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Original article

Safety and efficacy of golimumab in Chinese patients with active ankylosing spondylitis: 1-year results of a multicentre, randomized, double-blind, placebo-controlled phase III trial

Chunde Bao[1], Feng Huang[2], Muhammad Asim Khan[3], Kaiyin Fei[4], Zhong Wu[4], Chenglong Han[4] and Elizabeth C. Hsia[4,5]

Abstract

Objective. The aim of this study was to assess the efficacy and safety of golimumab in Chinese patients with active AS.

Methods. Two hundred and thirteen patients were randomized in a 1:1 ratio to receive either s.c. injections of placebo from weeks 0 to 20 followed by golimumab 50 mg from weeks 24 to 48 (group 1, $n = 105$) or golimumab 50 mg from weeks 0 to 48 (group 2, $n = 108$), both every 4 weeks. Placebo crossover occurred at week 24, while early escape was at week 16. The primary endpoint was an improvement of at least 20% in the Assessment of SpondyloArthritis international Society (ASAS20) criteria at week 14. Major secondary endpoints included week 24 ASAS20 response and week 14 change scores for BASFI and BASMI.

Results. Golimumab treatment elicited significantly better responses than placebo in week 14 ASAS20 response [49.1% (53/108) *vs* 24.8% (26/105), respectively, $P < 0.001$], week 24 ASAS20 response (50.0% *vs* 22.9%, $P < 0.001$) and mean improvements in BASFI (−1.26 *vs* 0.11, $P < 0.001$) and BASMI (−0.42 *vs* −0.19, $P = 0.021$) scores at week 14. Additionally, golimumab treatment led to significant improvements in the mental and physical components of health-related quality of life (HRQoL) and sleep problems at week 24, all of which were further improved through week 52. During the 16-week placebo-controlled study period, 31.4% and 30.6% of patients had adverse events (AEs) in groups 1 and 2, respectively; similar AE reporting rates were observed through week 24 (34.3% and 32.0%) and among the golimumab-treated patients through week 56 (41.2%).

Conclusion. Golimumab significantly reduced clinical symptoms/signs and improved physical function, range of motion and HRQoL in Chinese patients with active AS without unexpected safety concerns.

Trial registration: ClinicalTrials.gov, NCT01248793.

Key words: spondyloarthritis, spondyloarthropathy, ankylosing spondylitis, tumour necrosis factor, biologic, China, Asia.

[1]Shanghai Renji Hospital, Shanghai, [2]Chinese PLA General Hospital, Beijing, China, [3]Case Western Reserve University, Cleveland, OH, [4]Janssen Research & Development, LLC, Spring House, PA and [5]University of Pennsylvania School of Medicine, Philadelphia, PA, USA. hap//contradistinctionst2/show/NCT01248793

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Correspondence to: Chunde Bao, Department of Rheumatology, Shanghai Renji Hospital, Shanghai Jiaotong University School of Medicine, 145 Shandong Rd(c), Shanghai 200001, China.
E-mail: baochunde_1678@126.com

Chunde Bao and Feng Huang contributed equally to this study.

Introduction

AS is a chronic inflammatory disease of unknown aetiology involving the axial skeleton (sacroiliac, hip and shoulder joints and spine), entheses and less commonly, joints more peripheral to the spine [1]. Chronic inflammation of entheses, primarily in the axial skeleton, leads to new bone formation resulting in syndesmophytes and spinal ankylosis that in turn can limit range of motion and lead to disability. Although patients may experience

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a variety of musculoskeletal symptoms (chronic back pain, chest pain and tenderness around peripheral joints as a result of enthesitis), the most common presenting symptom is chronic lower back pain and stiffness. Common extra-articular manifestations or associations can include anterior uveitis, psoriasis and IBD [1]. Thus symptoms of early disease may be limited to inflammatory back pain, while those of more advanced or later stages of AS can include co-morbidities such as osteoporosis and cardiovascular manifestations (aortic valve involvement with or without heart block), as well as physical deformities related to spinal ankylosis and hip joint involvement [1, 2].

The prevalence of AS in China has been reported to range from 0.2% to 0.54% [3] and is similar to that seen in other parts of the world [4]. The clinical features and disease management of SpA in general are also similar between Asian countries and other parts of the world [4, 5]. Traditional AS treatments, consisting mainly of exercise and NSAIDs, and oral SSZ in the subset of patients with peripheral arthritis [6], have demonstrated limited efficacy. More recently, biologic therapies targeting the proinflammatory cytokine TNF-α have demonstrated efficacy in both Chinese and western AS patient populations [2, 7–10].

Golimumab is a newer monoclonal antibody that antagonizes the effects of TNF by binding with high affinity and specificity to soluble and transmembrane TNF [11]. Golimumab has demonstrated significant efficacy and an acceptable safety profile in a large cohort of patients with active AS [12]. The current study was undertaken to evaluate the efficacy and safety of golimumab in Chinese patients with AS as part of the global golimumab development programme.

Patients and methods

Patients

Eligible adult ($\geqslant$18 years of age) patients had a diagnosis of AS for at least 3 months defined as definite by the 1984 modified New York criteria [13]. Eligible patients also had a BASDAI of $\geqslant$4 (0–10 cm scale) and a visual analogue scale (VAS) score for total back pain of $\geqslant$4 (0–10 cm scale). Patients were allowed to continue receiving stable doses of MTX, SSZ and HCQ during study participation, while those who had received prior biologic anti-TNF therapy were not eligible for the study (see Results and Table 1 for details of baseline patient characteristics and medication use). Patients with complete ankylosis of the spine, defined as the presence of bridging syndesmophytes at all intervertebral levels of the cervical and lumbar spine on lateral view spinal radiographs, were also excluded. Eligible patients also met prespecified tuberculosis (TB) screening criteria based on results of the purified protein derivative (PPD) skin test, Quantiferon-TB Gold In-tube blood test and chest X-ray at baseline.

Study design

This multicentre phase 3 study (ClinicalTrial.gov, NCT01248793) had a 24-week, randomized, double-blind, placebo-controlled phase followed by s.c. administration of golimumab 50 mg to all patients from week 24 forward. The study was conducted according to the Declaration of Helsinki and good clinical practice guidelines. The protocol was reviewed and the study approved by all institutional review boards. All patients provided written informed consent prior to study participation.

Eligible patients were randomly assigned in a 1:1 ratio to receive s.c. injections of placebo (group 1) or golimumab 50 mg (group 2). Randomization was stratified using block methodology by investigational study site and by the patient's screening CRP level ($\geqslant$15 mg/l or $<$15 mg/l). Golimumab and placebo were supplied as sterile liquid (Janssen Research & Development, Spring House, PA, USA) for s.c. injection at week 0 and every 4 weeks through week 48.

At week 16, patients with $<$20% improvement from baseline in both total back pain and morning stiffness measures entered double-blind early escape (EE), whereby those in group 1 were started on golimumab 50 mg and those in group 2 continued to receive golimumab 50 mg. At week 24, all patients still receiving placebo crossed over to golimumab 50 mg s.c. injections. The final golimumab injection was scheduled for week 48, final efficacy assessments were conducted at week 52 and final safety assessments were conducted at week 56.

Study assessments and endpoints

An independent assessor trained by the sponsor and experienced in performing AS-related assessments was designated at each study site to perform all musculoskeletal assessments. Independent assessors had no access to any other patient or study-related data. The primary study endpoint was the proportion of patients achieving at least 20% improvement in Assessment of SpondyloArthritis international Society criteria (ASAS20) [14] at week 14. Details of this and other clinical assessments, including the BASFI [15], BASDAI [16] and BASMI [17], ASAS40 response, ASAS5/6 response, ASAS partial remission, the 36-item Short Form Health Survey (SF-36) health-related quality of life (HRQoL) questionnaire [18] and the Jenkins Sleep Evaluation Questionnaire (JSEQ) [19], are provided in supplementary data available at *Rheumatology* Online.

Serum golimumab concentrations were detected using a validated electrochemiluminescent immunoassay [20]. The detection of antibodies to golimumab was performed with a validated antigen-bridging immunoassay [21]. Safety assessments included adverse events (AEs) and routine laboratory analyses.

Statistical analyses

Efficacy and HRQoL parameters were assessed according to an intent-to-treat approach, while safety analyses included all treated patients according to the treatment they actually received. Serum golimumab concentrations were summarized among golimumab-treated patients.

TABLE 1 Summary of baseline demographics and disease characteristics among randomized patients

	Placebo	Golimumab 50 mg	Total
Patients randomized, *n*	105	108	213
Age, mean (S.D.) [median], years	30.6 (8.60) [29.0]	30.5 (10.27) [27.0]	30.5 (9.46) [29.0]
Male, *n* (%)	87 (82.9)	90 (83.3)	177 (83.1)
BMI, mean (S.D.) [median], kg/m^2	22.7 (3.02) [22.3]	21.8 (3.13) [21.5]	22.2 (3.10) [21.8]
Duration, mean (S.D.), years			
Back pain symptoms	7.5 (6.06)	6.8 (6.43)	7.1 (6.25)
SpA symptoms	6.6 (5.67)	6.1 (5.93)	6.4 (5.80)
AS diagnosis	3.7 (3.88)	4.2 (5.22)	3.9 (4.61)
CRP, mean (S.D.) [median], mg/l	18.6 (19.89) [11.5]	20.6 (21.23) [14.3]	19.7 (20.55) [12.4]
<15, *n* (%)	53/105 (50.5)	55/107 (51.4)	108/212 (50.9)
$\geqslant 15$, *n* (%)	52/105 (49.5)	52/107 (48.6)	104/212 (49.1)
BASDAI (0–10), mean (S.D.) [median]	6.5 (1.54) [6.7]	6.6 (1.31) [6.6]	6.5 (1.43) [6.6]
BASFI (0–10), mean (S.D.) [median]	5.0 (2.38) [4.8]	5.0 (2.35) [5.3]	5.0 (2.36) [5.1]
BASMI (0–10), mean (S.D.) [median]	3.8 (1.61) [3.6]	4.0 (1.88) [3.9]	3.9 (1.75) [3.7]
SF-36			
PCS score (0–100), mean (S.D.) [median]	33.9 (7.72) [34.7]	33.2 (7.81) [33.1]	33.6 (7.76) [33.8]
MCS score (0–100), mean (S.D.) [median]	36.2 (11.51) [37.8]	36.5 (10.51) [36.1]	36.4 (10.99) [36.8]
JSEQ score (0–20), mean (S.D.) [median]	9.2 (4.96) [9.0]	9.8 (4.87) [10.0]	9.5 (4.91) [10.0]
Baseline AS medication use, *n* (%)			
MTX	23 (21.9)	21 (19.4)	44 (20.7)
SSZ	56 (53.3)	58 (53.7)	114 (53.5)
HCQ	0 (0.0)	0 (0.0)	0 (0.0)
Corticosteroids	5 (4.8)	5 (4.6)	10 (4.7)
NSAIDs	76 (72.4)	72 (66.7)	148 (69.5)

JSEQ: Jenkins Sleep Evaluation Questionnaire; MCS: mental component summary; PCS: physical component summary; SF-36: 36-item Short Form Health Survey.

Continuous response parameters were compared using an analysis of variance on the van der Waerden normal scores, whereby normal scores are derived from ranks [22], and all statistical tests were two-sided and performed at $\alpha = 0.05$. Additional details of statistical methodology are provided in the supplementary data, available at *Rheumatology* Online.

Results

Patient disposition and baseline characteristics

Data for this report were collected beginning 9 September 2010; the last (week 56) evaluation was completed on 14 March 2012. The study was conducted at 12 Chinese sites. Of the 299 patients who consented to participate in the trial, 213 were randomized to treatment with placebo ($n = 105$) or golimumab 50 mg ($n = 108$). Ten of the 213 (4.7%) patients discontinued the study agent through week 56, most commonly resulting from withdrawal of consent. In addition, 61 (58.1%) of the placebo-randomized patients met the EE criteria and initiated golimumab 50 mg at week 16 (Fig. 1).

The 213 randomized Chinese patients had a median age of 29.0 years and a median BMI of 21.8 kg/m^2. The vast majority of patients were male (83.1%, 177/213) and HLA-B27 positive (200/212 with data, 94.3%).

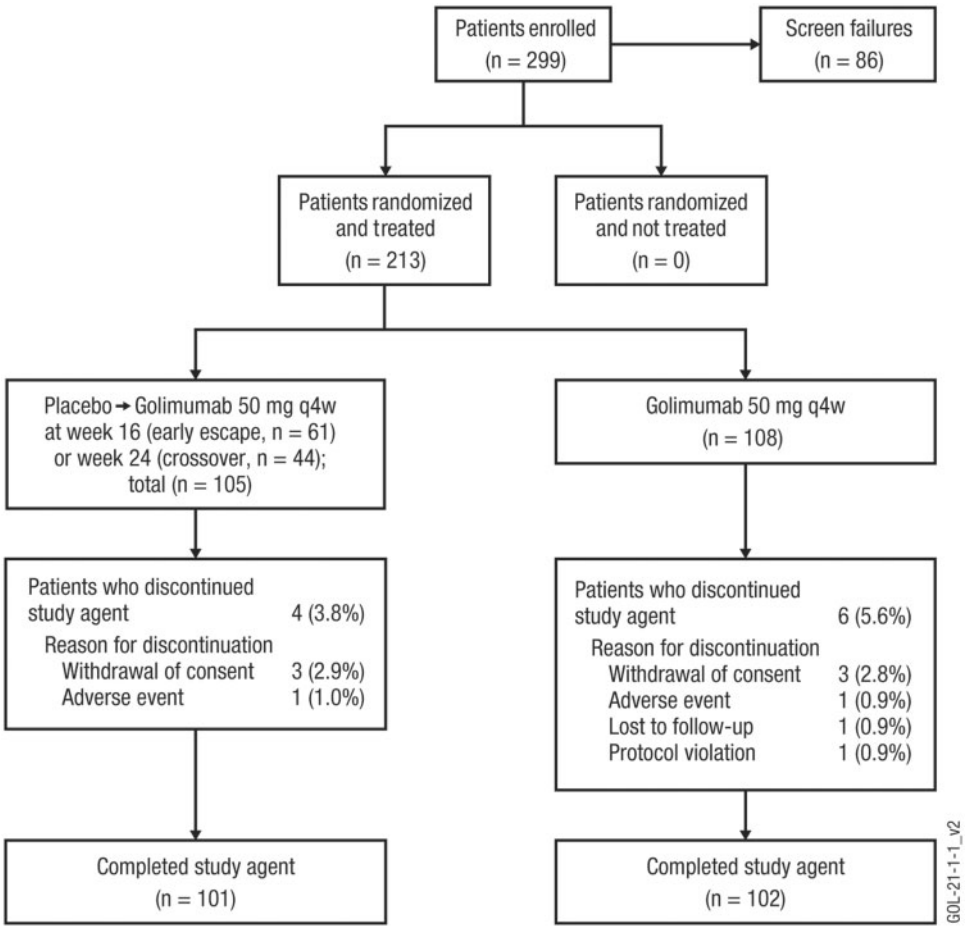
Screening CRP levels were <15 mg/l in 50.9% of patients, with an overall mean CRP of 19.7 (S.D. 20.6 mg/l, reference range <10 mg/l). On average, overall BASDAI (6.5) and BASFI (5.0) scores, both assessed on a scale of 0–10, indicated moderate degrees of disease activity and functional impairment, respectively. The most common baseline AS medications were NSAIDs (69.5%) and SSZ (53.5%). Baseline patient and disease characteristics were generally balanced across randomized treatment groups (Table 1). At baseline, 64 (30.0%) patients showed evidence of latent TB infection (49 of them had a positive PPD skin test). Treatment for latent TB was initiated either before or concomitantly with the first study agent administration according to local guidelines and consistent with methodology employed for the global golimumab clinical development programme [23, 24].

Clinical efficacy

Significantly greater proportions of patients in the golimumab than placebo group achieved an ASAS20 response at week 14 (49.1% *vs* 24.8%, $P < 0.001$) and week 24 (50.0% *vs* 22.9%, $P < 0.001$). At both time points, numerically greater treatment group differences were observed in patients with baseline CRP levels $\geqslant 15$ mg/l *vs* <15 mg/l (Table 2). At week 52, ~70% of all golimumab-treated patients had achieved an ASAS20 response (Fig. 2A).

Significant treatment group differences (golimumab *vs* placebo) were also observed for mean (S.D.) changes from baseline to week 14 in BASFI [−1.26 (2.57) *vs* 0.11 (2.10), $P < 0.001$] and BASMI [−0.42 (0.91) *vs* −0.19 (0.72),

FIG. 1 Patient disposition through week 52



Note that two of the four patients randomized to placebo who discontinued the study agent did so while still receiving placebo. q4w: every 4 weeks.

$P = 0.021$] scores (Table 2). Physical function and range of motion were further improved through week 52, with mean (S.D.) BASFI and BASMI changes from baseline of −2.18 (2.59) and −0.71 (0.92), respectively, in patients who started golimumab treatment at week 16 or 24 and −2.15 (2.54) and −0.76 (1.06), respectively, in patients receiving golimumab for a full year. Also among these two groups of golimumab-treated patients at week 52, 54.9% (50/91) and 55.3% (52/94), respectively, achieved at least a 2 U improvement in the BASFI and 33.3% (34/102) and 40.0% (42/105), respectively, achieved at least a 1 U improvement in the BASMI.

Significantly greater proportions of patients in the golimumab than placebo group achieved low disease activity (ASAS score <2 in each of the ASAS20 domains) at week 14 [15.7% (17/108) *vs* 1.0% (1/105), $P < 0.001$] and week 24 [18.5% (20/108) *vs* 2.9% (3/105), $P < 0.001$; Fig. 2D]. Significantly greater proportions of golimumab- than placebo-treated patients also achieved ASAS40 and ASAS5/6 responses at these time points (Fig. 2B and C, respectively). For all ASAS-based parameters, improvement continued through week 52, with response rates of ~70% for an ASAS20 response (Fig. 2A), ~30% for achievement of an ASAS score <2 (Fig. 2D), 50% for an ASAS40 response (Fig. 2B) and 63% for an ASAS5/6 response (Fig. 2C) among all golimumab-treated patients.

Similarly, significantly greater proportions of golimumab- than placebo-treated patients achieved BASDAI20, 50 and 70 responses at both week 14 and week 24 ($P < 0.001$ for all responses at both time points) and a BASDAI90 response at both week 14 ($P = 0.015$) and week 24 ($P = 0.001$). At week 16 and week 24, numerically higher proportions of golimumab-treated [29.6% (32/108) and 36.1% (39/108), respectively] than placebo-treated [12.4% (13/105) and 14.3% (15/105), respectively] patients achieved a BASDAI score <3. For all BASDAI-based parameters, improvement continued through week 52, with response rates of ~78% for BASDAI20 response (Fig. 3A), 56% for BASDAI50 response (Fig. 3B), 38% for BASDAI70 response (Fig. 3C), 15% for BASDAI90 response (Fig. 3D) and 50% for achievement of a BASDAI score <3 (Fig. 3E) among all golimumab-treated patients.

TABLE 2 Summary of primary and major secondary efficacy endpoints and quality of life assessments among randomized patients

	Placebo	Golimumab 50 mg
Patients randomized, *n*	105	108
ASAS20 at week 14 (1° endpoint), *n* (%)	26 (24.8)	53 (49.1)
P-value *vs* placebo		<0.001
CRP <15 mg/l	17/55 (30.9)	25/57 (43.9)
CRP ⩾15 mg/l	9/50 (18.0)	28/51 (54.9)
ASAS20 at week 24 (major 2° endpoint), *n* (%)	24 (22.9)	54 (50.0)
P-value *vs* placebo		< 0.001
CRP <15 mg/l	15/55 (27.3)	23/57 (40.4)
CRP ⩾15 mg/l	9/50 (18.0)	31/51 (60.8)
BASFI change from baseline to week 14 (major 2° endpoint)		
Mean (S.D.) [median]	0.11 (2.10) [0.18]	−1.26 (2.57) [−0.81]
P-value *vs* placebo		<0.001
BASMI change from baseline to week 14 (major 2° endpoint)		
Mean (S.D.) [median]	−0.19 (0.72) [−0.17]	−0.42 (0.91) [−0.33]
P-value *vs* placebo		0.021
SF-36 score change from baseline to week 14		
PCS, mean (S.D.) [median]	1.59 (6.12) [0.20]	6.25 (7.95) [5.45]
P-value *vs* placebo		<0.001
MCS, mean (S.D.) [median]	0.82 (9.44) [1.50]	3.86 (8.92) [3.55]
P-value *vs* placebo		0.020
SF-36 score change from baseline to week 24		
PCS, mean (S.D.) [median]	2.00 (6.13) [1.70]	6.89 (8.34) [6.60]
P-value *vs* placebo		<0.001
MCS, mean (S.D.) [median]	0.44 (9.79) [0.00]	3.34 (9.31) [3.10]
P-value *vs* placebo		0.019
JSEQ score change from baseline to week 14		
Mean (S.D.) [median]	−0.6 (4.36) [0.0]	−2.5 (5.12) [−2.0]
P-value *vs* placebo		0.013
JSEQ score change from baseline to week 24		
Mean (S.D.) [median]	−0.6 (4.44) [0.0]	−2.8 (4.93) [−2.0]
P-value *vs* placebo		<0.001

ASAS20: at least 20% improvement in the Assessment of SpondyloArthritis international Society response criteria; JSEQ: Jenkins Sleep Evaluation Questionnaire; MCS: mental component summary; PCS: physical component summary; SF-36: 36-item Short Form Health Survey.

HRQoL

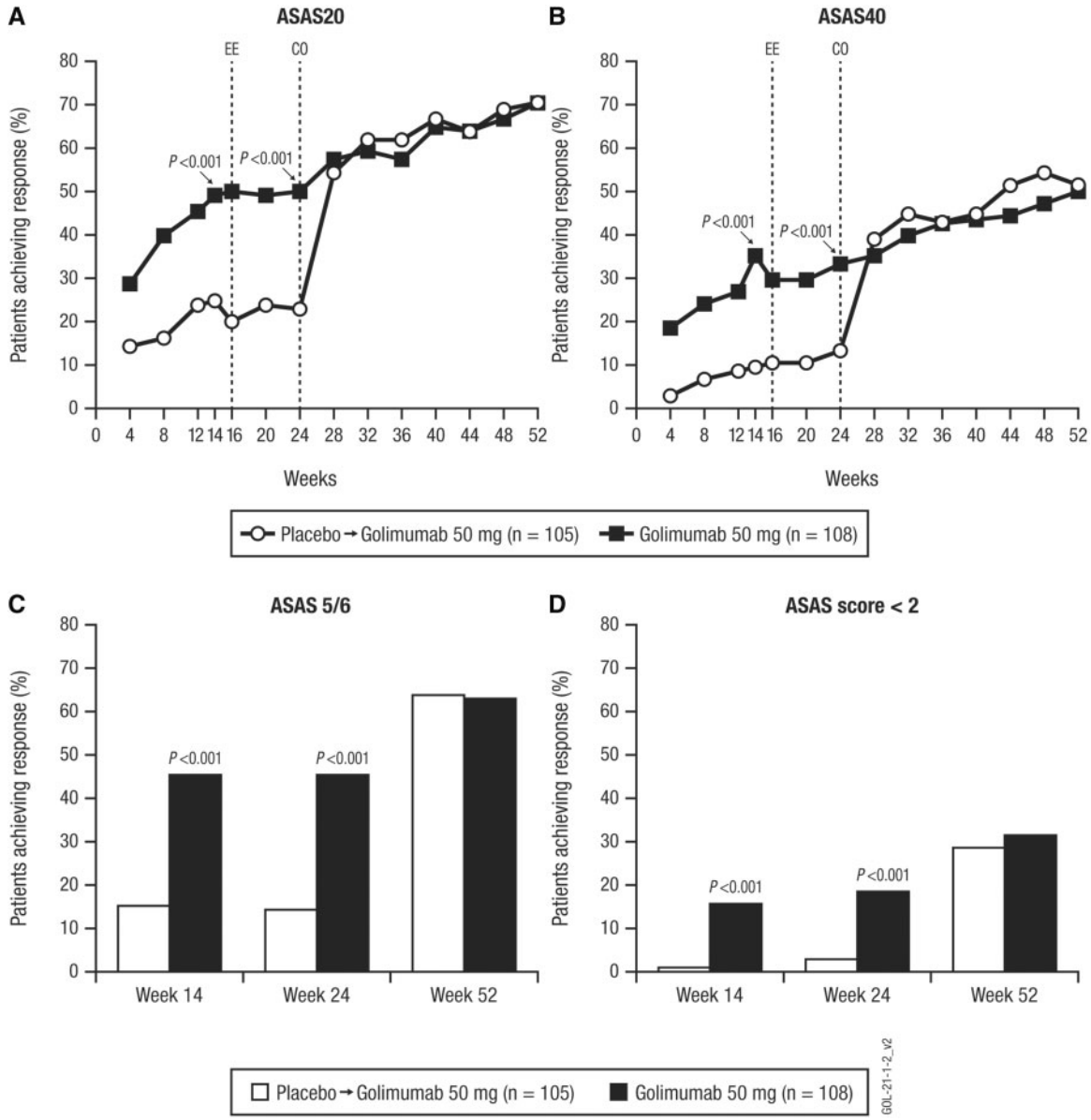
At both week 14 and week 24, median changes from baseline were significantly greater in the golimumab than placebo groups for both the physical component summary (PCS; 5.5 *vs* 0.2 at week 14 and 6.6 *vs* 1.7 at week 24, $P < 0.001$ for both comparisons) and mental component summary (MCS; 3.6 *vs* 1.5, $P = 0.020$ at week 14 and 3.1 *vs* 0.0, $P = 0.019$ at week 24) scores (Table 2). Median SF-36 PCS and MCS scores were further improved at week 52 in the golimumab group (7.6 and 4.5, respectively), with similar median improvements observed in patients who started golimumab at week 16 or 24 (7.5 and 4.3, respectively). Similar improvements were observed in each of the SF-36 subscales, with significant improvement observed in physical functioning, role-physical, bodily pain, general health, vitality, social functioning and mental health at both week 14 and week 24 (data not shown).

Also at week 14 and week 24, the median changes from baseline in JSEQ scores were significantly greater in the golimumab than placebo groups (−2.0 *vs* 0.0 at both time points; $P = 0.013$ at week 14 and $P < 0.001$ at week 24) (Table 2). The median JSEQ score was further improved through week 52 in patients who received a full year of golimumab therapy (−3.0); patients who started golimumab at week 16 or 24 had a median improvement of −2.0 from baseline to week 52.

Golimumab pharmacokinetics and antibodies to golimumab

Following s.c. administration of golimumab 50 mg every 4 weeks, serum golimumab concentrations generally achieved steady state by week 12, at which time the median [interquartile range (IQR)] trough serum golimumab concentration was 0.85 μg/ml (0.61, 1.10). Golimumab exposure was generally maintained through week 24 and week 52, at which time the median (IQR) trough serum golimumab concentrations were 0.88 μg/ml (0.61, 1.15) and 0.83 μg/ml (0.59, 1.22), respectively. No golimumab-treated patients who had

FIG. 2 Proportions of patients achieving ASAS responses through week 52



Responses include (**A**) at least 20% improvement (ASAS20), (**B**) at least 40% improvement (ASAS40) and (**C**) at least 20% improvement in five of six ASAS domains (ASAS5/6), as well as (**D**) an ASAS score <2. ASAS: Assessment of SpondyloArthritis international Society; EE: early escape; CO: crossover.

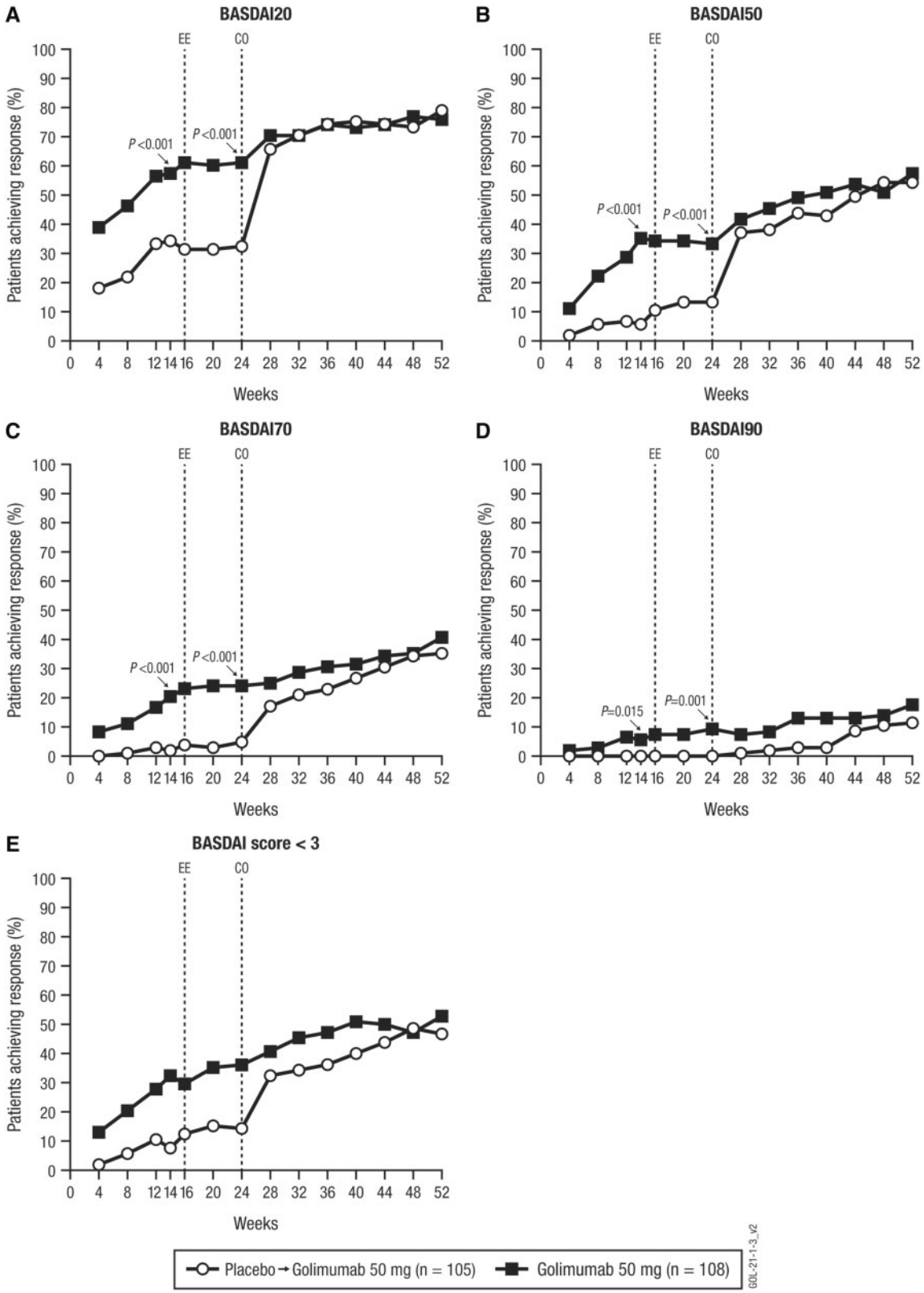
appropriate serum samples tested positive for antibodies to golimumab through week 52.

No apparent differences in median trough serum golimumab concentrations were observed between ASAS20 or ASAS40 responders and non-responders at week 24. Patients who met EE criteria appeared to have median trough serum golimumab concentrations similar to those who did not meet EE criteria, while at week 52 these non-responders appeared to have lower median (IQR) serum golimumab concentrations [0.67 μg/ml (0.52, 1.11)] *vs* responding patients [0.91 μg/ml (0.62, 1.25)]. Given that the apparent discrepancy may be related to the large variability in trough serum golimumab concentrations, no definitive conclusions can be drawn regarding the relationship between golimumab exposure and clinical response based on data reported herein. This variability also precluded conclusions regarding the effect of body weight on drug exposure.

Adverse events

Similar proportions of placebo- and golimumab-treated patients (31.4% *vs* 30.6%, respectively) had AEs through

FIG. 3 Proportions of patients achieving BASDAI responses through week 52



Responses include (**A**) at least 20% (BASDAI20), (**B**) at least 50% (BASDAI50), (**C**) at least 70% (BASDAI70) and (**D**) at least 90% (BASDAI90) improvement, as well as (**E**) a BASDAI score <3. EE: early escape; CO: crossover.

week 16. Through week 24, 34.3% of placebo- and 32.0% of golimumab-treated patients had AEs. Through week 56, 41.2% of golimumab-treated patients reported an AE. At all time points, the most commonly reported AEs were upper respiratory tract infections and liver transaminase elevations (Table 3).

No deaths occurred. Ovarian cancer occurred in a 56-year-old woman with a 10-year history of ovarian cysts. At the time the patient was diagnosed with right ovary mucinous cystadenocarcinoma (day 29), she had received only one dose of golimumab (day 1). The AE was considered serious and not reasonably related to study medication. This patient as well as a patient who received golimumab 50 mg in EE with increased transaminase levels (non-serious) discontinued the study agent. Additional serious AEs included enteritis, tuberculous pleurisy, tibial fracture, uveitis and epistaxis. They each occurred following receipt of at least one golimumab injection, but only the tuberculous pleurisy (see below for additional details) was considered to be possibly related to study agent. No other opportunistic infections were reported.

Sixty-four patients screened positive for latent TB and received treatment. One of these patients, who had a positive skin test but negative Quantiferon test and radiographic findings, developed tuberculous pleurisy during study participation. This 29-year-old male patient received isoniazid therapy for latent TB beginning at study outset and continuing for 9 months. He did not report a prior history of active or latent TB, signs or symptoms of active TB or any recent contact with an individual with active TB. He had developed mild symptoms of upper respiratory tract infection ~2 weeks prior to the first administration of study agent. The event was reported as recovered/resolved ~1 week later. The patient received placebo at weeks 0, 4, 8 and 12, followed by golimumab 50 mg at weeks 16, 20, 24, 28, 32, 36, 40, 44 and 48. Although he had received and completed 9 months of isoniazid therapy, he was hospitalized for severe symptoms of tuberculous pleurisy at ~7 weeks after the last dose of golimumab. Treatment included isoniazid, rifampicin, ethambutol and pyrazinamide, as well as thoracentesis. The outcome of the patient was later noted by the investigator as resolved.

Three patients, all receiving golimumab 50 mg, had an injection site reaction (one patient each with erythema, induration and pruritus). All reactions were mild and none led to study agent discontinuation. No anaphylactic, serum sickness–like or demyelination events were reported through week 56. Five patients (2.4%) had transient elevations of at least three times the upper limit of normal in serum alanine aminotransferase and of aspartate aminotransferase in one patient (0.5%) through week 56. For all of these patients, the abnormal levels had returned to within normal limits by the last follow-up assessment.

Discussion

We conducted this multicentre, phase 3, randomized, double-blind, placebo-controlled study of s.c. golimumab 50 mg every 4 weeks to assess golimumab efficacy and safety in Chinese patients with active AS. At week 14, golimumab-treated patients exhibited significant improvement in signs and symptoms of AS, as well as in physical

Table 3 Summary of AEs through week 24 and week 56 among treated patients

	Week 24				Week 56
		Golimumab			
	Placebo	Placebo → golimumab 50 mg	Golimumab 50 mg	All golimumab 50 mg	All golimumab 50 mg
Patients treated, *n*	105	61	108	169	211
Mean duration of follow-up, weeks	19.1	8.0	23.5	17.9	45.6
Mean exposure, number of administrations	4.7	2.0	5.9	4.5	10.3
Patients with ⩾1 AE, *n* (%)	36 (34.3)	12 (19.7)	42 (38.9)	54 (32.0)	87 (41.2)
Common AEs, *n* (%)		(⩾2% of all golimumab-treated patients)			(⩾3% of patients)
Upper respiratory tract infection	18 (17.1)	2 (3.3)	18 (16.7)	20 (11.8)	35 (16.6)
Transaminases increased	1 (1.0)	3 (4.9)	4 (3.7)	7 (4.1)	10 (4.7)
ALT increased	4 (3.8)	1 (1.6)	5 (4.6)	6 (3.6)	11 (5.2)
LFT abnormal	5 (4.8)	2 (3.3)	4 (3.7)	6 (3.6)	13 (6.2)
AST increased	1 (1.0)	2 (3.3)	3 (2.8)	5 (3.0)	—
Hepatic enzyme increased	1 (1.0)	2 (3.3)	2 (1.9)	4 (2.4)	—
Injections with injection site reactions, *n* (%)	0/498 (0.0)	0/121 (0.0)	1/632 (0.2)	1/753 (0.1)	3/2183 (0.1)
Patients with ⩾1 injection site reaction, *n* (%)	0 (0.0)	0 (0.0)	1 (0.9)	1 (0.6)	3 (1.4)

AEs: adverse events; ALT: alanine aminotransferase; LFT: liver function test; AST: aspartate aminotransferase.

function and range of motion, compared with placebo-treated patients.

Numerically greater treatment group differences were observed in patients with baseline CRP levels $\geqslant$15 mg/l *vs* $<$15 mg/l. Greater golimumab treatment effects among patients with more baseline inflammation have also been observed in the global AS population evaluated in the GO-RAISE trial [12] as well as in AS patients treated with the anti-TNF agent infliximab [25].

While the large variability in trough serum golimumab concentrations precluded definitive conclusions regarding the relationships between golimumab exposure and clinical response and between golimumab exposure and body weight based on data reported herein, the impact of body weight on serum golimumab concentrations in these Chinese patients has been evaluated relative to AS patients who participated in the global golimumab clinical development programme. After categorization of body weight as $\leqslant$70 kg or $>$70 kg, slight differences in median serum golimumab concentrations between Chinese patients and those in the global GO-RAISE study were observed; however, the distributions (IQRs) of serum golimumab concentrations overlapped substantially between the two populations. As a result of this large variability in both Chinese and global AS patients, serum golimumab concentrations through week 24 in patients treated with only golimumab 50 mg were not considered to be different between the populations within each body weight category (data not shown).

Golimumab-treated patients also demonstrated significant improvements in the mental and physical components of quality of life and sleep problems, as assessed using the SF-36 and JSEQ, at week 24 compared with placebo-treated patients. All of these improvements were further enhanced through week 52.

In the first randomized, placebo-controlled study that prospectively evaluated the effect of an anti-TNF agent on sleep disturbance in $>$350 patients with AS (the golimumab GO-RAISE trial) [12], the JSEQ was determined to be an internally consistent and valid tool for assessing sleep disturbance in patients with active AS [26]. Patients in the GO-RAISE trial had significantly disturbed sleep at baseline, with mean/median baseline JSEQ scores of 9–11, representing ~8 days of sleep disturbance in the previous 30 days [26]. In the current trial of Chinese patients with active AS, similar levels of disturbed sleep were observed at baseline (mean/median JSEQ scores of 9–10).

Each point on the JSEQ scale is a categorical representation of the number of days with sleep disturbance, such that a two-category improvement does not represent a specific number of days, but instead demonstrates a level of change representing a significant reduction in sleep disturbance. For example, a score improvement from 2 to 0 would represent a reduction from 4–7 to 0 days with sleep disturbance, while an improvement from 5 to 3 would indicate a reduction from 22–30 to 8–14 days with sleep disturbance [26]. Patients who received golimumab had significantly reduced sleep disturbance after 24 weeks compared with those who received placebo in both the GO-RAISE trial [26] and the current trial. In addition, in the current trial conducted in China, the mean changes observed in JSEQ scores among golimumab-treated AS patients at week 14 (−2.5) and week 24 (−2.8) indicate that golimumab therapy can significantly and expeditiously reduce patient sleep disturbance.

During the 16-week placebo-controlled study period, as well as through week 24, AEs were reported by approximately one-third of both placebo- and golimumab-treated patients. A similar AE reporting rate was observed through week 56 among golimumab-treated patients (41.2%). These AE reporting rates compared favourably with those reported by AS patients evaluated in the GO-RAISE trial of golimumab, in which ~79% of patients reported AEs through week 24 [12]. This finding may be related in part to the younger age of the Chinese AS patients (median age 27–29 years) relative to those of the multinational cohort (median age 38–41 years) [12]. Through week 56, one patient had a malignancy diagnosed (ovarian cancer in a 56-year-old woman with a 10-year history of ovarian cysts) following receipt of only one dose of golimumab. One opportunistic infection was reported: tuberculous pleurisy occurred ~7 weeks after the last dose of golimumab and was successfully treated. Incidentally, this patient had received and completed 9 months of isoniazid therapy for latent TB (positive PPD skin test) before entering the study.

Findings reported herein regarding potential relationships between pharmacokinetics and clinical responses or body weight are limited by the large variability in trough serum golimumab concentrations. This report may also be limited by the relatively small patient population assessed for certain safety events and golimumab immunogenicity. To address one limitation, a publication is planned to assess TB occurrence in Chinese AS and RA patients relative to observations in the global golimumab programme.

We conclude that in Chinese patients with active AS, golimumab significantly reduced the clinical signs and symptoms of disease and improved physical function, range of motion and HRQoL without unexpected safety concerns.

Rheumatology key messages

- Subcutaneous golimumab demonstrated an acceptable safety profile in Chinese patients with active AS.
- Subcutaneous golimumab yielded significant and sustained clinical improvements in Chinese patients with active AS.

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Supplementary data

Supplementary data are available at *Rheumatology* Online.

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