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Efficacy and Safety of Intravenous Golimumab Through One Year in Patients With Active Psoriatic Arthritis

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Objective. The present study was undertaken to evaluate the safety and efficacy of intravenous (IV) golimumab in patients with active psoriatic arthritis (PsA) through 1 year.

Methods. GO-VIBRANT was a phase III, randomized, placebo-controlled trial of 480 adults with active PsA. Patients were randomized to receive IV placebo (n = 239) or golimumab 2 mg/kg (n = 241) at weeks 0, 4, and every 8 weeks, with placebo crossover to golimumab at weeks 24, 28, and every 8 weeks thereafter. Efficacy through week 52 was assessed using the American College of Rheumatology (ACR) ≥20%, 50%, or 70% improvement criteria (ACR20/50/70), and the Psoriasis Area and Severity Index ≥75% improvement criteria (PASI75). Radiographic progression was measured using the PsA-modified Sharp/van der Heijde score (SHS). Adverse events (AEs) were monitored through week 60.

Results. The primary and major secondary end points through week 24 were achieved. At week 52, 76.8% of patients in the golimumab group and 77.0% in the placebo-crossover group achieved an ACR20 response, 58.1% and 53.6%, respectively, achieved an ACR50 response, and 38.6% and 33.9%, respectively, achieved an ACR70 response. Among patients with ≥3% body surface area affected, 71.9% in the golimumab group and 60.6% in the placebo-crossover group achieved a PASI75 response at week 52. Mean change from baseline in total SHS at week 52 was –0.5 in the golimumab group and 0.8 in the placebo-crossover group. Through week 60, 50.9% of all golimumab-treated patients had ≥1 AE, and 5.2% had ≥1 serious AE. There were no opportunistic infections, 2 malignancies, and 1 death in patients treated with golimumab.

Conclusion. Sustained improvements in joint and skin disease in patients with PsA were maintained through 1 year in the GO-VIBRANT study. No new safety signals for IV golimumab were identified.

INTRODUCTION

Psoriatic arthritis (PsA) is characterized by joint disease affecting either or both the peripheral joints and the axial skeleton along with psoriatic lesions (1). Progression of radiographic joint damage and the presence of enthesitis and dactylitis can lead to decreased physical function and disability. The totality of these symptoms contributes to the significant psychosocial burden of PsA (2).

In the phase III GO-VIBRANT study (A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial of Golimumab, an Anti-TNFα Monoclonal Antibody, Administered Intravenously, in Subjects With Active Psoriatic Arthritis), adult patients with active PsA showed greater improvements in the signs and symptoms of PsA and less radiographic progression through week 24 when receiving intravenous (IV) golimumab compared with those who received placebo (3). Improvements in health-related quality of life (HRQoL) were also greater for patients in the golimumab group

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SIGNIFICANCE & INNOVATIONS

- Intravenous golimumab 2 mg/kg was effective in reducing the signs and symptoms of active psoriatic arthritis in adult patients with a robust response through 1 year of treatment.
- Improvements in health-related quality of life in adult patients treated with intravenous golimumab 2 mg/kg were maintained through 1 year.
- Patients who crossed over from placebo to golimumab 2 mg/kg at week 24 generally achieved efficacy responses similar to those of patients who received golimumab from baseline in this 1-year study.
- The safety profile observed in this study was consistent with the known safety profile of anti–tumor necrosis factor agents, including previous studies of golimumab.

(3). Adverse events (AEs) through week 24 were consistent with the known safety profile of IV golimumab. Efficacy and safety through 1 year are reported herein.

PATIENTS AND METHODS

Patients and study design. Details of the study design and eligibility criteria for patients in the GO-VIBRANT trial have been previously described (3). Briefly, adult patients with a diagnosis of PsA for at least 6 months were eligible for the phase III GO-VIBRANT study. Patients had to have active PsA (≥5 swollen and ≥5 tender joints at screening and baseline and C-reactive protein [CRP] level ≥0.6 mg/dl at screening) despite current or previous therapy with disease-modifying antirheumatic drugs (≥3 months) and/or nonsteroidal antiinflammatory drugs (≥4 weeks) or an intolerance to these therapies. Patients who had been treated previously with biologics were excluded.

Eligible patients were randomly assigned to receive IV infusions of golimumab 2 mg/kg at weeks 0, 4, and every 8 weeks thereafter or placebo at weeks 0, 4, 12, and 20. Randomization was stratified by geographic region and baseline treatment with methotrexate (MTX) (yes/no). At week 16, if patients met the early escape criteria (<5% improvement in swollen and tender joint counts), specific changes in concomitant medications were permitted at the discretion of the investigator. At week 24, all patients in the placebo group crossed over to receive golimumab 2 mg/kg at week 24, week 28, and every 8 weeks thereafter. The final study agent infusion was administered at week 52. Concomitant treatment with stable doses of MTX (≤25 mg/week) was permitted for patients treated with MTX ≥3 months prior to the first golimumab administration. Stable doses of concomitant oral corticosteroids and nonsteroidal antiinflammatory drugs were also permitted.

Assessments. Changes in peripheral arthritis signs and symptoms were assessed using the American College of Rheumatology (ACR) response criteria (4) based on a swollen joint count (66 joints) and a tender joint count (68 joints). Disease activity was also assessed using the Disease Activity Score in 28 joints using the CRP level (DAS28-CRP) criteria for response and remission (5). DAS28-CRP response and remission analyses were prespecified and based on the criteria validated for use in patients with rheumatoid arthritis (5). DAS28-CRP response included good and moderate responses (a good response was defined as a score ≤3.2 with an improvement >1.2 from baseline, and a moderate response was defined as a score >3.2 with an improvement >1.2 from baseline or a score ≤5.1 and an improvement >0.6 to ≤1.2 from baseline). DAS28-CRP remission was defined as a score <2.6. Physical function was evaluated using the Health Assessment Questionnaire disability index (HAQ DI) (6). Enthesitis was evaluated using the Leeds Enthesitis Index (7), which was specifically designed for patients with PsA. Dactylitis was evaluated using a scoring system from 0 to 3 for each digit (0 = no dactylitis, 1 = mild dactylitis, 2 = moderate dactylitis, and 3 = severe dactylitis) (8,9). The proportion of patients with ≥50% improvement in the Bath Ankylosing Spondylitis Disease Activity Index criteria for 50% improvement (BASDAI 50) (10) was determined among patients with investigator-assessed spondylitis with peripheral arthritis. Radiographic progression was measured using the PsA-modified Sharp/van der Heijde score (SHS) (11). Among patients with ≥3% body surface area involvement, the proportions of patients with ≥75%, ≥90%, and 100% improvement in the Psoriasis Area and Severity Index (PASI75/90/100) (12) were also determined through week 52. Changes in psoriatic nail involvement were assessed using the modified Nail Psoriasis Severity Index (mNAPSI) (scale 0–3) (13) among patients with a baseline score >0. HRQoL was evaluated with the Short Form 36 health survey physical component summary (SF-36 PCS) and mental component summary (SF-36 MCS) scores (14). Odds ratios and 95% confidence intervals were calculated using a logistic regression model. As a post hoc analysis, selected efficacy end points of interest were also evaluated in patients who did not achieve an ACR20 response at week 52.

The proportion of patients achieving minimal disease activity (MDA) was determined at week 52. MDA is a composite measure defined as meeting ≥5 of the following 7 criteria: tender joint count ≤1, swollen joint count ≤1, PASI ≤1 or body surface area involvement ≤3%, visual analog scale (VAS) score ≤15 on a patient assessment of pain, VAS score ≤20 on a patient global assessment of disease activity, a HAQ DI score ≤0.5, and ≤1 tender entheseal point (15).

Patients were monitored for AEs through week 60. Serum samples were analyzed for the presence of antibodies to golimumab using a highly sensitive, drug-tolerant, enzyme immunoassay. Immunogenicity analyses included patients who had a baseline sample and at least 1 golimumab infusion and 1 postbaseline sample. Serum samples were also analyzed to measure golimumab concentrations. Pharmacokinetic analyses included all patients who had received at least 1 golimumab infusion and had available serum samples.

Statistical analysis. Efficacy outcomes through week 52 are reported by randomized treatment group and summarized using descriptive statistics (counts and percentages for discrete variables; mean ± SDs for continuous variables). There was no formal hypothesis testing after week 24. Treatment failure rules were not applied to clinical efficacy end points after week 24. Missing data were imputed using the last observation carried forward for continuous variables and for missing components of composite end points. For dichotomous responder-type end points with completely missing components, nonresponder imputation was applied for missing data.

RESULTS

Patients. Detailed patient demographic and disease characteristics have been previously published and were generally well-balanced between the treatment groups (3). A total of 480 patients were randomized to receive placebo (n = 239) or golimumab 2 mg/kg (n = 241) at baseline. Patient disposition through week 24 has been reported in detail (3). Through week 60, 53 patients discontinued the study agent. One patient withdrew from the study before receiving the study agent; 27 patients discontinued study treatment before week 24 and have been previously described (3). After week 24, 8 patients in the placebo-crossover group and 17 patients in the golimumab group discontinued study treatment through week 52 (Figure 1). Reasons for discontinuation from week 24 through week 52 included AEs (n = 14) and withdrawal of consent (n = 4).

Clinical efficacy and patient-reported outcomes. Greater proportions of patients in the golimumab group achieved an ACR20, ACR50, and ACR70 response at weeks 14 and 24 when compared with placebo (3). Following placebo-crossover

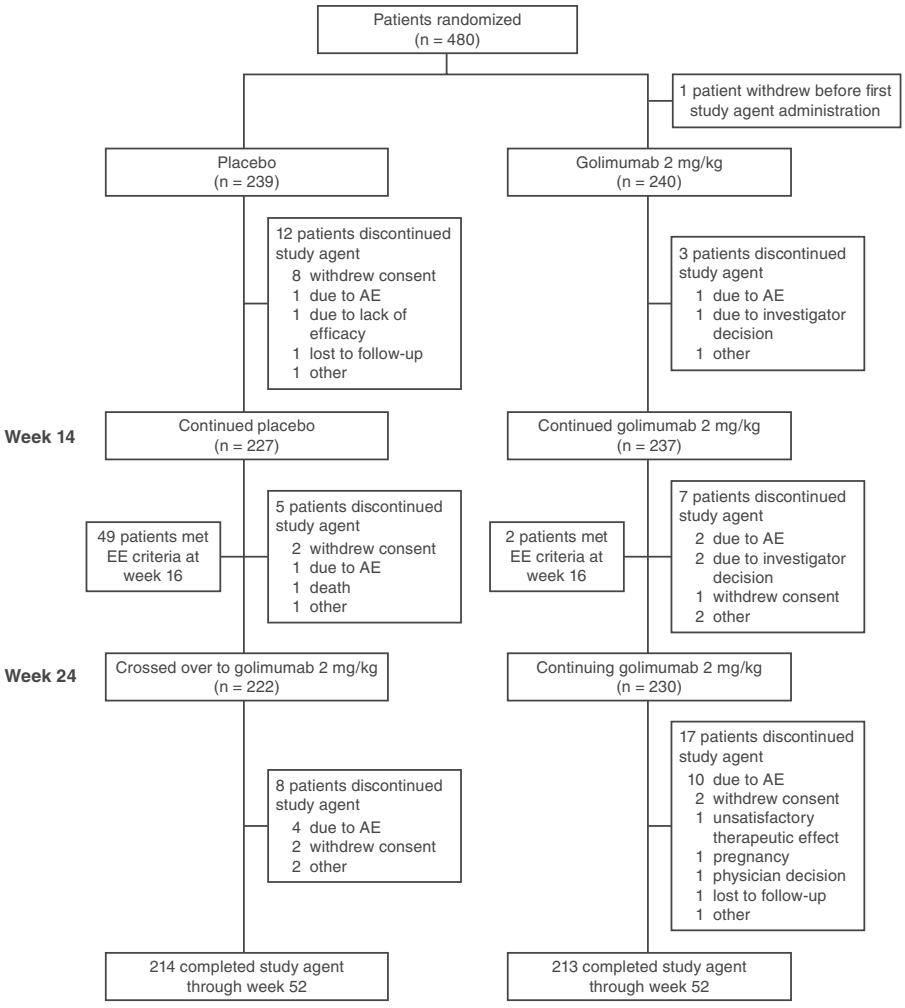

Figure 1. Patient disposition through week 52. AE = adverse event; EE = early escape.

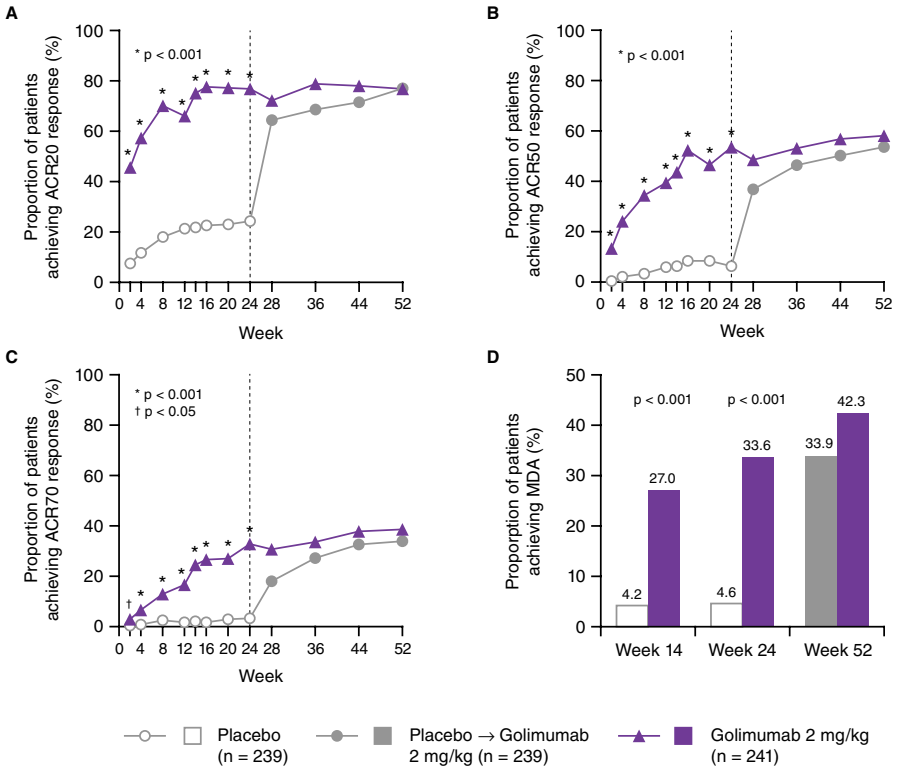

Figure 2. Proportions of patients achieving an ACR20 response (**A**), ACR50 response (**B**), ACR70 response (**C**), and minimal disease activity (MDA) (**D**) through week 52. ACR 20/50/70 = American College of Rheumatology 20%, 50%, and 70% improvement criteria. The broken line indicates the time of placebo crossover to golimumab.

to golimumab at week 24, the proportions of ACR responders in the placebo-crossover group approached those in the golimumab group at week 28. ACR response rates were maintained through week 52 in both groups (Figure 2). Similar to results through week 24, there was no meaningful difference between the treatment groups in the proportions of patients achieving an ACR20, ACR50, and ACR70 response who did and did not receive concomitant MTX at baseline (Table 1). Among patients in the golimumab group who achieved an ACR20, ACR50, or ACR70 response at week 24, 87.6% (162 of 185), 79.1% (102 of 129), and 74.7% (59 of 79), respectively, maintained this response at week 52. At week 52, 42.3% and 33.9% of patients in the golimumab group and the placebo-crossover group, respectively, achieved MDA.

Patients randomized to golimumab had greater mean improvements in the DAS28-CRP score compared with the placebo group at weeks 14 (–2.3 versus –0.6) and 24 (–2.5 versus –0.7). At week 52, the mean improvement in the placebo-crossover group (–2.4) was similar to that in the golimumab group (–2.6). Additionally, greater proportions of patients in the golimumab group achieved a DAS28-CRP response (92.5% versus 40.2%; $P < 0.001$) and remission (score <2.6, 36.5% versus 4.6%; $P < 0.001$) at week 14 and week 24 (92.9% versus 39.7%; $P < 0.001$ and 41.9% versus 7.1%; $P < 0.001$, respectively). DAS28-CRP response and remission rates were maintained at week 52 in the golimumab group, with the placebo-crossover group having similar response rates (Table 1).

Among patients with dactylitis or enthesitis at baseline, the mean changes from baseline in dactylitis and enthesitis scores, respectively, were similar in the 2 treatment groups at week 52, when all patients had been receiving golimumab (Table 1). Greater proportions of patients in the golimumab group had resolution of dactylitis at week 14 (74.6% versus 25.0%) and week 24 (78.4% versus 35.5%) and resolution of enthesitis at week 14 (47.6% versus 22.1%) and week 24 (60.5% versus 29.8%). The proportions of patients with resolution of dactylitis or enthesitis were maintained at week 52 in the golimumab group, with similar results in the placebo-crossover group (Table 1).

Among patients with physician-reported spondylitis with peripheral arthritis at baseline, 54.1% of patients in the golimumab group and 40.4% of patients in the placebo-crossover group had a BASDAI 50 response at week 52, and 37.7% and 24.6%, respectively, had a BASDAI 70 response.

Among patients with ≥3% body surface area affected at baseline, 71.9% in the golimumab group and 60.6% of patients in the placebo-crossover group had a PASI75 response at week 52 (Table 1); 56.1% and 41.9%, respectively, had a PASI90 response, and 28.6% and 18.7%, respectively, had a PASI100 response. Additionally, 58.2% of patients in the golimumab group and 52.5% in the placebo-crossover group had both a PASI75 response and an ACR20 response at week 52. Among patients with fin-

Table 1. Clinical efficacy and health-related quality of life at week 52*

	Placebo to golimumab 2 mg/kg	Golimumab 2 mg/kg
Patients, no.	239	241
ACR20	184 (77.0)	185 (76.8)
MTX at baseline		
Yes	133 (76.9)	127 (77.9)
No	51 (77.3)	58 (74.4)
ACR50	128 (53.6)	140 (58.1)
MTX at baseline		
Yes	90 (52.0)	94 (57.7)
No	38 (57.6)	46 (59.0)
ACR70	81 (33.9)	93 (38.6)
MTX at baseline		
Yes	53 (30.6)	61 (37.4)
No	28 (42.4)	32 (41.0)
DAS28-CRP response	206 (86.2)	224 (92.9)
DAS28-CRP remission	98 (41.0)	117 (48.5)
Patients with spondylitis with peripheral joint involvement, no.	57	61
BASDAI 20	37 (64.9)	44 (72.1)
BASDAI 50	23 (40.4)	33 (54.1)
BASDAI 70	14 (24.6)	23 (37.7)
Patients with ≥3% BSA with psoriasis involvement at baseline, no.	198	196
PASI75	120 (60.6)	141 (71.9)
PASI90	83 (41.9)	110 (56.1)
PASI100	37 (18.7)	56 (28.6)
Change from baseline in HAQ DI		
No.	236	237
Mean ± SD	−0.56 ± 0.55	−0.66 ± 0.63
Change from baseline in CRP		
No.	239	241
Mean ± SD	−1.2 ± 2.1	−1.1 ± 3.1
Patients with enthesitis at baseline, no.	181	185
Change from baseline in enthesitis score		
Mean ± SD	−2.2 ± 1.9	−2.1 ± 1.7
Patients with enthesitis score of 0 at week 52	115 (63.5)	117 (63.2)
Patients with dactylitis at baseline, no.	124	134
Change from baseline in dactylitis score		
Mean ± SD	−8.9 ± 10.1	−8.0 ± 8.9
Patients with dactylitis score of 0 at week 52	96 (77.4)	109 (81.3)
Health-related quality of life		
Change from baseline in SF-36 PCS score		
No.	236	237
Mean ± SD	9.0 ± 8.2	10.6 ± 8.9
Change from baseline in SF-36 MCS score		
No.	236	237
Mean ± SD	3.8 ± 9.5	5.4 ± 10.8

* Values are the number (%) unless indicated otherwise. ACR 20/50/70 = American College of Rheumatology 20%, 50%, and 70% improvement criteria; MTX = methotrexate; DAS28-CRP = Disease Activity Score in 28 joints using the C-reactive protein (CRP) level; BASDAI 20/50/70 = Bath Ankylosing Spondylitis Disease Activity Index 20%, 50%, and 70% improvement criteria; BSA = body surface area; PASI 75/90/100 = Psoriasis Area and Severity Index 75%, 90%, and 100% improvement criteria; HAQ DI = Health Assessment Questionnaire disability index; SF-36 PCS/MCS = Short Form 36 health survey physical/mental component summary.

gernail involvement at baseline (mNAPSI score >0), the mean improvement from baseline in mNAPSI score was greater in the golimumab group than in the placebo group at week 24 (−11.4 versus −3.7; $P < 0.001$). At week 52, the mean improvement from baseline in mNAPSI score was similar in both treatment groups (golimumab, −12.1; placebo-crossover, −12.9).

A total of 111 patients (placebo-crossover, n = 56; golimumab, n = 55) were ACR20 nonresponders at week 52. Among these patients, 40.0% in the placebo-crossover group and 76.8% in the golimumab group had achieved an ACR20 response at an earlier time point. Although these patients did not demonstrate a high level of clinical efficacy as defined by ACR response, there was some evidence of a positive clinical response in this group of patients. For example, 33.3% and 58.7%, respectively, achieved a PASI75 response, and 18.8% and 37.0% achieved a PASI90 response at week 52 (see Supplementary Table 1, available on the *Arthritis Care & Research* web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.23905/abstract).

Table 2. Radiographic results at week 52*

	Placebo to golimumab 2 mg/kg	Golimumab 2 mg/kg
Change from baseline in total SHS score	0.8 ± 3.0	−0.5 ± 2.5
Change from baseline in erosion score	0.5 ± 2.3	−0.5 ± 2.0
Change from baseline in joint space narrowing score	0.2 ± 1.1	−0.04 ± 0.9
Patients with a change from baseline in total SHS score ≤0, no. (%)	129 (54.4)	170 (71.7)
Patients with a change from baseline in total SHS score >SDC, no. (%)	37 (15.6)	13 (5.5)

* Values are the mean ± SD unless indicated otherwise. Smallest detectable change (SDC) = 2.42. SHS = psoriatic arthritis–modified Sharp/van der Heijde score.

HRQoL. Through week 24, patients in the golimumab group had greater mean improvements in HRQoL compared with patients in the placebo group (3). Mean changes in SF-36 PCS and MCS scores were maintained in the golimumab group at week 52 (Table 1). Mean changes in the placebo-crossover group at week 52 were similar to those observed in the golimumab group after all patients had been receiving golimumab after week 24.

Radiographic progression. At week 24, the mean change in the total SHS was –0.4 in the golimumab group and 2.0 in the placebo group (3). At week 52, the mean change from baseline in the golimumab group was –0.5 and 0.8 in the placebo-crossover group (Table 2). At week 52, 54.4% of patients in the placebo-crossover group and 71.7% of patients in the golimumab group showed a change from baseline in total SHS of ≤0.

AEs. Through week 60, 50.9% of all patients who had received golimumab (including placebo-crossover patients) experienced ≥1 AE (Table 3). Infections were the most common type of AE, occurring in 22.8% of all golimumab-treated patients. Ten patients (2.2%) had a total of 11 serious infections while receiving golimumab: pneumonia and empyema in 1 patient, pneumonia in 2 additional patients, pulmonary tuberculosis (TB) in 2 patients, and singular events of infected dermal cyst, acute pyelonephritis, periodontitis, urinary tract infection, and acute hepatitis of mixed etiology (Epstein-Barr virus–associated and autoimmune). Both cases of active TB occurred in patients who had screened negative for latent TB and had a negative QuantiFERON-TB Gold test prior to entering the study; 1 patient lived in Ukraine and the other in Lithuania. There were no opportunistic infections during the study. One demyelinating event, noninfectious encephalitis, occurred prior to week 24 (3). A total of 24 golimumab-treated patients (5.2%) had a serious AE (SAE) through week 60. With the exception of pneumonia and pulmonary TB, SAEs were singular events.

Two patients were diagnosed with a malignancy prior to week 24, both in the placebo group (3), and 2 patients were diagnosed with a malignancy after week 24 (gastric cancer in the placebo-crossover group and colon cancer in the golimumab group). There were 3 deaths in this study; 2 occurred through week 24 in the placebo group (acute cardiovascular failure and cardiorespiratory insufficiency due to metastasis) (3), and 1 death occurred after week 24 in the golimumab group and was a result of the acute hepatitis of mixed etiology.

A total of 3,122 golimumab infusions were administered through week 52; 4 golimumab-treated patients (0.9%) had infusion reactions. Two reactions occurred prior to week 24 (3), and 2 (fatigue and throat irritation) occurred after week 24. None of the infusion reactions were considered by the investigator to be serious or severe.

At baseline, 204 patients (85.4%) in the placebo group and 209 patients (87.1%) in the golimumab group had an alanine aminotransferase (ALT) level of less than or equal to the upper limit of normal (ULN). Among these patients, 20.6% (42 of 204) and 31.6% (66 of 209), respectively, had a postbaseline ALT level

Table 3. Adverse events (AEs) through week 60*

	Weeks 0–24 Placebo	Weeks 24–60 Placebo to golimumab 2 mg/kg	Weeks 0–60	
			Golimumab 2 mg/kg	All golimumab 2 mg/kg†
Patients, no.	239	220	240	460
Mean duration of follow-up, no. weeks	23.2	36.1	57.4	47.2
Patients who discontinued due to an AE	3 (1.3)	3 (1.4)	14 (5.8)	17 (3.7)
Patients with ≥1 AE	97 (40.6)	90 (40.9)	144 (60.0)	234 (50.9)
Patients with ≥1 infection	37 (15.5)	38 (17.3)	67 (27.9)	105 (22.8)
Tuberculosis	0	0	2 (0.8)	2 (0.4)
Opportunistic infections	0	0	0	0
Demyelinating events	0	0	1 (0.4)	1 (0.2)
Patients with ≥1 infusion reaction	0	2 (0.9)	2 (0.8)	4 (0.9)
Patients with ≥1 SAE	8 (3.3)	5 (2.3)	19 (7.9)	24 (5.2)
Serious infections	2 (0.8)	3 (1.4)	7 (2.9)	10 (2.2)
Malignancies	2 (0.8)	1 (0.5)	1 (0.4)	2 (0.4)
Deaths	2 (0.8)	0	1 (0.4)	1 (0.2)

* Values are the number (%) unless indicated otherwise. SAE = serious adverse event.
† Includes all patients who received at least 1 administration of golimumab.

of more than the ULN through week 24. Through week 60, a total of 401 golimumab-treated patients had a baseline ALT less than or equal to the ULN; among these, 157 (39.1%) had maximum postbaseline ALT levels above the ULN. Most of those patients (n = 146, 93%) had elevations <3 times the ULN, 9 (6%) had elevations ≥3 to <5 times the ULN, and 2 patients (1%) had a postbaseline ALT level ≥5 to <8 times the ULN; both had normal bilirubin levels throughout the study. No golimumab-treated patient had an ALT level ≥8 times the ULN through week 60.

A total of 36 golimumab-treated patients received TB prophylaxis. Of these, 34 had normal ALT levels at baseline, with 19 having postbaseline elevations. Fourteen of these patients had a maximum ALT level <2 times the ULN, 3 patients had a maximum ALT level ≥2 to <3 times the ULN, and 2 patients had a maximum ALT level ≥3 to <5 times the ULN. The 2 patients who had an elevated ALT level at baseline and received TB prophylaxis had a maximum postbaseline ALT level <2 times the ULN.

Three patients discontinued golimumab due to an AE of elevated ALT level. One patient with an ALT level ≥5 to <8 times the ULN was diagnosed with steatohepatitis, and golimumab treatment was discontinued after the week-24 infusion. Another patient who discontinued the study agent due to an elevated ALT level received golimumab at weeks 0, 4, 12, and 20, followed by placebo at week 24. The patient was then diagnosed with acute hepatitis of mixed etiology (fatal outcome, described earlier) with an ALT level ≥3 to <5 times the ULN, and study treatment was discontinued. A third patient had slightly elevated baseline ALT levels (>1 to <2 times the ULN) and a postbaseline maximum ALT level ≥5 to <8 times the ULN. This patient was diagnosed with MTX-induced toxic hepatitis before week 24 (3) and was later diagnosed with chronic hepatitis at week 42, after which golimumab therapy was discontinued.

Pharmacokinetics and immunogenicity. Trough serum golimumab concentrations reached steady state by approximately week 12 and were maintained through week 52 (median 0.61 μg/ml). Among patients with available serum samples after the first study of golimumab administration, 22% tested positive for antibodies to golimumab through week 52 (n = 46 of 220, 21% in the placebo-crossover group; n = 53 of 230, 23% in the golimumab group). The incidence of antibodies to golimumab was higher in patients without baseline treatment with MTX (n = 39 of 134, 29%) compared to those with baseline treatment with MTX (n = 60 of 316, 19%); however, there was no difference in the incidence of neutralizing antibodies (35.9% and 36.7% of those with antibodies, respectively).

At week 52, an ACR20, ACR50, or ACR70 response was achieved by 86.3%, 64.5%, and 41.7%, respectively, of all golimumab-treated patients who tested negative for antibodies to golimumab (n = 351) and by 81.1%, 51.1%, and 28.9%, respectively, of golimumab-treated patients who tested positive for antibodies to golimumab (n = 99). The ACR20 response rates were consistent across peak titer groups, while ACR50 and ACR70 responses tended to be similar in patients who tested negative for antibodies to golimumab and in patients who were positive for antibodies in the lower peak titer groups (e.g., <1:10). Patients with higher titers tended to have lower ACR50 and ACR70 response rates. However, the relatively small number of patients in each titer group limits the interpretation of these results.

Among the 351 patients who tested negative for antibodies to golimumab, 1 (0.3%) had an infusion reaction (throat irritation) through week 52. Of the 99 patients who tested positive for antibodies to golimumab, 3 (3.0%) had an infusion reaction through week 52; these were headache, fatigue, and infusion-related reaction (1 patient each). The event of infusion-related reaction resulted in the discontinuation of the study agent (3).

DISCUSSION

In the GO-VIBRANT study, patients in the golimumab group had greater improvements in joint and skin disease and HRQoL on average through week 24 when compared with placebo (3). ACR response rates for placebo patients who crossed over to golimumab at week 24 were similar to those in the golimumab group after week 36. In the golimumab group, clinical efficacy and improvements in HRQoL were maintained at week 52. Overall, the proportions of patients achieving ACR, BASDAI, and PASI responses were similar between the treatment groups at week 52, when all patients had been receiving golimumab for several months. ACR response rates were similar between patients who were receiving concomitant MTX and those who received golimumab monotherapy.

An exploratory analysis was performed to evaluate various clinical efficacy and HRQoL outcomes in patients who were ACR20 nonresponders at week 52. Although these patients did not meet the ACR20 response criteria, they often demonstrated improvements in skin disease and enthesitis and dactylitis. These factors may have contributed to these patients remaining in the trial and continuing golimumab therapy despite not achieving an ACR20 response.

Through week 24, the mean change in total PsA-modified SHS score was significantly greater for patients in the placebo group (2.0) compared with those in the golimumab group (–0.4). Patients in the golimumab group continued to demonstrate minimal radiographic progression at week 52, with a mean change from baseline of –0.5. Patients in the placebo group who crossed over to golimumab at week 24 appeared to have less radiographic progression after initiating golimumab therapy at week 24 than they did during the placebo period, with a mean change from baseline to week 52 of 0.8.

Patients receiving concomitant MTX had a lower incidence of antibodies to golimumab than patients receiving golimumab monotherapy, which is consistent with previous studies of other anti–tumor necrosis factor (anti-TNF) agents in patients with PsA (16). ACR20, ACR50, and ACR70 response rates tended to be higher for patients who tested negative to antibodies to golimumab compared with those who tested positive. Among patients who were positive for antibodies to golimumab, ACR20 response rates were generally consistent across titers. ACR50 and ACR70 response rates tended

to be lower with increasing titers; however, the small number of patients in each titer group limited the interpretation of these results, and the presence of antibodies to golimumab did not preclude clinical response.

The safety profile of IV golimumab 2 mg/kg in the GO-VIBRANT study was consistent with that observed with other anti-TNF therapies, including previous trials of patients who received either subcutaneous golimumab or IV golimumab. Through week 60, infections were the most common type of AE, occurring in 22.8% of all patients who received at least 1 golimumab administration. Few infusion reactions occurred, and none were serious or severe. There were no opportunistic infections, anaphylactic reactions, or serum sickness reactions. Among golimumab-treated patients, 2 malignancies (gastric cancer and colon cancer) and 1 death occurred (acute hepatitis). Among patients with a baseline ALT less than or equal to the ULN, 20.6% in the placebo group and 31.6% in the golimumab group had a postbaseline ALT level greater than the ULN through week 24. Through week 60, among 401 golimumab-treated patients with a baseline ALT level less than or equal to ULN, 39.1% had a postbaseline ALT level above the ULN; most cases were mild and transient. Three patients discontinued study treatment due to an AE of elevated ALT level. It should be noted that a majority of patients (70%) were receiving concomitant MTX (3). Elevated transaminases are a common occurrence with MTX treatment (17), which makes it difficult to distinguish the effects of golimumab on ALT levels in this population.

Four golimumab-treated patients experienced an infusion reaction. Three of these patients tested positive for antibodies to golimumab, with 1 discontinuing study treatment as a result of an infusion-related reaction. The vast majority of the 99 patients who tested positive for antibodies to golimumab did not experience an infusion reaction.

The GO-VIBRANT study was not powered to detect rare safety events, and follow-up was limited to ~1 year. However, the totality of the results through 1 year of the GO-VIBRANT study shows a durable response to IV golimumab 2 mg/kg across several clinical efficacy, HRQoL, and radiographic end points with no new safety signals.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Hsia had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Husni, Kavanaugh, Harrison, Kim, Lo, Leu, Hsia.

Acquisition of data. Kavanaugh, Murphy, Rekalov, Harrison, Lo, Hsia.

Analysis and interpretation of data. Husni, Kavanaugh, Murphy, Rekalov, Harrison, Kim, Lo, Leu, Hsia.

ROLE OF THE STUDY SPONSOR

Employees of the study sponsor participated in study design, data collection, analysis and interpretation of the data, and writing the manuscript. All authors approved the manuscript for submission. Publication of this article was not contingent upon approval by Janssen Research & Development. Rebecca Clemente, PhD, of Janssen Scientific Affairs provided writing support, and Stephen Xu, MS, of Janssen Research & Development provided statistical support.

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