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

Results Through Week Twenty-Four of the GO-VIBRANT Study

Arthur Kavanaugh,[1] M. Elaine Husni,[2] Diane D. Harrison,[3] Lilianne Kim,[3] Kim Hung Lo,[3] Jocelyn H. Leu,[3] and Elizabeth C. Hsia[4]

Objective. **To evaluate the safety and efficacy of intravenous (IV) golimumab treatment in psoriatic arthritis (PsA).**

Methods. **In this phase III, randomized, double-blind, placebo-controlled trial, patients were randomly assigned to receive IV placebo (n = 239) or golimumab at 2 mg/kg (n = 241) at weeks 0, 4, 12, and 20. The primary end point was the proportion of patients meeting the American College of Rheumatology 20% improvement criteria (achieving an ACR20 response) at week 14. Controlled secondary end points included change from baseline in Health Assessment Questionnaire disability index (HAQ DI) score at week 14, proportions of patients with ACR50 and ACR70 responses and ≥75% improvement on the Psoriasis Area and Severity Index (a PASI75 response) at week 14, and change from baseline at week 24 in the total modified Sharp/van der Heijde score (SHS) with modifications for patients with PsA.**

Results. **At week 14, an ACR20 response was achieved by 75.1% of patients in the golimumab group compared with 21.8% of patients in the placebo group ($P < 0.001$). Greater proportions of golimumab-treated patients had an ACR50 response (43.6% versus 6.3%), an ACR70 response (24.5% versus 2.1%), and a PASI75 response (59.2% versus 13.6%) at week 14 ($P < 0.001$ for all). Patients in the golimumab group had greater mean changes at week 14 in HAQ DI score (–0.60 versus –0.12; $P < 0.001$). At week 24, the mean change in total PsA-modified SHS was –0.4 in the golimumab group and 2.0 in the placebo group ($P < 0.001$). Through week 24, 40.6% of patients in the placebo group and 46.3% of patients in the golimumab group had ≥1 adverse event (AE); infections were the most common type.**

Conclusion. **Patients receiving IV golimumab at 2 mg/kg had significantly greater improvements in the signs and symptoms of PsA and less radiographic progression through week 24. AEs were consistent with those seen with other anti–tumor necrosis factor agents.**

Psoriatic arthritis (PsA) can be characterized by peripheral arthritis, axial arthritis/spondylitis, enthesitis, dactylitis, and skin and nail psoriasis. The introduction of anti–tumor necrosis factor (anti-TNF) therapies greatly improved clinical, radiographic, and quality-of-life outcomes for patients with moderate-to-severe PsA compared with earlier conventional therapies (1). Current treatment recommendations for PsA generally advise treatment with biologic therapies, including anti-TNF agents, for patients with active disease despite conventional therapy, such as disease-modifying antirheumatic

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[1]Arthur Kavanaugh, MD: University of California at San Diego, La Jolla, California; [2]M. Elaine Husni, MD, MPH: Cleveland Clinic, Cleveland, Ohio; [3]Diane D. Harrison, MD, MPH, Lilianne Kim, PhD, Kim Hung Lo, PhD, Jocelyn H. Leu, PharmD, PhD: Janssen Research & Development, LLC, Spring House, Pennsylvania; [4]Elizabeth C. Hsia, MD, MSCE: Janssen Research & Development, LLC, Spring House, Pennsylvania, and University of Pennsylvania, Philadelphia.
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Address correspondence to Elizabeth C. Hsia, MD, MSCE, Janssen Research & Development, LLC, 1400 McKean Road, PO Box 776, Spring House, PA 19477. E-mail: ehsia@its.jnj.com.
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drugs (DMARDs) and nonsteroidal antiinflammatory drugs (NSAIDs) (2–4).

In the GO-REVEAL trial, patients with PsA had significantly greater improvements in the signs and symptoms of PsA compared with placebo when treated with subcutaneous (SC) golimumab (5). Of note, golimumab is available as both SC and intravenous (IV) formulations. SC golimumab is approved for adults with PsA, rheumatoid arthritis (RA), and ankylosing spondylitis (6). IV golimumab is currently approved for patients with RA in a number of countries worldwide (7). In the Multinational Assessment of Psoriasis and Psoriatic Arthritis Survey, 26% of patients who had received biologic therapy expressed that they had experienced fear, anxiety, or inconvenience related to SC injections (8). Given the various biologic therapies available for patients with moderate-to-severe PsA, patient preference regarding mode and frequency of administration is an important factor to consider as part of shared decision-making when designing a treatment plan (4). The GO-VIBRANT study was performed to evaluate the safety and efficacy of IV golimumab in patients with active PsA. This report describes the results through week 24 of the GO-VIBRANT study. A list of investigators who randomized patients in the GO-VIBRANT trial is provided in Appendix A.

PATIENTS AND METHODS

Patients. Patients age ≥18 years were eligible for inclusion in the GO-VIBRANT study if they were diagnosed as having PsA for ≥6 months and met Classification Criteria for Psoriatic Arthritis (9) at screening. Patients had to have active PsA (defined as ≥5 of 66 swollen joints and ≥5 of 68 tender joints at screening and baseline and a high-sensitivity C-reactive protein [CRP] level of ≥0.6 mg/dl at screening) despite current or previous DMARD therapy (≥3 months) and/or NSAID therapy (≥4 weeks) or demonstrate intolerance to these agents.

Previous biologic therapy for PsA was not permitted. Concomitant use of methotrexate (MTX) (≤25 mg/week) was permitted for patients who had been receiving MTX for ≥3 months before the first golimumab administration; MTX doses had to have remained stable for ≥4 weeks. Patients could receive concomitant oral corticosteroids if they had been receiving a stable dose (≤10 mg prednisone/day) for ≥2 weeks prior to the first golimumab administration. Patients were also permitted to receive concomitant NSAIDs at the usual approved marketed doses if they had received stable doses for ≥2 weeks prior to the first golimumab administration.

Patients were randomly assigned to treatment groups by stratified block randomization using an interactive web response system. Randomization was stratified by geographic region and baseline MTX use (yes or no). Patients and investigators were blinded with regard to treatment group assignment for the duration of the study.

Study design. GO-VIBRANT is a phase III, multicenter, randomized, placebo-controlled trial. Eligible patients were randomized to receive IV infusions of placebo or golimumab at 2 mg/kg at weeks 0 and 4 and every 8 weeks. Infusions were administered during a period of 30 ± 10 minutes. At week 16, patients in both treatment groups with <5% improvement in swollen and tender joint counts entered early escape and were allowed one of the following changes in treatment at the investigator's discretion: an increase in corticosteroid dose (total dose ≤10 mg/day prednisone or equivalent), MTX dose (total dose ≤25 mg/week), or NSAID dose; or initiation of NSAIDs, corticosteroids (≤10 mg/day prednisone or equivalent), MTX (≤25 mg/week), sulfasalazine (≤3 gm/day), hydroxychloroquine (≤400 mg/day), or leflunomide (≤20 mg/day).

Assessments. The activity of peripheral arthritis was primarily evaluated using the American College of Rheumatology (ACR) criteria for improvement in RA (10). Physical function was evaluated using the Health Assessment Questionnaire disability index (HAQ DI) (11). Enthesitis was assessed with the Leeds Enthesitis Index (12), which was developed for patients with PsA and evaluates the presence or absence of tenderness in the following entheses (left and right): lateral elbow epicondyle, medial femoral condyle, and Achilles tendon insertion. The presence and severity of dactylitis was assessed in both hands and feet using a scoring system from 0 to 3 (0 = no dactylitis, 1 = mild dactylitis, 2 = moderate dactylitis, and 3 = severe dactylitis). For patients with investigator-assessed spondylitis with peripheral arthritis of PsA (n = 118), spondylitis was also assessed using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) (13). Skin response was evaluated using the Psoriasis Area and Severity Index (PASI), which ranges from 0 to 72 with higher scores indicating more severe disease, among patients with ≥3% body surface area involvement at baseline (14).

Health-related quality of life (HRQoL) was evaluated using the Short Form 36 health survey (SF-36) physical component summary (PCS) and mental component summary (MCS) scores (15). Minimal disease activity (MDA) was also evaluated as a composite measure with patients classified as achieving MDA if they met 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 of ≤15 on patient's assessment of pain; VAS score of ≤20 on patient's global assessment of disease activity; HAQ DI score of ≤0.5; and ≤1 tender entheseal point (16).

Radiographs were obtained at weeks 0 and 24 and were read by 2 independent assessors who were blinded with regard to treatment group and time point. Patients who entered early escape also had radiographs at week 16. Changes in radiographic damage were measured using the modified Sharp/van der Heijde score (SHS) with modifications for patients with PsA (i.e., inclusion of distal interphalangeal joints in the hands and pencil-in-cup/gross osteolysis deformities) (17).

Patients were monitored throughout the study, including routine laboratory assessments, for adverse events (AEs). Serum golimumab concentrations were recorded at prespecified time points through week 20. The presence of antibodies to golimumab was assessed through week 20 using a recently developed, highly sensitive, drug-tolerant enzyme immunoassay method in patients who received at least 1 administration

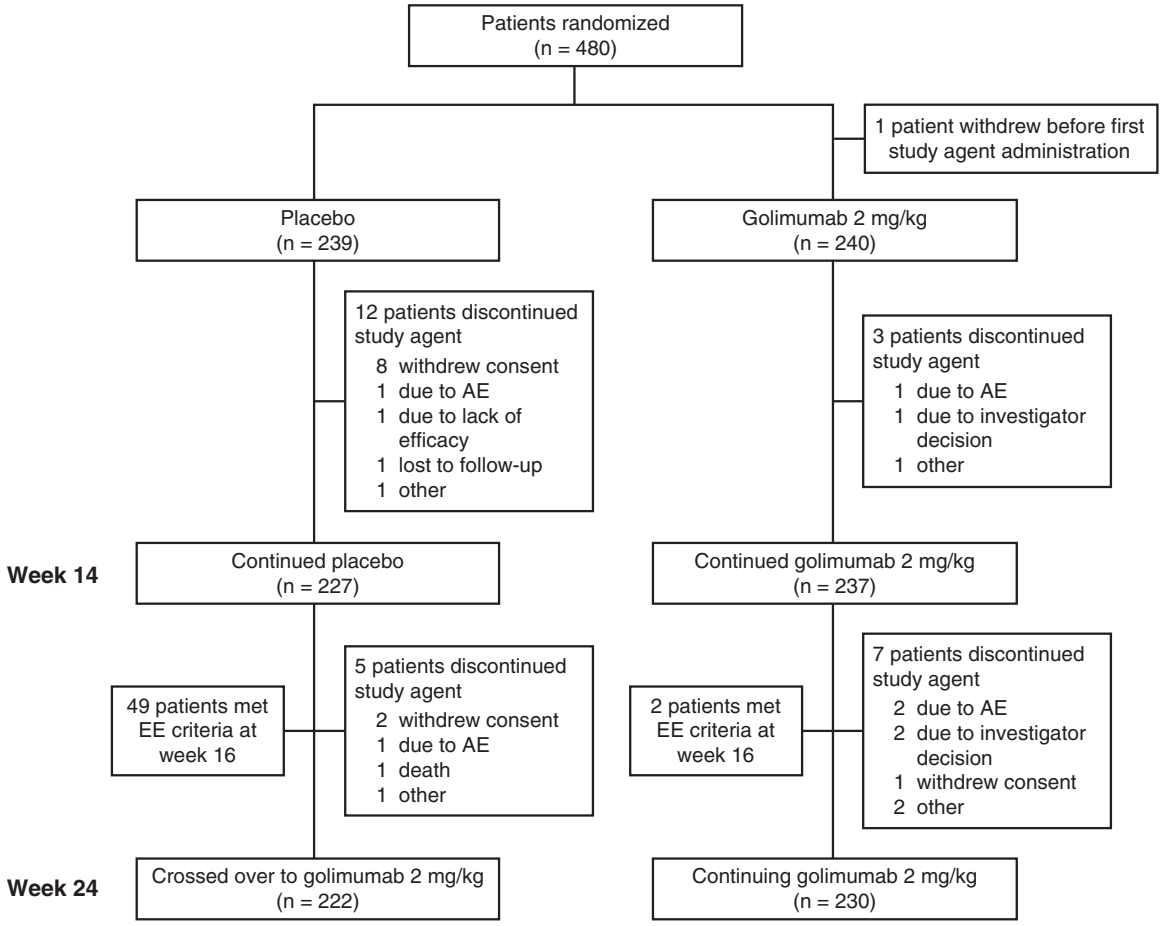

Figure 1. Patient disposition through week 24. AE = adverse event; EE = early escape.

of golimumab and had at least 1 postadministration sample available.

Statistical analysis. The primary end point was the proportion of patients meeting the ACR 20% improvement criteria (achieving an ACR20 response) (10) at week 14. Major secondary end points were the change from baseline in HAQ DI score at week 14, the proportion of patients with an ACR50 response at week 14, the proportion of patients with a ≥75% reduction in PASI scores (a PASI75 response) at week 14, and the change from baseline in total PsA-modified SHS at week 24. To control for multiplicity, the major secondary end points were tested sequentially (according to the order listed above) only if the primary end point achieved statistical significance. Other controlled end points were change from baseline in enthesitis score at week 14, change from baseline in dactylitis score at week 14, change from baseline in SF-36 PCS score at week 14, proportion of patients with an ACR50 response at week 24, proportion of patients with an ACR70 response at week 14, and change from baseline in SF-36 MCS score at week 14. Changes in enthesitis and dactylitis were evaluated among patients with these findings at baseline. These end points were tested sequentially in the order listed only if the primary and major secondary end points achieved statistical significance. For other efficacy analyses, nominal *P* values were provided for selected end points.

Efficacy data were analyzed by randomized treatment group (intent-to-treat analysis). For the primary end point analysis (proportion of patients achieving an ACR20 response) and all other composite end points, missing data for components were imputed using last observation carried forward methodology, and patients with missing data for all components at week 14 were classified as nonresponders. For signs and symptoms end points, patients were classified as nonresponders (treatment failure) if they discontinued study treatment due to lack of efficacy, initiated prohibited therapies or had an increase in dose of MTX or oral corticosteroids (other than early escape treatment), or met the early escape criteria and initiated or increased concomitant medications.

The change in total PsA-modified SHS was evaluated for randomized patients who had a baseline total PsA-modified SHS. Multiple imputations (18), using data from patients who had data at both week 0 and week 24, were used to impute week 24 radiograph scores for missing data and/or early escape. A linear regression model with baseline score, ln(CRP + 1), and MTX usage as covariates was used to generate missing data. Comparisons were made using a *t*-test from the aggregated data.

All statistical tests were performed at an alpha level of 0.05 (2-sided). Differences between treatment groups were tested using the Cochran-Mantel-Haenszel test for dichotomous end points and mixed-effects model repeated-measures methodology using observed data for continuous variables. For the primary end point, it was estimated that 220 patients in each treatment group would ensure 99% power to detect a significant difference between the groups, assuming a 20% ACR20 response rate in the placebo group and a 40% ACR20 response rate in the golimumab group at a 2-sided significance level of 0.05 (using a chi-square test). In addition, for the radiographic end point, it was estimated that 220 patients in each group would provide 90.7% power to detect a significant difference in the mean change in total PsA-modified SHS between treatment groups.

RESULTS

Patient disposition and baseline characteristics. Data for this report were collected from September 2014 to July 2016 at 90 sites in 11 countries (Belarus, Canada, Germany, Hungary, Lithuania, Poland, Romania, Russia,

Table 1. Baseline demographic and disease characteristics of the patients*

	Placebo (n = 239)	Golimumab 2 mg/kg (n = 241)
Age, years	46.7 ± 12.5	45.7 ± 11.3
Men, no. (%)	121 (50.6)	128 (53.1)
Duration of PsA, years	5.3 ± 5.9	6.2 ± 6.0
PsA subtype, no. (%)		
DIP joint involvement	21 (8.8)	18 (7.5)
Arthritis mutilans	13 (5.4)	10 (4.1)
Asymmetric peripheral arthritis	40 (16.7)	49 (20.3)
Polyarticular arthritis with absence of rheumatoid nodules	108 (45.2)	103 (42.7)
Spondylitis with peripheral arthritis	57 (23.8)	61 (25.3)
ACR core set of disease activity measures		
Swollen joint count, 0–66	14.1 ± 8.2	14.0 ± 8.4
Tender joint count, 0–68	26.1 ± 14.4	25.1 ± 13.8
Patient's assessment of pain, 0–10-cm VAS	6.4 ± 2.1	6.3 ± 2.0
Patient's global assessment of disease activity, 0–10-cm VAS	6.3 ± 2.1	6.5 ± 1.9
Physician's global assessment of disease activity, 0–10-cm VAS	6.4 ± 1.6	6.2 ± 1.7
HAQ DI score, 0–3	1.3 ± 0.6	1.3 ± 0.6
CRP, mg/dl	2.0 ± 2.0	1.9 ± 2.5
BASDAI		
No. of patients tested†	53	56
BASDAI score, 0–10 cm	6.4 ± 1.9	6.5 ± 1.8
Patients with dactylitis in ≥1 digit, no. (%)	124 (51.9)	134 (55.6)
Dactylitis score, 0–60	9.9 ± 10.1	9.3 ± 9.4
Patients with enthesitis, no. (%)	181 (75.7)	185 (76.8)
Enthesitis score, 0–6	3.2 ± 1.6	3.0 ± 1.6
Total PsA-modified SHS, 0–528	34.5 ± 53.5	35.5 ± 55.2
Patients with ≥3% body surface area involvement with psoriasis, no. (%)	198 (82.8)	196 (81.3)
PASI, 0–72	8.9 ± 9.0	11.0 ± 9.9
SF-36 PCS score, 0–100	34.0 ± 7.2	33.1 ± 6.9
SF-36 MCS score, 0–100	42.5 ± 10.2	43.5 ± 11.4
Concomitant medications		
MTX		
Patients, no. (%)	173 (72.4)	163 (67.6)
Dose, mg/week	14.9 ± 4.8	14.8 ± 4.7
Oral corticosteroids		
Patients, no. (%)	67 (28.0)	66 (27.4)
Dose, mg/day‡	7.6 ± 2.5	7.4 ± 2.6
NSAIDs		
Patients, no. (%)	167 (69.9)	173 (71.8)

* Except where indicated otherwise, values are the mean ± SD. DIP = distal interphalangeal; ACR = American College of Rheumatology; VAS = visual analog scale; HAQ DI = Health Assessment Questionnaire disability index; CRP = C-reactive protein; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; SHS = modified Sharp/van der Heijde score; PASI = Psoriasis Area and Severity Index; SF-36 = Short Form 36 health survey; PCS = physical component summary; MCS = mental component summary; MTX = methotrexate; NSAIDs = nonsteroidal antiinflammatory drugs.

† Patients with investigator-assessed spondylitis in addition to peripheral arthritis as their primary presentation of psoriatic arthritis (PsA).

‡ Dose equivalent to mg prednisone/day.

Table 2. Clinical efficacy and radiographic progression through week 24*

	Week 14		Week 24	
	Placebo (n = 239)	Golimumab 2 mg/kg (n = 241)	Placebo (n = 239)	Golimumab 2 mg/kg (n = 241)
Clinical efficacy				
ACR20 response	52 (21.8)	181 (75.1)†	58 (24.3)	185 (76.8)†
MTX use at baseline				
Yes	38/173 (22.0)	126/163 (77.3)	45/173 (26.0)	127/163 (77.9)
No	14/66 (21.2)	55/78 (70.5)	13/66 (19.7)	58/78 (74.4)
ACR50 response	15 (6.3)	105 (43.6)†	15 (6.3)	129 (53.5)†
MTX use at baseline				
Yes	12/173 (6.9)	70/163 (42.9)	11/173 (6.4)	85/163 (52.1)
No	3/66 (4.5)	35/78 (44.9)	4/66 (6.1)	44/78 (56.4)
ACR70 response	5 (2.1)	59 (24.5)†	8 (3.3)	79 (32.8)†
MTX use at baseline				
Yes	4/173 (2.3)	39/163 (23.9)	6/173 (3.5)	53/163 (32.5)
No	1/66 (1.5)	20/78 (25.6)	2/66 (3.0)	26/78 (33.3)
No. of patients with spondylitis and peripheral joint involvement	57	61	57	61
BASDAI20 response	12 (21.1)	41 (67.2)†	20 (35.1)	44 (72.1)†
BASDAI50 response	6 (10.5)	32 (52.5)†	2 (3.5)	28 (45.9)†
BASDAI70 response	1 (1.8)	21 (34.4)†	1 (1.8)	18 (29.5)†
No. of patients with ≥3% body surface area with psoriasis involvement at baseline	198	196	198	196
PASI75 response	27 (13.6)	116 (59.2)†	26 (13.1)	127 (64.8)†
MTX use at baseline				
Yes	20/142 (14.1)	78/131 (59.5)	21/142 (14.8)	86/131 (65.6)
No	7/56 (12.5)	38/65 (58.5)	5/56 (8.9)	41/65 (63.1)
PASI90 response	13 (6.6)	77 (39.3)†	15 (7.6)	84 (42.9)†
PASI100 response	9 (4.5)	33 (16.8)†	11 (5.6)	50 (25.5)†
Change from baseline in HAQ DI score				
No. of patients tested	222	233	221	231
Mean ± SD	–0.12 ± 0.47	–0.60 ± 0.53†	–0.14 ± 0.50	–0.63 ± 0.55†
Change from baseline in CRP				
No. of patients tested	239	241	239	241
Mean ± SD	–0.3 ± 1.9	–1.6 ± 2.5†	–0.2 ± 2.1	–1.5 ± 2.4†
No. of patients with enthesitis at baseline	181	185	181	185
Change from baseline in enthesitis score				
No. of patients tested	173	182	172	181
Mean ± SD	–0.8 ± 2.0	–1.8 ± 1.8†	–1.1 ± 2.1	–2.1 ± 1.8†
No. of patients with dactylitis at baseline	124	134	124	134
Change from baseline in dactylitis score				
No. of patients tested	115	130	116	130
Mean ± SD	–2.8 ± 7.0	–7.8 ± 8.6†	–5.0 ± 8.1	–8.2 ± 8.9†
Health-related quality of life				
Change from baseline in SF-36 PCS score				
No. of patients tested	222	233	221	231
Mean ± SD	2.7 ± 5.9	8.7 ± 7.6†	2.5 ± 6.2	9.5 ± 8.0†
Change from baseline in SF-36 MCS score				
No. of patients tested	222	233	221	231
Mean ± SD	1.0 ± 7.6	5.3 ± 9.9†	0.8 ± 7.6	5.5 ± 10.3†
Radiographic results				
Change from baseline in total PsA-modified SHS, mean ± SD	–	–	2.0 ± 0.3	–0.4 ± 0.1†
MTX use at baseline				
Yes	–	–	2.2 ± 4.3	–0.4 ± 1.9
No	–	–	1.7 ± 4.1	–0.4 ± 2.8
Change from baseline in erosion score, mean ± SD	–	–	1.3 ± 2.8	–0.3 ± 1.7†
Change from baseline in joint space narrowing score, mean ± SD	–	–	0.6 ± 1.7	–0.1 ± 1.1†
Patients with a change from baseline ≤0 in total PsA-modified SHS	–	–	102 (43.0)	170 (71.7)†
Patients with a change from baseline ≥SDC in total PsA-modified SHS	–	–	64 (27.0)	19 (8.0)†

* Except where indicated otherwise, values are the number or number/total number (%). ACR20 = American College of Rheumatology 20% improvement criteria; MTX = methotrexate; BASDAI20/50/70 response = ≥20%/50%/70% reduction in the Bath Ankylosing Spondylitis Disease Activity Index score; PASI75 = ≥75% improvement on the Psoriasis Area and Severity Index; HAQ DI = Health Assessment Questionnaire disability index; CRP = C-reactive protein; SF-36 = Short Form 36 health survey; PCS = physical component summary; MCS = mental component summary; PsA-modified SHS = modified Sharp/van der Heijde score with modifications for patients with psoriatic arthritis; SDC = smallest detectable change (2.49).
† $P < 0.001$ versus placebo.

Spain, Ukraine, and the US). A total of 817 patients were screened, and 480 patients were randomized to placebo (n = 239) or golimumab at 2 mg/kg (n = 241); 1 patient in the golimumab group was withdrawn from the study (met exclusion criteria) before receiving any study agent and was included in the efficacy analyses. Through week 14, 12 patients in the placebo group discontinued study agent; 3 patients in the golimumab group discontinued study agent, in addition to the 1 patient who withdrew before receiving study agent (Figure 1). After week 14, an additional 12 patients (5 in the placebo group and 7 in the golimumab group) discontinued study agent through week 24. At week 16, 51 patients met early escape criteria (49 in the placebo group and 2 in the golimumab group) and were eligible for prespecified treatment adjustments at the investigator's discretion. Among these patients, 29 (56.9%) did not have any change in treatment, 6 (11.8%) and 4 (7.8%) had an increase in MTX and NSAID dose, respectively, 5 (9.8%) initiated MTX, 4 (7.8%) initiated corticosteroids, 1 (2.0%) initiated NSAIDs, 1 (2.0%) initiated sulfasalazine, and 1 (2.0%) initiated leflunomide.

Demographic and disease characteristics were well balanced between the treatment groups (Table 1). Approximately 52% of all patients were men. The mean age at baseline was 46 years, and the mean duration of PsA was 5.8 years. At baseline, 70.0% of all patients were receiving concomitant MTX, 27.7% were receiving low-dose oral corticosteroids, and 70.8% were receiving NSAIDs, and the proportions of patients receiving these therapies were comparable between the treatment groups (Table 1).

Clinical efficacy and patient-reported outcomes. At week 14, 75.1% of patients in the golimumab group achieved an ACR20 response (primary end point) compared with 21.8% in the placebo group ($P < 0.001$) (Table 2). All major secondary end points were achieved (Table 2). Patients receiving golimumab had a greater mean change in HAQ DI score at week 14 compared with patients receiving placebo (–0.60 versus –0.12; $P < 0.001$), and greater proportions of patients in the golimumab group had an ACR50 response (43.6% versus 6.3%; $P < 0.001$) and a PASI75 response (59.2% versus 13.6%; $P < 0.001$) at week 14. In addition, patients in the golimumab group had less radiographic progression than those in the placebo group (Figure 2), with a mean change from baseline in total PsA-modified SHS of –0.4 in the golimumab group and 2.0 in the placebo group at week 24 ($P < 0.001$) (Table 2).

All additional controlled secondary end points showed greater improvements for patients in the golimumab group compared with those in the placebo group. Golimumab-treated patients had significantly greater mean changes from baseline in enthesitis scores (–1.8 versus –0.8; $P < 0.001$) and dactylitis scores (–7.8 versus –2.8; $P < 0.001$) at week 14 compared with placebo-treated patients. Greater proportions of patients in the golimumab

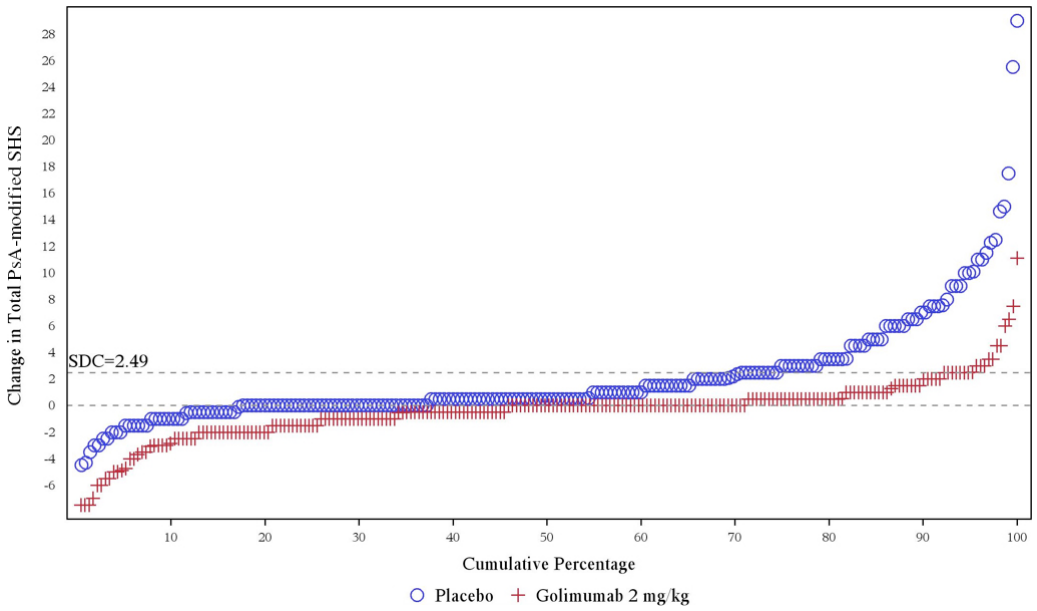

Figure 2. Cumulative probability plot of change from baseline in modified Sharp/van der Heijde score with modifications for patients with psoriatic arthritis (PsA-modified SHS). SDC = smallest detectable change.

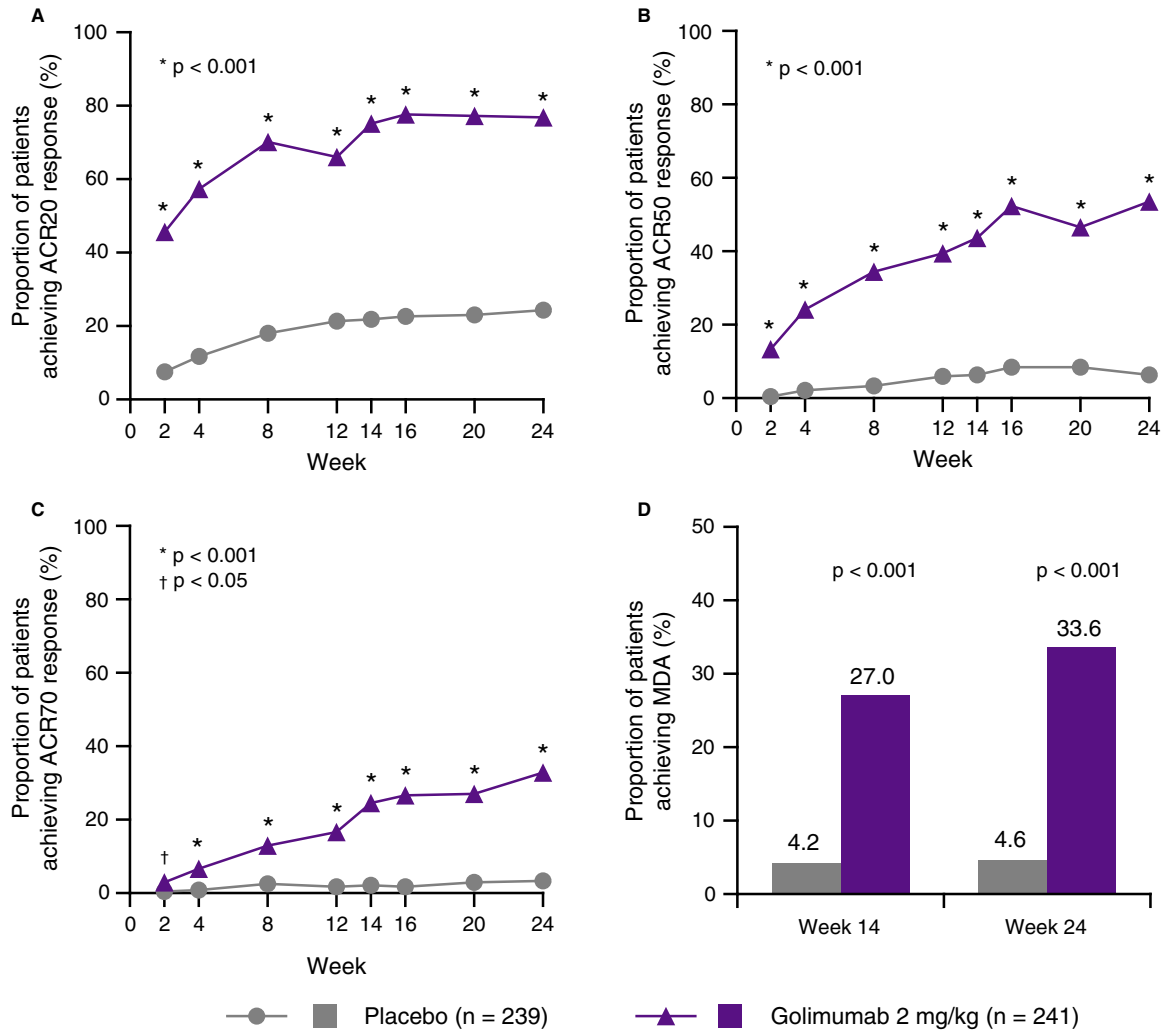

Figure 3. Proportion of patients meeting the American College of Rheumatology 20% improvement criteria (achieving an ACR20 response) (**A**), achieving an ACR50 response (**B**), achieving an ACR70 response (**C**), and achieving minimal disease activity (MDA) (**D**) through week 24.

group had an ACR50 response at week 24 (53.5% versus 6.3%; $P < 0.001$) and an ACR70 response at week 14 (24.5% versus 2.1%; $P < 0.001$). In addition, mean changes from baseline in SF-36 PCS scores (8.7 versus 2.7; $P < 0.001$) and MCS scores (5.3 versus 1.0; $P < 0.001$) at week 14 were significantly greater in the golimumab group than in the placebo group.

A greater proportion of golimumab-treated patients had an ACR20 response at week 2 (45.6% versus 7.5%; $P < 0.001$). Separation between the treatment groups was also observed at week 2 for ACR50 and ACR70 response and was maintained through week 24 (Figure 3). There were no apparent differences in the ACR20, ACR50, and ACR70 response rates between patients who received concomitant MTX at baseline and those who did not (Table 2).

Improvements in dactylitis and enthesitis scores were maintained at week 24 (Table 2). Patients in the golimumab group also continued to have greater mean improvements from baseline in HAQ DI, SF-36 PCS, and SF-36 MCS scores at week 24 (Table 2). Among patients with spondylitis with peripheral arthritis at baseline, greater proportions of golimumab-treated patients achieved a ≥20%/50%/70% reduction in the BASDAI score (a BASDAI20, BASDAI50, and BASDAI70 response) at week 14 and week 24 (Table 2).

The proportion of patients with a PASI75 response was maintained through week 24, with no apparent difference between patients who received baseline MTX and those who did not (Table 2). Additionally, the proportions of patients who achieved a PASI90 and PASI100 response were also greater in the

Table 3. AEs through week 24*

	Placebo (n = 239)	Golimumab 2 mg/kg (n = 240)
Duration of follow-up, mean weeks	23.2	23.9
Patients who discontinued due to an AE	3 (1.3)	5 (2.1)
Patients with ≥1 AE	97 (40.6)	111 (46.3)
Patients with ≥1 infection	37 (15.5)	45 (18.8)
Opportunistic infections	0	0
Demyelinating events	0	1 (0.4)
Patients with ≥1 infusion reaction	0	2 (0.8)
Patients with ≥1 SAE	8 (3.3)	7 (2.9)
Serious infections	2 (0.8)	1 (0.4)
Malignancies	2 (0.8)	0
Deaths	2 (0.8)	0

* Except where indicated otherwise, values are the number (%). AE = adverse event; SAE = serious AE.

golimumab group at week 14 and week 24 (nominal $P < 0.001$). In addition, greater proportions of patients in the golimumab group achieved the composite MDA response at both week 14 and week 24 (Figure 3).

Radiographic progression. Mean changes in total PsA-modified SHS from baseline to week 24 were similar for patients who did and those who did not receive MTX at baseline (Table 2). A greater proportion of patients in the golimumab group experienced a change from baseline of ≤0 (71.7% versus 43.0%; $P < 0.001$) (Table 2). Patients in the golimumab group demonstrated mean improvements from baseline in both erosion (–0.3) and joint space narrowing (–0.1), while patients in the placebo group had mean increases in erosion scores (1.3) and joint space narrowing scores (0.6) ($P < 0.001$ for both).

AEs. Through week 24, 40.6% of patients in the placebo group and 46.3% in the golimumab group had at least 1 AE (Table 3); infections were the most common type of AE. No opportunistic infections or active tuberculosis (TB) were reported through week 24. There were no anaphylactic or serum sickness–like reactions through week 24. One patient in the golimumab group was diagnosed as having a demyelinating event, noninfectious encephalomyelitis, ~16 weeks after the first golimumab administration; the patient was not hospitalized, and study drug was discontinued.

The incidence of serious AEs (SAEs) was similar between the treatment groups through week 24 (Table 3). Eight patients (3.3%) in the placebo group experienced at least 1 SAE, including pneumonia, acute cardiac failure, abnormal liver function test result, cerebral hematoma, cataract, humerus fracture, renal failure, pneumonia aspiration, and deep vein thrombosis. Two malignancies occurred, both in the placebo group (non–small cell lung cancer and esophageal neoplasm). Two deaths occurred, both in the placebo group (1 from acute cardiovascular failure and 1 from cardiorespiratory insufficiency due to metastasis [from the esophageal neoplasm]). Seven patients (2.9%) in the golimumab group had an SAE: pleomorphic adenoma, myocardial infarction, pneumonia, abnormal liver function test result, neuritis, drug-induced liver injury (MTX-induced toxic hepatitis), and pustular psoriasis.

Mild transaminase elevations were common in both groups. For alanine aminotransferase (ALT), 34% of patients in the golimumab group and 26% of patients in the placebo group had a maximum postbaseline value that was elevated but <3× the upper limit of normal (ULN). Most of these patients had values <2× the ULN. Few patients had values ≥3× the ULN; 2.9% in the golimumab group and 0.4% in the placebo group had maximum values ≥3× to <5× the ULN, and 1.7% and 0.4%, respectively, had values ≥5× the ULN.

Among the 240 patients treated in the golimumab group, 22 received TB prophylaxis. Of these, 9 had a maximum postbaseline ALT value that was abnormal through week 24 (8 with an ALT level <2× the ULN and 1 with an ALT level ≥3× to <5× the ULN).

In the golimumab group, 163 patients received MTX at baseline. Of these, 43 patients had ALT levels in the normal range at baseline and a maximum postbaseline value that was abnormal through week 24. Most of these patients (n = 41) had a value <3× the ULN; 2 had a value ≥3× to <5× the ULN. Among the 77 patients in the golimumab group who were not receiving MTX at baseline, 23 had ALT levels in the normal range at baseline and a maximum postbaseline value that was abnormal through week 24. Most of these patients (n = 21) had a value <3× the ULN, 1 had a value ≥3× to <5× the ULN, and 1 had a value ≥5× the ULN.

Pharmacokinetics and immunogenicity. Median trough serum golimumab concentrations reached steady state at week 12 and were maintained at week 20 (0.59 μg/ml) after IV administration of golimumab at 2 mg/kg at weeks 0 and 4 and every 8 weeks thereafter. Median serum golimumab concentrations were generally similar over time regardless of baseline MTX usage. Antibodies to golimumab were detected using a highly sensitive, drug-tolerant immunoassay method in 44 of 226 golimumab-treated patients (19.5%) through week 20, and antibody titers were generally low in these patients (39 of these patients had titers below 1:100, while 2 patients had the highest titer of 1:768); 16 of the 44 patients positive for antibodies to

golimumab were positive for neutralizing antibodies. Median trough golimumab concentrations were generally lower in patients who tested positive for antibodies to golimumab, with golimumab concentrations decreasing as peak titers increased. Among the 41 patients who tested positive for antibodies to golimumab and had available ACR response data, 30 (73%) had an ACR20 response, 12 (29%) had an ACR50 response, and 5 (12%) had an ACR70 response at week 20. Among the 170 patients who tested negative for antibodies to golimumab and had available ACR response data, 144 (85%) had an ACR20 response, 90 (53%) had an ACR50 response, and 55 (32%) had an ACR70 response at week 20.

Two patients experienced infusion reactions. One infusion reaction (headache) occurred at week 0 in a patient who later tested positive for antibodies to golimumab; the reaction was moderate in intensity and did not lead to study discontinuation. The other infusion reactions (tightness of the chest, anxiety, and dyspnea) occurred at week 20 in a patient who tested positive for antibodies to golimumab. The reactions in this patient were assessed as moderate in intensity, and the infusion reaction tightness of chest led to discontinuation of study agent administration; electrocardiogram findings were normal, and results of a troponin test were negative.

DISCUSSION

In the GO-VIBRANT study, improvements in PsA disease activity were significantly greater with IV golimumab at 2 mg/kg compared with placebo for adult patients with active PsA. The primary end point was achieved, with 75.1% of golimumab-treated patients having an ACR20 response at week 14 compared with 21.8% of patients in the placebo group. In addition, greater proportions of golimumab-treated patients achieved high levels of response, reflected in ACR50 and ACR70 responses and MDA. Separation between the treatment groups was observed as early as week 2 and maintained through week 24.

Improvements in enthesitis and dactylitis through week 24 were greater in the golimumab group. Among patients with spondylitis with peripheral arthritis as their primary arthritis presentation of PsA, BASDAI20, BASDAI50, and BASDAI70 response rates were also greater with golimumab. Additionally, skin response with IV golimumab was robust, with >40% of patients achieving a PASI90 response and 25% achieving skin clearance (a PASI100 response) at week 24. Patients in the golimumab group also experienced significantly less radiographic progression through week 24, and a greater proportion of golimumab-treated patients demonstrated no progression through week 24. Improvements in physical function and HRQoL were also greater in the golimumab group, as evidenced by improvements in the SF-36 PCS and MCS scores, which are relevant to patients with PsA.

AEs observed through week 24 of this trial were consistent with results of previous trials of SC and IV golimumab in patients with rheumatic diseases (5,19–22) as well as with the safety profiles of other anti-TNF agents (23,24). It should be noted that this study was not powered to detect rare safety events. Infections were the most common type of AE among patients who received golimumab; there were no cases of opportunistic infections or active TB through week 24. Few infusion reactions occurred, and none were considered to be serious or severe. Through week 24, 2 patients (both in the placebo group) were diagnosed as having a malignancy. Two deaths occurred, both in the placebo group. The incidence of SAEs (3%) was low and balanced between the treatment groups. Elevations in ALT have been associated with anti-TNF therapies (25) and were also noted in this study (most were mild). Concomitant treatment for latent TB or with MTX did not have effects on this pattern in the current study.

Forty-four patients tested positive for antibodies to golimumab using a highly sensitive, drug-tolerant assay, which was consistent with other rheumatic indications tested with the same assay. The higher incidence of antibodies to golimumab in comparison to the previous assay (5) was expected due to the higher sensitivity of the current assay. The majority of patients who tested positive for antibodies to golimumab in the GO-VIBRANT study had low titers, which did not have an apparent effect on golimumab concentrations, efficacy, or safety. Higher titers of antibodies may be associated with lower golimumab concentrations and efficacy. However, this should be interpreted with caution because there were few patients with high titers in this study. Development of antibodies to golimumab did not preclude clinical response in this population.

One of the overarching principles in the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis PsA treatment recommendations is the concept that treatment decisions should be individualized for patients, taking into account patient preferences in addition to other factors such as disease activity and treatment history (2). In addition to safety and efficacy, patient preferences regarding the characteristics of SC and IV therapies, including mode and frequency of administration and the ability to self-administer therapy

at home or receive treatment in a medical facility, play a role in determining treatment. Prior studies of patient preference with anti-TNF therapies have shown that while some patients prefer the flexibility to self-administer SC treatments at home (26,27), other patients express fear or anxiety regarding self-injection (8) and prefer the additional interactions with health care providers when receiving an IV medication (26,27). Therefore, given the various therapies available for patients with moderate-to-severe PsA, patient preference regarding mode and frequency of administration is an important factor to consider as part of shared decision-making when designing a treatment plan (4). Currently, golimumab is the only anti-TNF therapy with both SC and IV formulations, which may allow a more individualized treatment plan for some patients.

Through week 24 of the GO-VIBRANT trial, patients with PsA treated with IV golimumab at 2 mg/kg at weeks 0 and 4 and every 8 weeks thereafter experienced significantly greater improvements in measures of disease activity (both joint and skin), HRQoL, and radiographic progression compared with patients receiving placebo. The AEs reported in this trial were consistent with the established safety profile of anti-TNF agents, including SC and IV golimumab, in patients with rheumatic diseases. The study will continue through 1 year, including patients who crossed over from placebo to golimumab at week 24, and those data will be presented in a subsequent publication.

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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 published. 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. Kavanaugh, Husni, Harrison, Kim, Lo, Leu, Hsia.

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

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

ROLE OF THE STUDY SPONSOR

Authors who are employees of the study sponsor, Janssen Research & Development, LLC, were involved in the study design, collecting and analyzing the data, and interpreting the results. All authors reviewed and approved the manuscript prior to submission. Writing support was provided by Janssen Scientific Affairs, LLC. Publication of this article was not contingent upon approval by Janssen Research & Development, LLC.

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APPENDIX A: INVESTIGATORS RANDOMIZING PATIENTS IN THE GO-VIBRANT TRIAL

Investigators who randomized patients in the GO-VIBRANT trial are as follows: Olga Degtereva, Vitaly Krivenchuk, Valentina Luchko, Anatoly Rekun, Ivan Timkin (Belarus); Proton Rahman (Canada); Rieke Alten, Siegfried Wassenberg, Juergen Wollenhaupt (Germany); Attila Bartha, Bela Gomor, Agota Kranicz, Bernadette Rojkovich, Gabriella Sulyok, Edit Toth, Eszter Varga (Hungary); Asta Baranauskaite, Vida Basijokiene, Loreta Bukauskiene, Virginija Lietuvininkiene, Marija Tamulaitiene, Algirdas Venalis (Lithuania); Anna Dudek, Maria Glowacka-Kulesz, Pawel Hrycaj, Slawomir Jeka, Marek Krogulec, Marcin Mazurek, Malgorzata Miakisz, Anna Olak-Popko, Jacek Olas, Jolanta Weglowska, Piotr Wiland, Rafal Wojciechowski, Anna Zubrzycka-Sienkiewicz (Poland); Codrina Ancuta, Relu Liviu Craciun, Octavian Petre (Romania); Evgenia Akatova, Olga Bugrova, Larisa Eliseeva, Olga Ershova, Larisa Knyazeva, Valerii Marchenko, Alexey Maslyanskiy, Galina Matsievskaya, Tatiana Mikhaylova, Nino Mosesova, Natalya Nikulenkova, Dmitry Platonov, Tatiana Raskina, Olga Reshetko, Pavel Shesternya, Nataliya Shilkina, Evgeniya Shmidt, Oleg Uryasev, Natalia Vezikova, Irina Vinogradova, Sergey Yakushin (Russia); Juan Povedano Gomez, Maria Dolores Lopez Montilla (Spain); Olena Garmish, Yuriy Gasanov, Olena Grishyna, Halyna Hrytsenko, Mykola Iabluchanskyi, Oleg Iaremenko, Olexandr Kuryata, Ganna Kuzmina, Olena Levchenko, Lyudmyla Prystupa, Dmitro Rekalov, Valentyna Romaniuk, Sergii Shevchuk, Svitlana Smiyan, Mykola Stanislavchuk, Vira Tseluyko, Samvel Turianitsia, Nataliya Ursol, Victoriia Vasylets, Viacheslav Zhdan (Ukraine); Tina Bunch, Paul Caldron, Mary Ann Domingo, Gerald Ho, John Hull, Akgun Ince, Ramina Jajoo, Frederick Murphy, Rakesh Patel (United States).