumab at week 16, also suggesting that patients with early disease were more likely to achieve BASDAI 50 and ASDAS inactive disease. Of note, complete ankylosis at baseline was reported for 2 patients in the early disease cohort and 6 patients in the late disease cohort. Finally, the sensitivity analysis confirmed that patients who achieved clinical response at week 16 or 52 tended to have a shorter AS (IBP) symptom duration than that observed in nonresponders, across all clinical efficacy endpoints evaluated.

The IV golimumab benefit-risk profile appeared to be favorable across the early disease and late disease subgroups. Despite the small numbers of patients composing the early and late disease subgroups, golimumab was well tolerated through week 60 of treatment, with a lower proportion of patients with early disease than late disease reporting ≥1 AE. The true differences in the proportions of patients with early or late disease reporting at least 1 AE or infection through week 60 remain unclear because of low numbers of patients in each cohort. The safety profile of golimumab in these patients was consistent with the known profile of golimumab in other rheumatic conditions as well as with other TNFi.[27]

Substantial delays in diagnosis of AS by physicians have been recognized worldwide (6.7 years on average), highlighting the need for additional awareness for physicians and patients with back pain.[3] Further, there is mounting evidence that early and effective treatment of inflammation may slow or prevent disease progression, supporting early treatment of patients with AS to reduce the likelihood of radiographic progression.[17] Accordingly, earlier recognition of clinical manifestations and subsequently earlier diagnosis of AS is paramount to management and potential reduction in long-term sequelae including worse functional impairment, greater radiographic progression, poorer quality of life, greater work disability, unemployment, health care costs, and reduced response to treatment.[28,29] In this post hoc analysis, treatment with IV golimumab in patients with early disease (median onset of AS [IBP] symptoms, 2–3 years) appeared to be associated with an early positive response at week 16 and a higher proportion of patients achieving inactive disease after 1 year of treatment (37%–44%) compared with patients with late disease (4%–14%). Of note, patients with early disease had less severe disease characteristics at baseline (e.g., lower BASFI and enthesitis scores) compared with those with late disease. Overall, in this post hoc analysis, patients treated earlier in the disease course tended to have better outcomes at 1 year.

Although some previous studies in AS patients failed to identify any association between symptom or disease duration and clinical response to therapy,[30–33] these findings are likely due to their observational design with ensuing bias and confounding.

In contrast, the findings from GO-ALIVE (a placebo-controlled randomized clinical trial) that AS patients with early disease had better clinical responses at 1 year following golimumab compared with late disease are in keeping with several other reports.[15,34–37] Based on the findings from 2 small placebo-controlled, randomized studies of patients with active AS, 73% of those with shorter disease duration (≤10 years) achieved a BASDAI 50 response compared with 58% of patients with disease duration of 11 to 20 years and 31% of patients with disease duration of more than 20 years.[37] Findings from an exploratory analysis of 4 randomized, placebo/active-controlled studies with etanercept (n = 1281)[15,34–36] reported that 34% with early disease (≤2 years) achieved partial remission compared with 22% to 30% with longer disease duration (30% for >2–5 years, 27% for >5–10 years, and 22% for >10 years; all $p < 0.05$).[16] Overall, the findings from these studies and GO-ALIVE suggest that earlier treatment in the course of the disease may lead to better outcomes for patients with AS, potentially because their disease represents active inflammation that may be reversible; although, additional research to support this is needed. Patients with late disease may be more likely to have greater disease severity at initiation of therapy and possibly irreversible damage.

Limitations of this study include the small sample size and post hoc nature of the analysis. Further, the definition of early versus late disease was based on self-reported duration of IBP. While this symptom reasonably categorizes a patient's length of disease, recall bias may have affected the accuracy of the IBP duration reported. Median AS duration since diagnosis by a physician differed between the placebo and golimumab treatment groups among patients with late disease (6.8 vs. 13.0 years, respectively). This difference may have been due to chance alone or to the small sample size. However, this variable was not used to categorize patients as having early or late disease due to known delays from symptom onset to a physician diagnosis of AS.[3,4] In this post hoc analysis, patient-reported IBP was therefore felt to be a more accurate estimate of disease duration for defining the early and late disease cohorts. Finally, although no patient included in the early and late disease cohorts had received a prior TNFi and other biologics were not permitted prior to study entry, patients could have received other nonbiologic medications, which was not factored into the efficacy assessments.

In summary, IV golimumab provided clinically meaningful improvements in signs and symptoms of AS through 1 year regardless of duration of IBP symptoms; furthermore, greater proportions of patients with early versus late disease were able to achieve inactive disease. These data support timely treatment for optimal outcomes for patients with AS, in keeping with the emergence of a treat-to-target strategy for AS.[38,39] This post hoc analysis also shows that BASDAI 50 and ASDAS inactive disease responses were discriminating outcomes for patients with early versus late disease. Further research is needed to determine the long-term benefits of initiating treatment to patients earlier in the disease process.

KEY POINTS

- Patients with early and late disease demonstrated improvements in AS symptoms through 1 year of IV golimumab treatment.
- Among IV golimumab-treated patients, greater proportions of those with early disease than late disease (as defined by duration of IBP) achieved BASDAI 50 (60% vs. 42%) and ASDAS inactive disease responses (37% vs. 4%) at 1 year, supporting the importance of prompt diagnosis and treatment of AS.
- Intravenous golimumab was well tolerated through 1 year of treatment, with a lower proportion of patients with early disease (46%) than late disease (61%) reporting at least 1 AE.
- These findings are in keeping with the concept that earlier treatment leads to better outcomes in patients with AS.

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