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Original article

Long-term tolerability and efficacy of golimumab in active non-radiographic axial spondyloarthritis: results from open-label extension

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Abstract

Objectives. We report the open-label extension (OLE) of the GO-AHEAD study evaluating the long-term efficacy and safety of golimumab (GLM) in patients with non-radiographic axial spondyloarthritis (nr-axSpA).

Methods. Patients [both GLM- and placebo (PBO)-treated in the double-blind phase] received GLM 50 mg every 4 weeks during the OLE (36-week treatment; additional 8-week safety follow-up; GLM/GLM and PBO/GLM groups). All patients who entered and received $\geq$1 dose of study treatment in the OLE were included in the efficacy and safety analyses. The primary efficacy evaluations were the proportions of patients achieving 20% and 40% improvement in the ASAS criteria (ASAS20 and ASAS40, respectively). Responders' analyses were calculated using a non-responder imputation approach.

Results. Of 198 patients randomised, 189/198 (95.5%) entered the OLE; 174/198 patients (87.9%) completed all visits. Although the proportion of responders increased from week 16 to week 52 in the OLE in both GLM/GLM and PBO/GLM groups, the GLM/GLM group had a higher proportion of responders than the PBO/GLM group throughout the OLE from week 16 to week 52 (ASAS20: 71.1% to 83.9% *vs* 40.0% to 75.0%, respectively; ASAS40: 56.7% to 76.3% *vs* 23.0% to 59.4%, respectively; ASAS partial remission: 33.0% to 53.8% and 18.0% to 45.8%). In the OLE, the overall incidence of AEs was lower in the GLM/GLM *vs* PBO/GLM groups (41.9% and 54.2%).

Conclusions. Sustained improvement in clinical efficacy was observed at 52 weeks in patients with nr-axSpA following GLM treatment. GLM was well tolerated and provided substantial long-term benefits to patients with nr-axSpA.

Trial registration. NCT01453725; United States National Library of Medicine clinical trials database; www.clinicaltrials.gov.

Key words: efficacy, golimumab, non-radiographic axial spondyloarthritis, open-label, safety, spondyloarthritis

Rheumatology key messages

- Following 16 weeks of randomised treatment, open-label treatment with golimumab for 36 weeks produced sustained improvement.
- Patients who switched from placebo to golimumab in the open-label extension experienced noticeable improvement.
- These results demonstrate that golimumab provides substantial long-term benefits in patients with non-radiographic axial spondyloarthritis.

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Introduction

Golimumab (GLM), an anti-tumor necrosing factor (anti-TNF) monoclonal antibody, is approved by the European Medicines Agency (EMA [1]) and the US Food and Drug Administration (FDA [2]) for the treatment of rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and ulcerative colitis, and by the EMA also for non-radiographic axial spondyloarthritis (nr-axSpA). In the 16-week, double-blind, randomised, placebo (PBO)-

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controlled, multicentre, phase 3 GO-AHEAD base study conducted in patients with active nr-axSpA [3], GLM [50 mg every 4 weeks (Q4W), subcutaneous (s.c.)] significantly improved the signs and symptoms of nr-axSpA *vs* PBO. GLM was well tolerated and had a favorable benefit-risk profile. The results of the 44-week open-label extension (OLE) of the GO-AHEAD study, designed to evaluate the long-term safety and efficacy of GLM in patients with active nr-axSpA, are presented here.

Methods

This OLE was the second part of a phase 3, randomised, double-blind clinical study [3] (Fig. 1A). The study protocol (Merck protocol 006; NCT01453725) was approved by the institutional review board or independent ethics committee at each investigational site. The study was performed in accordance with the Declaration of Helsinki and the guidelines for Good Clinical Practice. Written informed consent was obtained from all patients prior to their participation in the study.

The study details have been described previously [3]. Briefly, the study enrolled adult patients (age 18–45 years) who had chronic back pain for $\geq$3 months and were diagnosed with active nr-axSpA for $\leq$5 years' duration. Additionally, patients met the ASAS classification criterion [4] either if they were positive for sacroiliitis on MRI and had at least one of the SpA features or if they were HLA-B27 positive and had $\geq$2 SpA features. Patients had active disease at screening and at baseline, as defined by a spinal pain score of $\geq$4 and a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score of $\geq$4.0 on a 10-cm visual analogue scale (VAS). An additional inclusion requirement was an inadequate response to or intolerance to $\geq$1 NSAID or the inability to tolerate a maximal dose of NSAIDs for 30 days. Key exclusion criteria included radiographic evidence (based on central reading at screening) of grade II sacroiliitis bilaterally or grade III or IV sacroiliitis unilaterally and previous treatment with TNF-targeted therapies.

Patients received GLM (50 mg, s.c.) or PBO at weeks 0, 4, 8 and 12 (double-blind phase). Patients who successfully completed the double-blind phase entered the OLE. All patients (irrespective of their treatment in the double-blind phase) received GLM (50 mg, s.c.) at week 16 and Q4W thereafter, with the final dose administered at week 48. Thus, the OLE population comprised two groups: those who had received PBO during Part 1 and switched to GLM during Part 2 (PBO/GLM) and those who were administered GLM during both parts of the study (GLM/GLM).

After proper training in the s.c. injection technique, patients were allowed to self-inject the medication in the clinic at weeks 16 and 20, and thereafter away from the clinic, if approved by the physician. The efficacy evaluations were conducted until week 52. Patients were followed up until week 60, 12 weeks after the last dose of GLM, via phone call for safety evaluations.

Efficacy endpoints

The proportions of patients achieving 20% and 40% improvement in the ASAS criteria (ASAS20 and ASAS40, respectively) [5] were evaluated at weeks 20, 24, 32, 40 and 52 in both the GLM/GLM and PBO/GLM groups. Additionally, ASAS partial remission (PR) [6] and 50% improvement in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI50) [7] were evaluated at the same timepoints. Other endpoints included the Bath Ankylosing Spondylitis Functional Index (BASFI) score [8], Ankylosing Spondylitis Disease Activity Score (ASDAS) [based on C-reactive protein (CRP) levels] [9], Bath Ankylosing Spondylitis Metrology Index [BASMI (scored on a scale of 0–10)] [10], CRP level, ASAS 5/6 [5], swollen joint count (SJC), tender joint count (TJC), total back pain, BASDAI [7], BASDAI morning stiffness (average of the last two questions of the BASDAI), Physician's Global Assessment (PGA), and the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) [11]. Quality of life (QoL) outcomes were assessed using the Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL) [12], 36-item Short Form Health Survey (SF-36) [13], EuroQol group 5 Dimensions Health Questionnaire (EQ-5D-3L) Index, EQ-5D Health State [14], and Work Productivity and Activity Impairment (WPAI) [15] at weeks 16 and 52.

Safety

Safety evaluations included monitoring of adverse events (AEs), vital signs, physical examination, and serum chemistry and hematology throughout the study (up to week 60). AEs of clinical interest included elevated aspartate transaminase (AST) or alanine transaminase (ALT) [$\geq$3 $\times$ upper limit of normal (ULN)], elevated bilirubin ($\geq$2 $\times$ ULN) with alkaline phosphatase ($<$2 $\times$ ULN), as well as monitoring of clinically significant opportunistic infections, tuberculosis and hypersensitivity reactions.

Immunogenicity

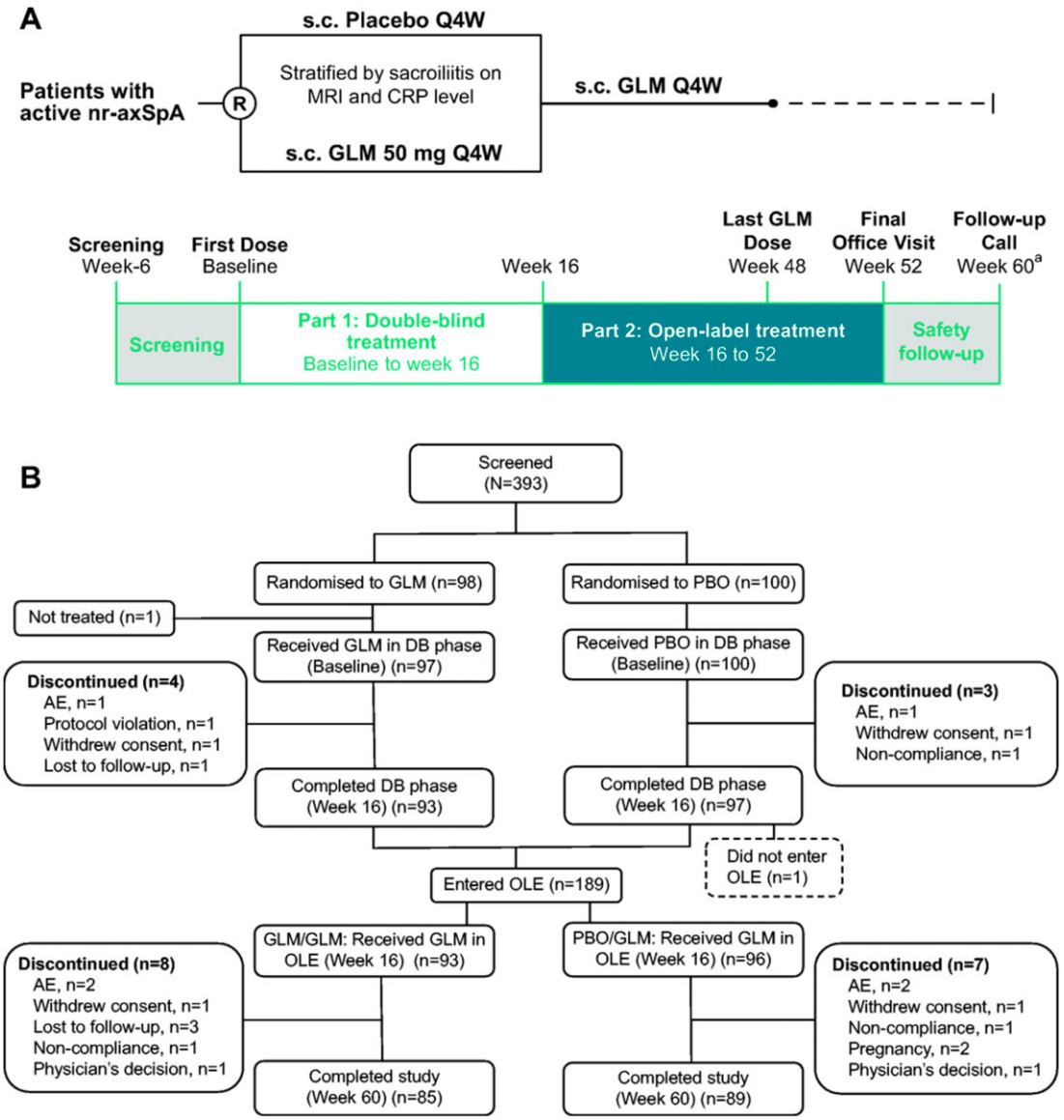
Antibodies to GLM and trough GLM concentrations were determined from serum samples collected at baseline, day 1, week 16 and week 52.

Statistical analysis

All patients who received $\geq$1 dose of study treatment in the OLE were included in the efficacy and safety analyses.

No formal hypotheses were tested in the OLE. Prespecified descriptive statistics of the efficacy endpoints (counts and percentages for binary-outcome-type variables such as ASAS20, ASAS40 and ASAS PR) were calculated by treatment group (GLM/GLM and PBO/GLM), using a non-responder imputation (NRI) approach, which assigns a value of 'non-response' for visits where all four components were missing. If 1–3 components were missing, an LOCF was applied for that component. For BASDAI50, if three or more of the five components of BASDAI were missing at a post-baseline visit, then last observation carried forward

FIG. 1 (**A**) Study design and (**B**) CONSORT diagram showing trial disposition



(**A**) CRP: C-reactive protein; GLM: golimumab; MRI: magnetic resonance imaging; Q4W: every 4 weeks; R: randomisation; s.c.: subcutaneous; nr-axSpA: nonradiographic axial spondyloarthritis. [a]For patients who discontinued early, safety follow-up was 12 weeks after the last dose of trial medication. (**B**) AE: adverse event; DB: double-blind; GLM: golimumab; OLE: open-label extension; PBO: placebo.

imputation was used for that visit value. For continuous variables, observed data were used in the analyses and summaries, as prespecified in the protocol. ASDAS was calculated only when all the components were available. For all other continuous endpoints [i.e. BASDAI inflammation score, BASFI score, BASMI score, MASES score, PGA measured with visual analogue scale (VAS), SJC, and TJC], only the observed data were used in the analyses and summaries; no missing data were imputed.

Disease activity was characterised as low disease activity (ASDAS <2.1) and inactive disease (ASDAS <1.3) in a *post hoc* analysis using NRI [16]. The pre-specified responder analyses were conducted with the denominators as per the size of the treatment groups at the beginning of the OLE only, excluding subjects who did not enter the OLE. In a *post hoc* analysis, performed using an alternative approach, the denominators were the number of subjects who entered the double-blind phase at week 0 in the GLM/GLM group instead of those who entered the OLE only. For the pre-specified responder analyses, sustainability of response was evaluated descriptively by comparing the percentages of responders after week 16 to the percentage at week 16.

Sustainability was also assessed in a *post hoc* analysis by evaluating 'loss of acceptable status', defined as ASDAS >2.1 status at two consecutive visits in the OLE, after achieving ASDAS <2.1 at week 16. The proportion of patients who did not achieve ASDAS <2.1 at the end of part 1 was summarized; of these patients, the proportion that went on to achieve ASDAS <2.1 at the end of part 2 was also summarised. Subgroup analysis included evaluation of efficacy endpoints and overall AEs in patients with objective signs of inflammation [high CRP levels (>ULN, 9 mg/l) and/or evidence of sacroiliitis on magnetic resonance imaging (MRI) at baseline (CRP+ and/or MRI+ subgroup) *vs* normal CRP levels (≤9 mg/l) and no evidence of sacroiliitis on MRI at baseline (CRP-neg and MRI-neg subgroup)].

Safety endpoints were summarised descriptively.

Results

Patient disposition

In total, 198 patients were randomised to either s.c. GLM 50 mg or PBO; 189 (95.5%) patients were included in the OLE (GLM/GLM group, 93; PBO/GLM group, 96; Fig. 1B). Of these 189 patients, 153 were in the CRP+ and/or MRI+ subgroup (GLM/GLM group, 76; PBO/GLM group, 77), while a small number of patients ($n = 36$) were negative for objective signs of inflammation as per both CRP and MRI.

Overall, 174/198 randomised patients (87.9%) completed both parts (double-blind phase and OLE) of the study (GLM/GLM group, 85; PBO/GLM group, 89; Fig. 1B).

Baseline characteristics

Both treatment groups had similar baseline demographics, except for gender, as previously reported [3]. Baseline characteristics of the CRP+ and/or MRI+ subgroup were consistent with those of the overall study population [3].

Exposure and adherence

The median (Q1, Q3) GLM concentration at week 52 in the OLE was comparable between patients in the GLM/GLM group [0.836 (0.383, 1.31) μg/ml] and PBO/GLM group [0.686 (0.425, 1.11) μg/ml]. This was consistent with the median (Q1, Q3) concentration observed at week 16 in the double-blind phase of the study [0.768 (0.448, 1.32) μg/ml] for the GLM-treated patients. The adherence rate (defined as the total number of doses taken divided by the total number of doses the patient was supposed to take during the treatment period) was 99% in the OLE.

Clinical efficacy

In the GLM/GLM group, the ASAS20 responders increased from 71.1% (69/97 at week 16) to 83.9% (78/93 at week 52) in the OLE (Fig. 2A). In the PBO/GLM group, after patients switched to GLM, the ASAS20 responders increased from 40.0% (40/100 at week 16) to 75.0% (72/96 at week 52) in the OLE. Consistent with this, the ASAS40 responders increased in both the GLM/GLM and PBO/GLM groups from week 16 to week 52 in the OLE [GLM/GLM: 55/97 (56.7%) to 71/93 (76.3%); PBO/GLM: 23/100 (23.0%) to 57/96 (59.4%)] (Fig. 2B). The proportion of patients with BASDAI50 response also increased from week 16 to week 52 in the OLE in both the GLM/GLM [56/97 (57.7%) to 77/93 (82.8%)] and PBO/GLM [30/100 (30.0%) to 61/96 (63.5%)] groups (Fig. 2C). Similarly, the ASAS PR also increased from week 16 to week 52 in the OLE in both the GLM/GLM [32/97 (33.0%) to 50/93 (53.8%)] and PBO/GLM [18/100 (18.0%) to 44/96 (45.8%)] groups (Fig. 2D).

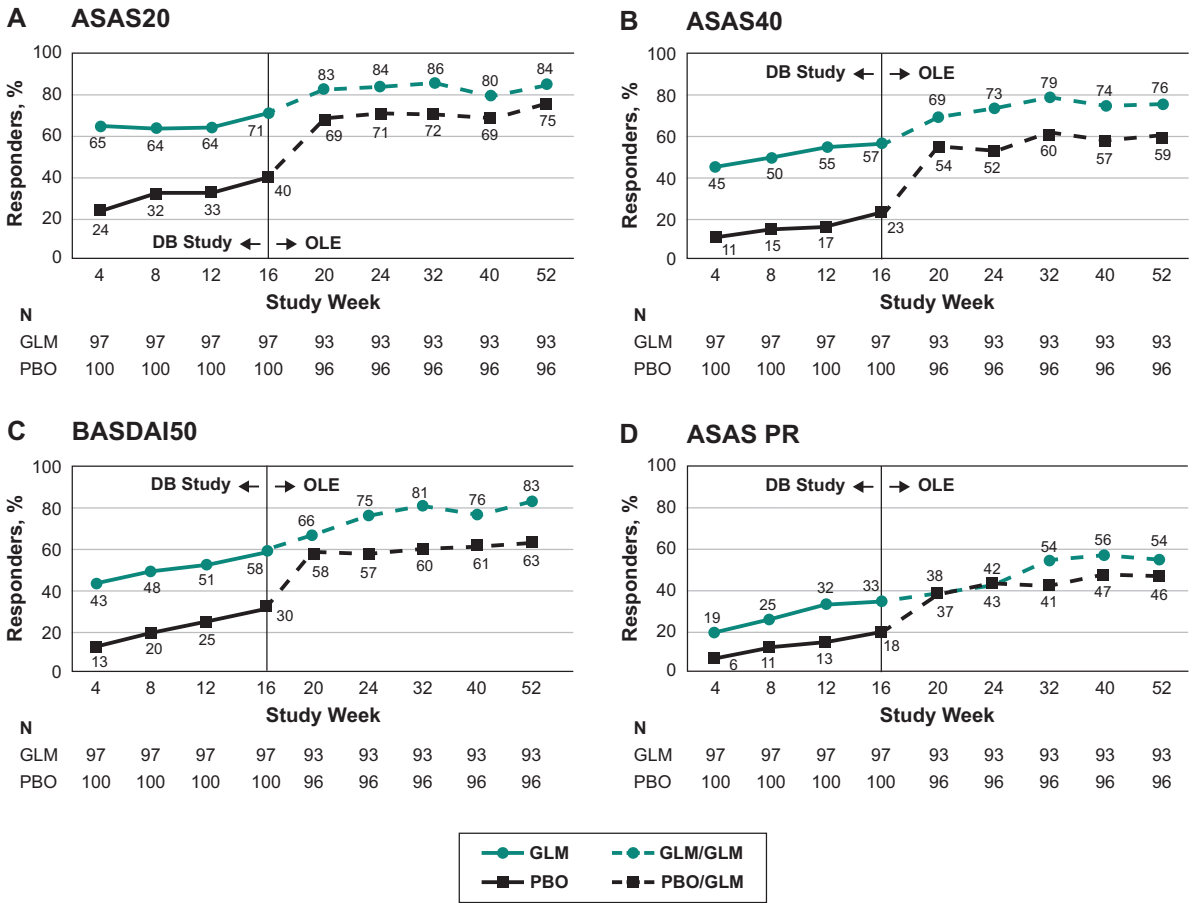
Patient dropout throughout the study (in both double-blind phase and OLE) had minimal impact on the efficacy endpoints measured using non-responder analyses, as shown by results from the *post hoc* analysis of the GLM/GLM group using the denominator based on the original number of subjects entering the double-blind phase at week 0 ($n = 97$). In this *post hoc* analysis, the results did not change materially; in the OLE, ASAS20 response increased from 71.1% (69/97 at week 16) to 80.4% (78/97 at week 52), ASAS40 response increased from 56.7% (55/97 at week 16) to 73.2% (71/97 at week 52), BASDAI50 response increased from 57.7% (56/97 at week 16) to 79.4% (77/97 at week 52), and ASAS PR increased from 33.0% (32/97 at week 16) to 51.5% (50/97 at week 52).

Overall, for ASAS20, ASAS40, BASDAI50 and ASAS PR, in the OLE, the proportions of responders in the GLM/GLM group continued to increase from week 16 to week 32, after which these responses generally plateaued until the end of the efficacy assessment period at week 52. The PBO/GLM group showed notable improvements in ASAS responses in the OLE starting at week 20, after switching to GLM at week 16.

In the CRP+ and/or MRI+ subgroup [$n = 153$ (GLM/GLM, $n = 76$; PBO/GLM, $n = 77$)], the proportion of ASAS20 responders increased in the GLM/GLM group from 76.9% (60/78) at week 16 to 85.5% (65/76) at week 52 in the OLE. In the PBO/GLM group, after patients switched to GLM, the proportion of ASAS20 responders increased from 37.5% (30/80) at week 16 to 75.3% (58/77) at week 52. Consistent with this, the proportion of ASAS40 responders increased in both the GLM/GLM and PBO/GLM groups from week 16 to week 52 [GLM/GLM: 47/78 (60.3%) to 60/76 (78.9%); PBO/GLM: 18/80 (22.5%) to 46/77 (59.7%)].

In the CRP-neg and MRI-neg subgroup [$n = 36$ (GLM/GLM, $n = 17$; PBO/GLM, $n = 19$)], the proportion of ASAS20 responders increased in the GLM/GLM group from 47.4% (9/19) at week 16 to 76.5% (13/17) at week 52 in the OLE. In the PBO/GLM group, after patients switched to GLM, the ASAS20 responders increased from 50.0% (10/20) at week 16 to 73.7% (14/19) at week 52. Consistent with this, the proportion of ASAS40 responders increased in both the GLM/GLM and PBO/GLM groups from week 16

FIG. 2 Proportion of responders over the study duration by endpoint



(**A**) ASAS20, (**B**) ASAS40, (**C**) BASDAI50 and (**D**) ASAS PR. NRI approach was used for ASAS20, ASAS40 and ASAS PR responder analysis; LOCF approach was used for BASDAI50. ASAS: Assessment of SpondyloArthritis international Society; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; DB: double-blind; GLM: golimumab; NRI: non-responder imputation; OLE: open-label extension; PBO: placebo; PR: partial remission. DB study (up to week 16): GLM, n = 97; PBO, n = 100. OLE (weeks 20–52): GLM/GLM, n = 93; PBO/GLM, n = 96.

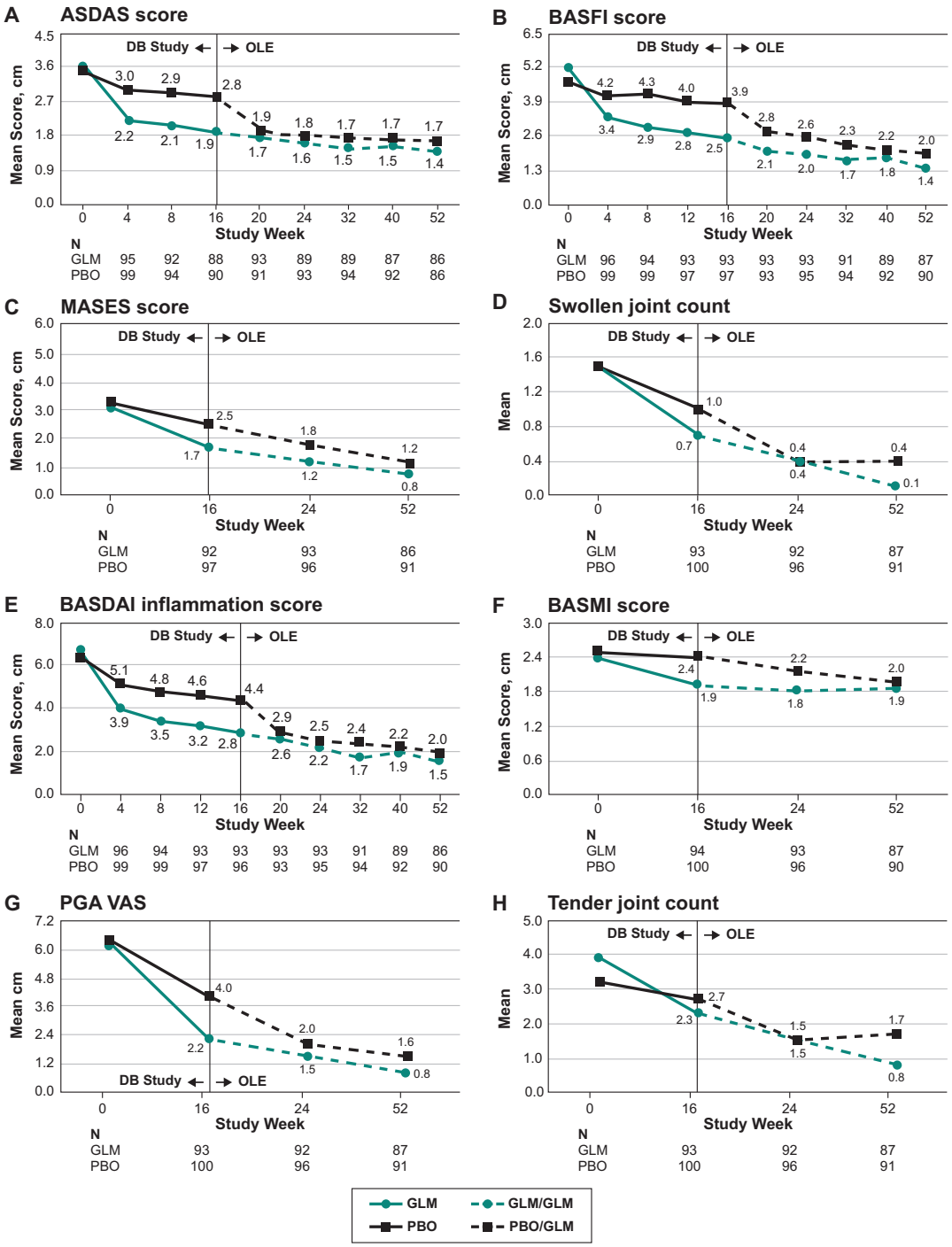
to week 52 [GLM/GLM: 8/19 (42.1%) to 11/17 (64.7%); PBO/GLM: 5/20 (25.0%) to 11/19 (57.9%)].

Post hoc analysis of disease activity states using the NRI approach showed that the proportion of patients in the OLE with ASDAS <2.1 increased from 57.5% (56/97) at week 16 to 80.6% (75/93) at week 52 in the GLM/GLM group, with >70% of patients in this group having achieved ASDAS <2.1 by week 20 (Supplementary Figure S1, available at *Rheumatology* online). In the PBO/GLM group, the proportion of patients in the OLE with ASDAS <2.1 increased from 24% (24/100) at week 16 to 63.5% (61/96) at week 52 (Supplementary Figure S1, available at *Rheumatology* online). In addition, in the PBO/GLM group, after switching to GLM, 54.0% (41) of the 76 patients in the OLE who had not achieved ASDAS <2.1 at week 16 achieved ASDAS <2.1 at week 52. In the GLM/GLM group, 63.4% (26) of the 41 patients in the OLE who had not achieved ASDAS <2.1 at week 16 achieved ASDAS <2.1 at week 52. The proportion of GLM/GLM patients in the OLE with inactive disease (ASDAS <1.3) increased from 29.9% (29/97) at week 16 to 52.7% (49/93) at week 52, while the proportion of PBO/GLM patients in the OLE increased from 12% (12/100) at week 16 to 44.8% (43/96) at week 52 (Supplementary Figure S1, available at *Rheumatology* online). All other clinical endpoints, including the BASFI, also demonstrated similar improvements in both the GLM/GLM and PBO/GLM groups in the OLE (Fig. 3, Supplementary Table S1, available at *Rheumatology* online).

Sustainability

The efficacy responses observed in patients in the GLM/GLM group from week 16 were durable and were maintained through week 52 in the OLE. For ASAS20, of the 69 responders at week 16, 94.2% were also responders at week 52 in the OLE. For ASAS40, of the 55 responders at week 16, 89.1% were also responders at week 52 in the OLE. Similarly, of the 56 BASDAI50 responders at week 16, 91.1% maintained their BASDAI50 response at week 52 in the OLE, and of the 32 patients who were in ASAS PR at week 16, 87.5% sustained their ASAS PR

Fig. 3 Continuous efficacy endpoints over the study duration



(**A**) ASDAS score, (**B**) BASFI score, (**C**) MASES score, (**D**) swollen joint count, (**E**) BASDAI inflammation score, (**F**) BASMI score, (**G**) PGA VAS and (**H**) tender joint count. ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; DB: double-blind; GLM: golimumab; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; OLE: open-label extension; PBO: placebo; PGA: Physician's Global Assessment; VAS: visual analogue scale. Denominators for analysis of DB phase (weeks 0–16): GLM, $n = 97$; PBO, $n = 100$. Denominators for OLE (weeks 20–52): GLM/GLM, $n = 93$; PBO/GLM, $n = 96$. The n for each time point is shown in each panel.

status at week 52 in the OLE. Of the patients with ASDAS <2.1 at week 16 [GLM, $n = 56$ (70%); PBO, $n = 24$ (30%)], loss of acceptable status was observed in six (10.7%) and one (4.2%) patient in the GLM/GLM and PBO/GLM groups, respectively in the OLE.

QoL endpoints

The mean changes from baseline in QoL endpoints in the OLE in the GLM/GLM at week 52 showed similar or better improvement than that observed at week 16. Patients in the PBO/GLM group in the OLE experienced a marked improvement in all QoL endpoints by week 52 after switching from PBO to GLM at week 16 (Fig. 4, Supplementary Table S2). The increases in the SF-36 physical function measure (Supplementary Table S2) were consistent with the improvement seen in BASFI mentioned above. Improvements in WPAI were noted during the OLE in patients who received GLM (Fig. 5).

Safety

In the OLE, 91 (48.1%) of the 189 patients who received the study medication reported AEs (Table 1). The incidence of overall AEs was lower in patients in the GLM/GLM group *vs* patients in the PBO/GLM group (41.9% and 54.2%, respectively). A total of 28 (14.8%) patients had drug-related AEs (GLM/GLM, $n = 12$; PBO/GLM, $n = 16$). The most common treatment-related AEs included nasopharyngitis (GLM/GLM, $n = 2$; PBO/GLM, $n = 3$) and upper respiratory tract infection and headache (GLM/GLM, $n = 2$; PBO/GLM, $n = 2$, each) (Table 1). Four participants in the PBO/GLM mg group had injection site reactions (data not shown).

Three (3.2%) patients in the GLM/GLM group in the OLE had elevated ALT levels; in one of these patients, the ALT elevation was considered to be a severe AE and was associated with other hepatic AEs [elevated AST, GGT, hepatic steatosis, and hepatomegaly (diagnosed via ultrasound); all were considered by the investigator to be not drug related]. Bilirubin levels were elevated in six (6.5%) patients in the GLM/GLM group and two (2.1%) patients in the PBO/GLM group. Extra musculoskeletal manifestation AEs included one case each of iridocyclitis and psoriasis in the PBO/GLM group; in both cases, the patients had prior histories of the respective AEs.

For patients in the OLE who remained on GLM for ~52 weeks (GLM/GLM group), the incidence of overall AEs was 55.7% and incidence of drug-related AEs was 18.6%; 6.2% of patients experienced one or more severe AEs and 3.1% of patients each had serious AEs and discontinuations due to AEs. The severe AEs included one case each of duodenitis, bacterial infection, hyperhidrosis, pruritus, and increased ALT and AST, and two cases of headache in the GLM 50 mg group. All other AEs resolved, except for increased ALT and AST for which the outcome was unknown. No deaths were reported in the study.

Immunogenicity

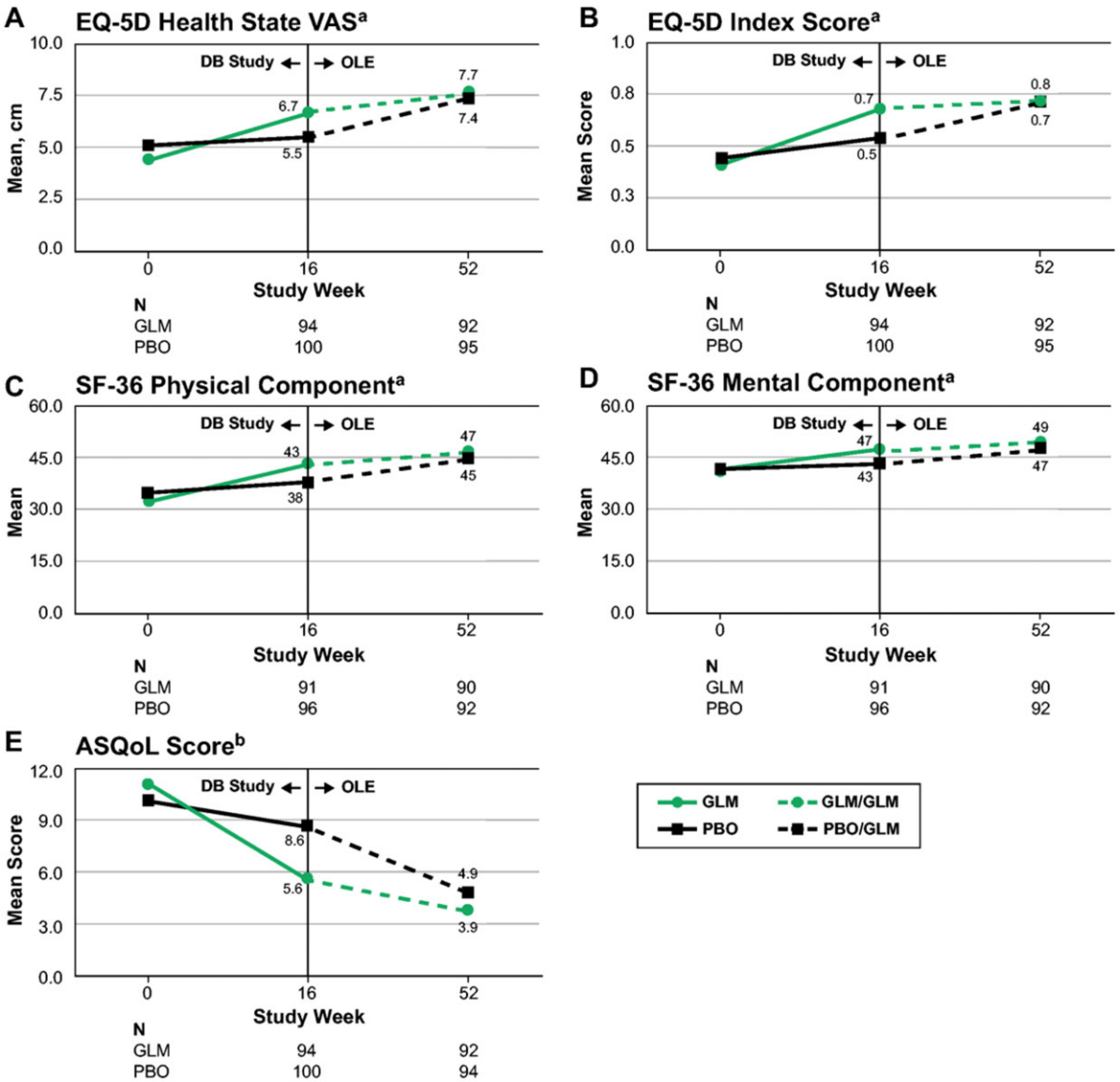
The incidence of patients in the OLE with at least one serum sample positive for antibodies to GLM through week 52 was 9.2% (9/98) in the PBO/GLM group and 5.3% (5/95) in the GLM/GLM group. The titers of the 14 patients positive for antibodies to GLM ranged from 1:10 to 1:1280; they also tested positive for neutralising antibodies. Three patients who were positive for antibodies to GLM discontinued the study (i.e. by week 32, week 40 and week 44, respectively) and showed GLM concentrations below the lowest limit of quantification. All three discontinuations were due to withdrawal by subject.

Discussion

In this OLE of the phase 3 GO-AHEAD study, GLM was found to be efficacious and generally tolerable for long-term use up to 1 year in patients with active nr-axSpA. Overall, for the ASAS20, ASAS40, BASDAI50 and ASAS PR endpoints, the proportions of responders in the GLM/GLM group still increased from week 16 to week 32 and were then generally sustained through week 52. Our results are consistent with the published literature on other anti-TNF therapies. In the phase 3 ABILITY-1 trial, adalimumab was associated with sustained clinical and functional improvements over a 3-year treatment period in patients with nr-axSpA [17]. Patients with early active nr-axSpA on etanercept in the phase 3 EMBARK study showed improvement from week 12 in the clinical composite measures; health and productivity outcomes were sustained up to 48 weeks of treatment [18]. In the RAPID-axSpA phase 3 trial, certolizumab pegol demonstrated improvements in the clinical efficacy outcomes at 24 and 96 weeks that were sustained through 4 years of treatment [19]. Taken together, these results imply that long-term anti-TNF treatment has the potential to improve clinical outcomes. However, comparative head-to-head trials between these agents are lacking, with no recommended hierarchy for the first prescription of an anti-TNFα agent in the treatment of nr-axSpA [20].

Clinical improvements in ASAS20 and ASAS40, albeit smaller than those observed in the CRP+ and/or MRI+ subgroup, were also observed in the CRP-neg and MRI-neg population in the OLE. While these data suggest that patients without objective signs of inflammation at baseline also responded to GLM treatment during the OLE, these results should be interpreted with caution due to the small number of patients in this group ($n = 36$). It should also be noted that this is a population for which neither GLM nor any other anti-TNF is indicated. There is preliminary evidence of some benefit with adalimumab during long-term, open-label extension treatment in such patients [17]. Some active nr-axSpA patients who were CRP/MRI-neg at baseline became positive over the course of follow-up [21]. Such patients could become responsive to anti-TNF therapy.

FIG. 4 Mean scores of QoL measurements over the study duration

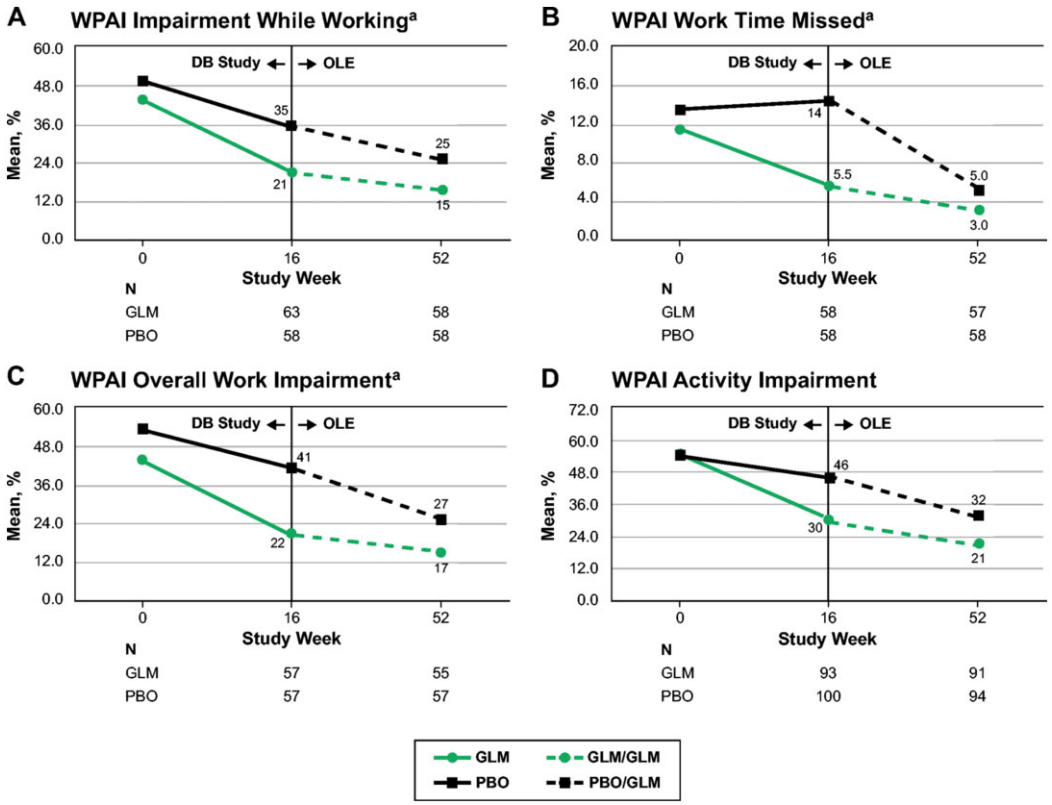


(**A**) EQ-5D Health State VAS, (**B**) EQ-5D Index Score, (**C**) SF-36 Physical Component, (**D**) SF-36 Mental Component, (**E**) ASQoL Score. ASQoL Ankylosing Spondylitis Quality of Life Questionnaire. DB: double-blind; EQ-5D: EuroQol group 5 Dimensions Health Questionnaire; GLM: golimumab; OLE: open-label extension; PBO: placebo; QoL: quality of life; SF-36: 36-item Short Form Health Survey; VAS: visual analogue scale. Denominators for analysis of DB phase (weeks 0–16): GLM, $n = 97$; PBO, $n = 100$. Denominators for OLE (weeks 20–52): GLM/GLM, $n = 93$; PBO/GLM, $n = 96$. The n for each time point is shown in each panel; [a]increase from baseline indicates improvement; [b]decrease from baseline indicates improvement.

In light of recommendations to manage patients according to a treat-to-target approach [22], disease activity was measured *post hoc* using ASDAS targets. Of the patients in the GLM/GLM group achieving low disease activity (ASDAS <2.1) at week 16, ~90% (49/56) showed sustained responses during the extension phase.

Overall, our results indicate that the improvements in composite clinical measures translate into improvements in physical function, QoL and work productivity in the long term. Patients who received GLM throughout the study showed continued improvement in QoL up to week 52. Further, notable improvements occurred in all aspects of WPAI overall, suggesting GLM treatment can be valuable in decreasing the considerable impact of axSpA on employment, which is especially relevant as it affects patients at a relatively young age [23].

FIG. 5 WPAI scores over the study duration



(**A**) Impairment while working, (**B**) Work time missed, (**C**) Overall work impairment, (**D**) Activity impairment. DB: double-blind; GLM: golimumab; OLE: open-label extension; PBO: placebo; WPAI: Work Productivity and Activity Impairment. Denominators for analysis of DB phase (weeks 0–16): GLM, $n = 97$; PBO, $n = 100$. Denominators for OLE (weeks 20–52): GLM/GLM, $n = 93$; PBO/GLM, $n = 96$. The n for each time point is shown in each panel; [a]responses completed only by patients who were employed.

TABLE 1 AEs occurring from week 16 to week 60

Patients with AEs[a] *n* (%)	GLM/GLM (*n* = 93)	PBO/GLM (*n* = 96)	Total (*n* = 189)
Any AE	39 (42)	52 (54)	91 (48)
Treatment-related AEs[b]	12 (13)	16 (17)	28 (15)
Nasopharyngitis	2 (2)	3 (3)	5 (3)
Upper respiratory tract infection	2 (2)	2 (2)	4 (2)
Headache	2 (2)	2 (2)	4 (2)
Serious AEs	2 (2)	3 (3)	5 (3)
Bacterial infection	1 (1)	0	1 (<1)
Duodenitis	1 (1)	0	1 (<1)
Migraine	0	1 (1)	1 (<1)
Uterine polyp	0	1 (1)	1 (<1)
Staphylococcal infection	0	1 (1)	1 (<1)
AEs leading to treatment discontinuation	1 (1)	2 (2)	3 (2)
Acute tonsillitis	1 (1)	0	1 (<1)
Bacterial infection	1 (1)	0	1 (<1)
Hepatitis B	0	1 (1)	1 (<1)
Rhinitis	0	1 (1)	1 (<1)
Deaths	0	0	0

AE: adverse event; GLM: golimumab; PBO: placebo. [a]Includes patients who received ≥1 dose of the study drug. [b]Treatment-related per the investigators and occurring in ≥3 patients.

GLM was generally safe and well tolerated. We did not find any notable differences in the types of AEs between the GLM/GLM and the PBO/GLM treatment groups. No new safety signals were identified in the treatment of nr-axSpA during this OLE.

Some limitations of the present study should be acknowledged. As is the nature of OLE studies, selection bias and a lack of generalisability are issues to consider, because the extension phase did not include patients who discontinued treatment or were lost to follow-up during Part 1. As active inflammation of the SI joints was assessed by MRI only at baseline and week 16, evaluation of MRI changes (inflammation or structural damage) was not possible during the OLE.

Conclusions

Sustained improvements in clinical efficacy, physical function, QoL and productivity were observed over 52 weeks in nr-axSpA patients treated with GLM. Patients who switched from PBO to GLM experienced a noticeable improvement after the switch. Overall, these results demonstrate that GLM is tolerable and can provide substantial long-term benefits to patients with nr-axSpA.

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Data availability statement

The data sharing policy, including restrictions, of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA, is available at http://engagezone.msd.com/ds_documentation.php. Requests for access to the clinical study data can be submitted through the EngageZone site or via email to dataaccess@merck.com.

Supplementary data

Supplementary data are available at *Rheumatology* online.

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