SUPPLEMENTAL MATERIALS

PATIENTS AND METHODS

Study design

As reported previously,[6] 405 patients were randomized (1:1.3:1.3) by centralized interactive voice response system (ClinPhone) to receive blinded subcutaneous injections of placebo, golimumab 50 mg, or golimumab 100 mg at weeks 0, 4, 8, 12, 16, and 20, with stratification by baseline methotrexate use. Golimumab (Janssen Biotech, Inc.; Horsham, PA) and placebo were supplied as sterile liquid for injection. At week 16, patients with <10% improvement in both swollen and tender joint counts could early escape from placebo to golimumab 50 mg or from golimumab 50 mg to 100 mg; patients randomized to golimumab 100 mg continued blinded 100 mg. Starting at week 24, all patients still receiving placebo crossed over to golimumab 50 mg such that all patients received blinded golimumab 50 mg or 100 mg every 4 weeks between the week-24 and week-52 database locks. Subsequently, patients received open-label subcutaneous golimumab (50 mg or 100 mg) injections every 4 weeks. Patients receiving golimumab 50 mg could escalate to 100 mg, while those receiving 100 mg could dose decrease to 50 mg, both at the investigator's discretion. Patients who discontinued golimumab treatment were followed for approximately 4 months and contributed follow-up data to efficacy and safety analyses. Week 268 was the last evaluation for this report (16 weeks after the last golimumab injection at week 252). Following the last golimumab injection of the trial, patients could transition to standard-of-care treatment for psoriatic arthritis, including commercially available biologics.

Statistical analyses

Sample size estimation for GO-REVEAL has been detailed.[6] Descriptive statistics were employed to summarize all efficacy findings through week 256 (up to 4 weeks after the last golimumab injection). Data related to clinical and radiographic efficacy were summarized according to randomized treatment groups. Clinical efficacy summaries were intent-to-treat (ITT) analyses, i.e., by randomized group irrespective of study treatment changes. Missing data for assessments involving response rates were imputed using last-observation-carried-forward methodology; patients who discontinued treatment due to lack of efficacy were considered nonresponders for dichotomous determinations. Analyses of radiographic scores from Reading Session #3, calculated as the two-reader average, were conducted for patients with radiographic scores at weeks 0, 104, and 256 using observed data.

Because the study protocol allowed increases/decreases in the golimumab dose during the open-label long-term extension, safety data were summarized for patients who received at least one dose of golimumab by the overall treatment received during the entire study period, i.e., 50 mg only, 100 mg only, or 50+100 mg. In this analysis, reported adverse events were summarized through week 268, with the exception of those that occurred after receipt of any commercial biologic (including commercial golimumab). Patients who received commercially available biologic treatment after discontinuing study golimumab, but who remained in the study, had adverse events reported up to week 268; these adverse events were excluded from safety summaries.

The incidences of rare events were calculated per 100 patient-years to account for different lengths of follow-up. Observed incidences of malignancy were compared with those

expected in the general United States population per the Surveillance, Epidemiology and End Results database (exclusive of nonmelanoma skin cancer).[10] Standardized incidence ratios and exact 95% confidence intervals were determined.

RESULTS

Patient disposition and baseline characteristics

The most common reasons for study agent discontinuation were adverse events and unsatisfactory therapeutic response (Table S1). Eighty patients increased the golimumab dose from 50 mg to 100 mg, and 54 decreased the golimumab dose from 100 mg to 50 mg at the discretion of the investigator during the extension; another 28 patients randomized to receive golimumab 50 mg increased the dose to 100 mg in early escape as mandated by the protocol (Table S1).

Baseline patient and disease characteristics were generally consistent among randomized treatment groups, with the exception of higher baseline psoriatic arthritis-modified Sharp/van der Heijde score in patients receiving methotrexate at baseline (Table 2). Despite the investigator's ability to adjust concomitant non-biologic disease-modifying antirheumatic drug, immunosuppressive, corticosteroid, and/or nonsteroidal anti-inflammatory drug treatment starting at week 52, the proportions of patients taking these medications and the mean doses at week 256 were generally similar to baseline use (Tables 1 and S2). Baseline characteristics also were consistent between the overall trial population (Table S2) and the subgroup of patients with radiographic scores at baseline, week 104, and week 256 (Table S3), which serves as the basis for radiographic analyses presented herein.

Efficacy

The two radiographic readers demonstrated good agreement in radiographic image scoring, with an intraclass correlation coefficient of 0.71 for change from baseline to week 256.

Golimumab pharmacokinetics and antibodies to golimumab

Dose-proportional pharmacokinetics were generally observed through 5 years of treatment among patients randomized to golimumab who did not change dose. Median serum golimumab concentrations were maintained over time and corresponded with the observed sustained clinical efficacy. Consistent with findings through week 24,[6] week 52,[7] and week 104,[8] a small number of patients developed antibodies-to-golimumab through week 256 (6.0% [20/335] among patients with ≥1 appropriate sample after the first administration of study agent). Antibody-to-golimumab development was less common in patients receiving (1.8% [3/165]) versus not receiving (10.0% [17/170]) baseline methotrexate.

Safety results

After discontinuation of study golimumab injections, 99 patients were treated with commercially available biologics through week 268; 19 of these patients (all treated with commercial golimumab) experienced an adverse event (AE). The AEs observed in the 19 patients were similar to those observed during receipt of study medication in the overall trial. One patient had a serious AE reported. The 65-year-old man, who had a 55-year history of smoking and received placebo and then golimumab 50 mg through week 248, started commercial golimumab at week 256. Stage 1 malignant non-small cell lung cancer was reported as a serious

AE approximately 11 weeks after the start of commercial drug and was resolved following surgical removal of the lesion.

Injection-site reactions, most commonly mild injection-site erythema, hematoma, and swelling, occurred in 37 (9%) patients through week 268 (Table 2). No relationship between antibody-to-golimumab status and the occurrence of injection-site reactions was observed, although the limited number of patients positive for antibodies-to-golimumab precludes drawing a definitive conclusion. No injection-site reaction was severe or resulted in treatment discontinuation. No patient experienced anaphylactic or serum sickness-like reactions.

Consistent with clinical laboratory findings reported through week 52 [7]and week 104,[8] a small number of golimumab-treated patients had more than one markedly abnormal postbaseline hematology or chemistry laboratory value through week 256 (Table 2).

Table S1. Patient disposition through week 252.

	Placebo	Golimumab 50 mg	Golimumab 100 mg
RANDOMIZED PATIENTS	113	146	146
TREATED PATIENTS	113	146	146
TREATMENT RECEIVED			
Golimumab 50 mg	102 (90.3%)	146 (100.0%)	0 (0.0%)
Placebo → Golimumab 50 mg in Early Escape (weeks 16-104)	51 (45.1%)	-	-
Dose Escalated to 100 mg (weeks 52-252)	*21/51*	-	-
-Dose Decreased to 50 mg (weeks 52-252)	*3/21*	-	-
Placebo → Golimumab 50 mg in Crossover (weeks 24-104)	51 (45.1%)	-	-
Dose Escalated to 100 mg (weeks 52-252)	*17/51*	-	-
-Dose Decreased to 50 mg (weeks 52-252)	*6/17*	-	-
Golimumab 50 mg only	-	118 (80.8%)	-
Dose Escalated to 100 mg (weeks 52-252)	-	*42/118*	-
-Dose Decreased to 50 mg (weeks 52-252)	-	*5/42*	-
Golimumab 50 mg → 100 mg in Early Escape (weeks 16-104)	-	28 (19.2%)	-
Dose Decreased to 50 mg (weeks 52-252)	-	3/28	
Golimumab 100 mg	38 (33.6%)	70 (47.9%)	146 (100.0%)

Table S1. Patient disposition through week 252.

	Placebo	Golimumab 50 mg	Golimumab 100 mg
Dose Decreased to 50 mg (weeks 52-252)	-	-	*37/146*
PATIENTS WHO DISCONTINUED STUDY AGENT	36 (31.9%)	51 (34.9%)	39 (26.7%)
Adverse event	14 (12.4%)	18 (12.3%)	18 (12.3%)
Worsening of psoriatic arthritis	*1 (0.9%)*	*0 (0.0%)*	*1 (0.7%)*
Unsatisfactory therapeutic effect	9 (8.0%)	8 (5.5%)	6 (4.1%)
Lost to follow-up	2 (1.8%)	5 (3.4%)	3 (2.1%)
Death	0 (0.0%)	1 (0.7%)	2 (1.4%)
Other	11 (9.7%)	19 (13.0%)	10 (6.8%)

Table S2. Baseline patient characteristics and concomitant medication use. Values are mean ± SD or n (%) unless otherwise noted

		Golimumab	
	Placebo	**50 mg**	**100 mg**
Number of patients randomized	113	146	146
Male	69 (61%)	89 (61%)	86 (59%)
Caucasian	110 (97%)	141 (97%)	142 (97%)
Age (years)	47.0 ± 10.6	45.7 ± 10.7	48.2 ± 10.9
PsA duration (years)	7.6 ± 7.9	7.2 ± 6.8	7.7 ± 7.8
Number of swollen joints (0-66)	13.4 ± 9.8	14.1 ± 11.4	12.0 ± 8.5
Number of tender joints (0-68)	21.9 ± 14.7	24.0 ± 17.1	22.5 ± 15.7
CRP (mg/dL)	1.3 ± 1.6	1.3 ± 1.6	1.4 ± 1.8
DAS28-CRP	4.9 ± 1.0	5.0 ± 1.1	4.9 ± 1.1
PsA-modified SHS of hands & feet[1] (0-528)	73	93	101
All patients, N =	17.1 ± 29.1	24.1 ± 36.8	19.8 ± 35.8
Patients receiving MTX, N =	43	48	52
	22.7 ± 35.1	29.4 ± 43.9	25.9 ± 42.6
Patients not receiving MTX, N =	30	45	49

Table S2. Baseline patient characteristics and concomitant medication use. Values are mean ± SD or n (%) unless otherwise noted

		Golimumab	
	Placebo	**50 mg**	**100 mg**
	9.1 ± 14.7	18.5 ± 26.6	13.3 ± 25.7
Patients with dactylitis	38 (34%)	50 (34%)	49 (34%)
Dactylitis score (1-60)	3.1 ± 2.1	6.3 ± 6.1	5.4 ± 6.7
Patients with enthesitis	88 (78%)	109 (75%)	115 (79%)
PsA-modified MASES score (1-15)	5.0 ± 4.1	5.7 ± 4.0	6.1 ± 4.1
Patients with ≥3% BSA	79 (70%)	109 (75%)	108 (74%)
BSA (%)	14.7 ± 15.7	16.2 ± 17.7	17.7 ± 18.3
PASI score (0-72)	8.4 ± 7.4	9.8 ± 8.6	11.1 ± 9.5
HAQ-DI score (0-3)	1.0 ± 0.5	1.0 ± 0.6	1.1 ± 0.6
Patients with fingernail involvement	83 (73%)	95 (65%)	109 (75%)
NAPSI score (0-8) of target fingernail	4.4 ± 2.2	4.7 ± 2.2	4.6 ± 2.1
SF-36 summary scores			
PCS score	31.9 ± 9.3	33.0 ± 10.7	32.8 ± 8.9
MCS score	47.6 ± 10.7	45.4 ± 12.2	45.0 ± 11.7
Patients receiving MTX	54 (48%)	71 (49%)	69 (47%)

Table S2. Baseline patient characteristics and concomitant medication use. Values are mean ± SD or n (%) unless otherwise noted

		Golimumab	
	Placebo	**50 mg**	**100 mg**
Dose (mg/week)	15.0 ± 4.4	14.8 ± 4.7	15.5 ± 5.1
Patients receiving oral corticosteroids	19 (17%)	19 (13%)	27 (19%)
Dose (mg/day)	5.8 ± 1.7	7.6 ± 2.4	6.0 ± 2.2
Patients receiving NSAIDs	88 (78%)	110 (75%)	110 (75%)

[1] Utilizing data derived from Reading Session #3. To assess PsA-specific radiographic damage, scores for the distal interphalangeal hand joints and pencil-in-cup/gross osteolysis deformities were added to the original SHS. The total PsA-modified SHS (0-528) is a sum of erosion (0-320) and joint space narrowing (JSN, 0-208) scores in 40 hand joints and 12 feet joints. Higher scores/larger increases in radiographic scores indicate more radiographic damage/progression.

BSA-body surface area, CRP-C-reactive protein, DAS28-28-joint count Disease Activity Score, HAQ-DI - Health Assessment Questionnaire Disability Index, MASES-Maastricht Ankylosing Spondylitis Enthesitis Score, MCS-mental component summary, MTX-methotrexate, NAPSI-Nail Psoriasis Severity Index, NSAIDs-nonsteroidal anti-inflammatory drugs, PASI-Psoriasis Area and Severity Index, PCS=physical component summary, PsA-psoriatic arthritis, SD-standard deviation, SF-36-36-item short-form health survey, SHS-Sharp/van der Heijde score

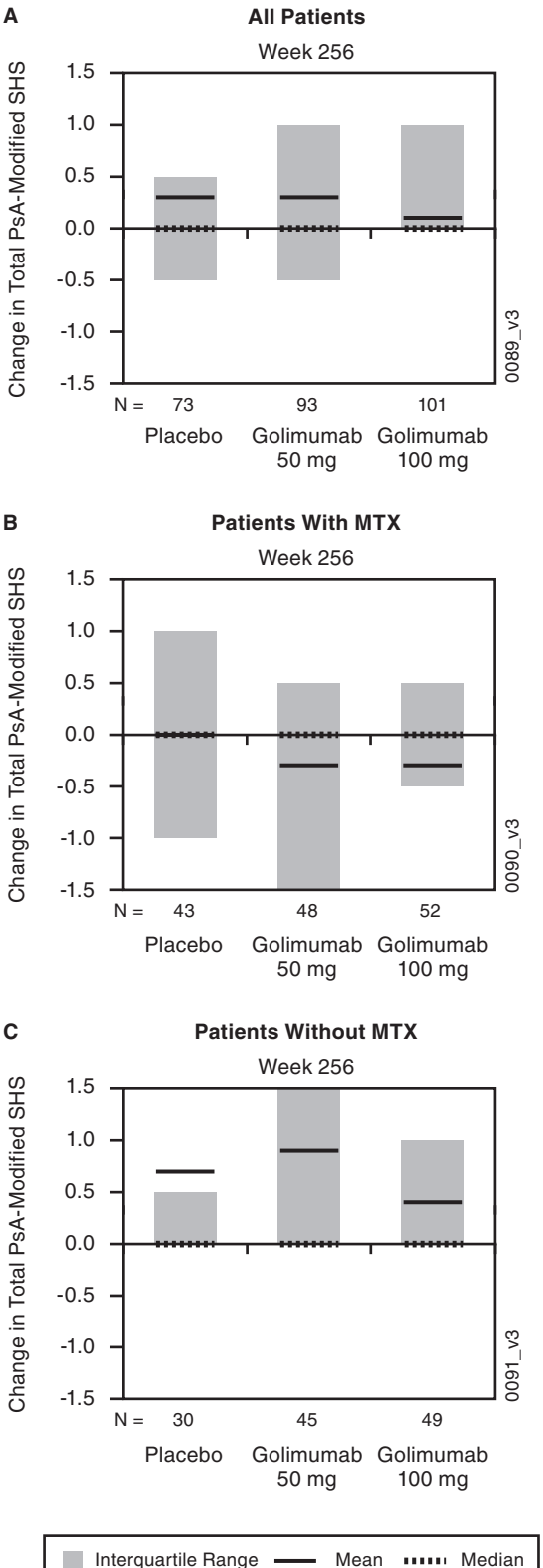
Table S3. Baseline patient characteristics for patients with radiographic data.[1] Values are mean ± SD or n (%) unless otherwise noted

		Golimumab	
	Placebo	**50 mg**	**100 mg**
Number of patients randomized	73	93	101
Male	45 (62%)	57 (61%)	56 (55%)
Caucasian	71 (97%)	89 (96%)	99 (98%)
Age (years)	45.8 ± 9.9	45.1 ± 9.8	46.9 ± 10.3
PsA duration (years)	8.2 ± 7.8	7.7 ± 6.4	8.1 ± 8.3
Number of swollen joints (0-66)	13.6 ± 9.6	13.8 ± 11.1	11.2 ± 7.9
Number of tender joints (0-68)	22.5 ± 15.1	23.5 ± 17.0	21.5 ± 15.2
CRP (mg/dL)	1.5 ± 1.7	1.4 ± 1.6	1.4 ± 1.8
DAS28-CRP	5.0 ± 1.0	5.0 ± 1.1	4.8 ± 1.0

[1] Utilizing radiographic data derived from Reading Session #3.

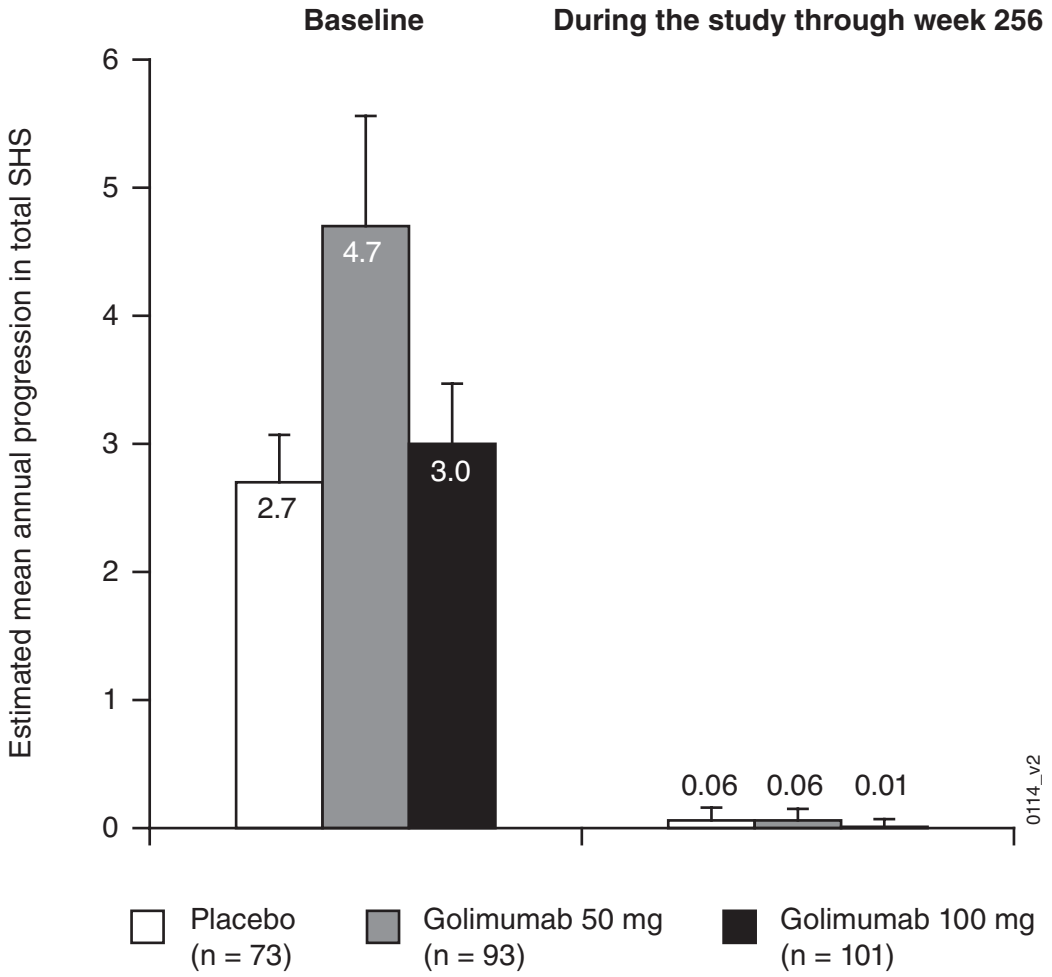
CRP-C-reactive protein, DAS28-28-joint count Disease Activity Score, PsA-psoriatic arthritis, SD-standard deviation

Figure S1: Changes from baseline in psoriatic arthritis (PsA)-modified Sharp/van der Heijde score (SHS). Analyses of radiographic data derived from Reading Session #3 were conducted for patients with radiographic scores at week 0, week 104, and week 256 by randomized treatment group, irrespective of treatment changes during the study. (Panel A: all patients, Panel B: patients with methotrexate [MTX] use at baseline, Panel C: patients with no MTX use at baseline). The placebo group includes patients who were originally randomized to placebo and later early escaped/crossed over at week 16/24 to receive golimumab 50 mg, with the possibility to increase golimumab from 50 mg to 100 mg after the week-52 database lock. The golimumab 50-mg group includes patients who were originally randomized to golimumab 50 mg and later early escaped at week 16 or dose escalated after the week-52 database lock to receive golimumab 100 mg. All patients could decrease the golimumab dose from 100 mg to 50 mg after the week-52 database lock.



PsA, psoriatic arthritis; SHS, Sharp/van der Heijde score.

Figure S2. Estimated mean annual progression in total psoriatic arthritis (PsA)-modified Sharp/van der Heijde score (SHS) at baseline and during the study through week 256 by randomized treatment group, irrespective of treatment changes during the study. The placebo group includes patients who early escaped/crossed over at week 16/24 to receive golimumab 50 mg, with the possibility to increase golimumab from 50 mg to 100 mg after the week-52 database lock. The golimumab 50-mg group includes patients who early escaped at week 16 or dose escalated after the week-52 database lock to receive golimumab 100 mg. All patients could decrease the golimumab dose from 100 mg to 50 mg after the week-52 database lock. Vertical whiskers represent upper bounds of standard error of the mean.



[1] Utilizing data derived from Reading Session #3.

[2] Estimated annual radiographic progression rate determined at baseline as baseline SHS score/duration of PsA at baseline for each patient and at week 256 as SHS change score at week 256/duration of golimumab treatment for each patient.