ONLINE SUPPLEMENTAL TEXT

Patients. Stable (≥2 weeks) approved regimens of nonsteroidal anti-inflammatory drugs and/or oral corticosteroids (≤10 mg/day prednisone or equivalent) were allowed prior to and throughout the study. Patients were screened for the presence of active or latent tuberculosis (TB) via medical history; physical examination; recent close contacts; and serum, skin and radiographic evaluations. Any patient with active TB was excluded from trial participation; patients with any evidence of latent TB could participate if they received appropriate treatment for latent TB prior to or simultaneously with the first administration of study agent.

Study design and assessments. The GO-FURTHER trial (ClinicalTrials.gov: NCT00973479, EudraCT 2008-006064-11) was conducted according to the Declaration of Helsinki and International Committee on Harmonization good clinical practices. The protocol was approved by each site's institutional review board or ethics committee; all patients provided written informed consent.

Golimumab and placebo were infused over 30 ± 10 minutes. Patients could receive standard prophylaxis for infusion reactions (e.g., acetaminophen, antihistamines), but not corticosteroids. Prophylaxis was provided only at the investigator's discretion.

For a particular radiograph, if the mean changes from baseline differed between the two readers by more than 10 points, an adjudicator (third reader) read all of the patient's radiographs in the reading session in a blinded fashion.

Statistical analyses. Sensitivity analyses conducted for the major radiographic endpoint included: 1) exclusion of patients missing baseline van der Heijde-Sharp (vdH-S) scores, 2) using observed data after a patient changed randomized treatment (dropout retrieved), 3) last-observation-carried-forward methodology for determining week-24 (wk24) scores for early escape patients, and 4) re-randomization test. Subgroup analyses based upon baseline disease characteristics, demographics, and medications were also conducted.

Safety analyses were performed for all patients who received ≥1 infusion of study agent. The adverse event data were summarized using Medical Dictionary for Regulatory Activities (version 10.1) system-organ class and preferred term.

As reported previously,[6] a sample size of 564 participants was estimated to provide a ≥99% power to detect significant treatment group differences in the primary endpoint. The sample size also ensured an adequate number of patients exposed to intravenous golimumab 2 mg/kg for safety assessments and provided a >90% power for the major radiographic secondary endpoint (wk24 change from baseline in vdH-S score), assuming mean changes from baseline in total vdH-S score of 1.2 with placebo+methotrexate (MTX) and 0.4 with golimumab+MTX, both with a standard deviation of 2.7.

Radiographic findings. The two primary readers demonstrated good inter-reader agreement in scoring the images on the treatment group, patient, and individual joint levels (data not shown). Based on a re-read of 10% of patients with radiographic evaluations at each time point (baseline, wk24, and wk52), the intra-class correlation coefficient (0.97) was high. Weighted Kappa statistics ranging from 0.69 to 0.76 across the three time points for erosion and joint space

narrowing scores of the hands and feet indicated agreement between the two primary readers at the individual joint level.

Among the 592 patients included in the analysis of radiographic data, 127 (21%) had a missing value for the change from baseline in total vdH-S score at wk24. The majority of the missing values (82/127) were due to a design element of the study, i.e., meeting early escape criteria at wk16, at which time the radiographic image was taken for patients who met early escape criteria instead of at wk24, and were replaced via linear extrapolation. The remaining 45 (8%) patients had missing values due to various reasons such as early discontinuation, unavailable images, and images that could not be scored or were taken outside of the window; the vast majority of these missing values were replaced using the median change from baseline among all patients in the same C-reactive protein level stratum at screening (< 1.5 mg/dL or ≥ 1.5mg/dL).

ONLINE SUPPLEMENTAL TABLE

Table S1 Summary of adverse events through week 52; treated patients

		Golimumab			
	Placebo + MTX	**Placebo + MTX → Golimumab 2 mg/kg + MTX at week 16**	**Placebo + MTX → Golimumab 2 mg/kg + MTX at week 24**	**Golimumab 2 mg/kg + MTX**	**All Golimumab 2 mg/kg + MTX**
Pts treated, N	197	68	121	395	584
Mean weeks of follow-up	21.0	36.0	27.0	49.8	43.5
Mean no. of administrations	4.2	4.9	3.9	6.6	5.9
Pts with AEs, n (%)	98 (49.7%)	40 (58.8%)	62 (51.2%)	275 (69.6%)	377 (64.6%)
Common AEs (>2% of golimumab-treated patients) by preferred term					
Upper resp tract infection	15 (7.6%)	5 (7.4%)	3 (2.5%)	41 (10.4%)	49 (8.4%)
Bronchitis	2 (1.0%)	3 (4.4%)	5 (4.1%)	24 (6.1%)	32 (5.5%)
Headache	5 (2.5%)	4 (5.9%)	2 (1.7%)	24 (6.1%)	30 (5.1%)
Nasopharyngitis	5 (2.5%)	3 (4.4%)	5 (4.1%)	21 (5.3%)	29 (5.0%)
Pharyngitis	2 (1.0%)	0	5 (4.1%)	22 (5.6%)	27 (4.6%)
Hypertension	5 (2.5%)	4 (5.9%)	1 (0.8%)	21 (5.3%)	26 (4.5%)
Urinary tract infection	6 (3.0%)	3 (4.4%)	3 (2.5%)	19 (4.8%)	25 (4.3%)
Rheumatoid arthritis	12 (6.1%)	5 (7.4%)	2 (1.7%)	18 (4.6%)	25 (4.3%)
Alanine aminotransferase increased	7 (3.6%)	4 (5.9%)	0	18 (4.6%)	22 (3.8%)
Dyspepsia	3 (1.5%)	0	4 (3.3%)	13 (3.3%)	17 (2.9%)
Aspartate aminotransferase increased	3 (1.5%)	2 (2.9%)	0	14 (3.5%)	16 (2.7%)
Back pain	4 (2.0%)	1 (1.5%)	4 (3.3%)	11 (2.8%)	16 (2.7%)

Table S1 Summary of adverse events through week 52; treated patients

		Golimumab			
	Placebo + MTX	**Placebo + MTX → Golimumab 2 mg/kg + MTX at week 16**	**Placebo + MTX → Golimumab 2 mg/kg + MTX at week 24**	**Golimumab 2 mg/kg + MTX**	**All Golimumab 2 mg/kg + MTX**
Sinusitis	3 (1.5%)	1 (1.5%)	3 (2.5%)	10 (2.5%)	14 (2.4%)
Influenza	4 (2.0%)	3 (4.4%)	0	10 (2.5%)	13 (2.2%)
Diarrhea	2 (1.0%)	0	1 (0.8%)	11 (2.8%)	12 (2.1%)
Nausea	3 (1.5%)	1 (1.5%)	3 (2.5%)	8 (2.0%)	12 (2.1%)
Pts with infusion reactions	1 (0.5%)	4 (5.9%)	0	17 (4.3%)	21 (3.6%)
Pts with serious AEs	6 (3.0%)	3 (4.4%)	4 (3.3%)	43 (10.9%)	50 (8.6%)
Pts with serious infections	1 (0.5%)	1 (1.5%)	1 (0.8%)	9 (2.3%)	11 (1.9%)
Pts with postbaseline abnormalities in ALT[1]					
Pts with TB prophylaxis	7/34 (20.6%)	4/16 (25.0%)	3/17 (17.6%)	24/48 (50.0%)	31/81 (38.2%)
Pts with no TB prophylaxis	32/148 (21.6%)	21/47 (44.7%)	25/93 (26.9%)	113/309 (36.6%)	159/449 (35.4%)

[1] Among patients with baseline ALT ≤ ULN.

AE – adverse event, ALT – alanine aminotransferase, MTX - methotrexate, pts – patients, TB - tuberculosis, ULN – upper limit of normal