

SYNOPSIS

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<u>Name of Sponsor/Company</u>	Janssen Research and Development, LLC*
<u>Name of Finished Product</u>	SIMPONI®
<u>Name of Active Ingredient(s)</u>	Golimumab

Protocol No.: C0524T18

Title of Study: A Phase 3 Multicenter, Randomized, Placebo-controlled, Double-blind Study to Evaluate the Safety and Efficacy of Golimumab Maintenance Therapy, Administered Subcutaneously, in Subjects with Moderately to Severely Active Ulcerative Colitis

Study Name: PURSUIT – Maintenance

EudraCT Number: 2006-003399-37

NCT No.: NCT00488631

Clinical Registry No.: CR014179

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Study Centers: 251 sites

Publication (Reference): None

Study Period: First subject in: 28 Sep 2007 and last subject last visit: 24 Oct 2011
Database lock: 17 Nov 2011

Phase of Development: 3

Objectives:

Primary Objectives

1. To evaluate the efficacy of 2 SC maintenance dose regimens of golimumab in maintaining clinical response through Week 54 in subjects with moderately to severely active ulcerative colitis (UC) who achieved clinical response with golimumab in 1 of the induction studies, C0524T16 or C0524T17.
2. To evaluate the safety of 2 SC maintenance dose regimens of golimumab in subjects with moderately to severely active UC.

Secondary Objectives

1. To evaluate the efficacy of golimumab maintenance dose regimens in maintaining clinical remission at Week 30 and Week 54.
2. To evaluate the efficacy of golimumab maintenance dose regimens in maintaining mucosal healing at Week 30 and Week 54.
3. To evaluate the efficacy of golimumab maintenance dose regimens in maintaining clinical remission at Week 30 and Week 54 for subjects in clinical remission at Week 0 of this study.
4. To evaluate the efficacy of golimumab maintenance dose regimens in achieving clinical remission and eliminating corticosteroid use at Week 54 among subjects receiving concomitant corticosteroids at Week 0 of this study.

Methods:**Study Design and Populations**

This was a Phase 3, multicenter, placebo-controlled, double-blind, parallel-group, randomized-withdrawal study. The last administration of study agent in the main study was at Week 52 and the final efficacy and safety evaluations in the main study were at Week 54. This CSR reports data through Week 54.

Subjects who were in clinical response to golimumab at Week 6 in C0524T16 or C0524T17 (ie, the target population) were randomized in a 1:1:1 ratio at Week 0 of this study to receive 1 of the following maintenance treatment regimens administered subcutaneously (SC) every 4 weeks (q4w) through Week 52: placebo, golimumab 50 mg, or golimumab 100 mg.

Subjects who were in clinical response to placebo and subjects who were not in clinical response to golimumab or placebo at Week 6 in C0524T16 or C0524T17 were not randomized but were eligible to be enrolled in the study (ie, the nonrandomized group) and received the following treatment regimens: placebo induction responders → placebo q4w through Week 52, placebo induction nonresponders → golimumab 100 mg q4w through Week 52, and golimumab induction nonresponders → golimumab 100 mg q4w through Week 52.

Subjects who successfully completed treatment (through Week 52) and the Week 54 safety and efficacy evaluations and who, in the opinion of the investigator, might benefit from continued treatment were eligible to participate in a study extension. The study extension began at Week 54 and is to continue through Week 228 or until marketing authorization is obtained for golimumab in the treatment of UC, or until a decision is made not to pursue an indication in UC, whichever occurs first.

Dose Adjustment

Subjects in the target population who subsequently lost response at any time during the study had their golimumab dose adjusted as follows:

- Placebo: Received golimumab 100 mg q4w
- Golimumab 50 mg: Rerandomized to receive golimumab 50 mg or 100 mg q4w
- Golimumab 100 mg:
 - Prior to the implementation of Protocol Amendment 3, subjects were rerandomized to receive golimumab 100 mg or 200 mg q4w.
 - After the implementation of Protocol Amendment 3, subjects received golimumab 100 mg q4w. Subjects who had been rerandomized to golimumab 200 mg q4w prior to implementation of Protocol Amendment 3 had their dose decreased to golimumab 100 mg q4w.

Among subjects in the nonrandomized group, placebo induction responders who subsequently lost response at any time during this study received golimumab 100 mg q4w. Placebo induction nonresponders and golimumab induction nonresponders were not eligible for a dose adjustment.

Subjects were eligible for a single dose adjustment through Week 52. If, by 16 weeks following the first administration of the adjusted dose, the subject did not show improvement in their UC disease activity, as assessed by the investigator, they were discontinued from study agent administrations.

Number of Subjects:

A total of 1228 subjects were enrolled in C0524T18. The numbers of subjects in each population were as follows:

- 464 subjects were in the target population (ie, were in clinical response to golimumab at Week 6 of an induction study; randomized subjects):
 - 154 subjects randomized to golimumab 50 mg
 - 154 subjects randomized to golimumab 100 mg
 - 156 subjects randomized to placebo

- 764 subjects were enrolled but not randomized (ie, nonrandomized subjects):
 - 129 placebo induction responders who continued to receive placebo
 - 230 placebo induction nonresponders who received golimumab 100 mg
 - 405 golimumab induction nonresponders who received golimumab 100 mg

Diagnosis and Main Criteria for Inclusion:

Subjects were eligible for this study if they received all study agent administrations and completed the Week 6 Mayo score evaluation in 1 of the induction studies, C0524T16 or C0524T17, and completed the Week 0 visit for this maintenance study on the same day as the Week 6 visit of the induction study (unless approval was received from the medical monitor to complete their Week 0 visit within 7 days of the Week 6 visit).

Subjects were not to be enrolled into this study if they increased the dose of their concomitant UC medications since Week 0 of induction study C0524T16 or C0524T17, initiated a concomitant UC medication since Week 0 of an induction study, or had undergone a colectomy (partial or total) or an ostomy (ie, temporary colostomy, permanent colostomy, ileostomy, or other enterostomy) since Week 0 of an induction study. Subjects with signs or symptoms of any of the following were not eligible for enrollment into this maintenance study: a granulomatous infection (including TB), a nontuberculous mycobacterial infection or opportunistic infection; infection with HIV, hepatitis B, or hepatitis C; any malignancy or possible lymphoproliferative disease; congestive heart failure (CHF); systemic lupus erythematosus; or demyelinating disease. Subjects who had a clinically significant infection since Week 0 of an induction study or who had a clinically significant hypersensitivity reaction in an induction study were not eligible for enrollment into this maintenance study.

Test Product, Dose, and Mode of Administration:

Golimumab was supplied as a sterile liquid for SC injection in single-use prefilled syringes. Each single-use prefilled syringe contained either 50 mg (0.5 mL fill of liquid) or 100 mg (1 mL fill of liquid) golimumab in an aqueous medium of histidine, sorbitol, and polysorbate 80 at pH 5.5.

Reference Therapy, Dose, and Mode of Administration:

Placebo was supplied by the sponsor as a sterile liquid for SC injection at a fill volume of 0.5 mL or 1.0 mL in single-use prefilled syringes. Each single-use prefilled syringe contained histidine, sorbitol, and polysorbate 80 at pH 5.5. No preservatives were present.

Duration of Treatment:

Duration of treatment in the main study was 52 weeks.

Criteria for Evaluation:Pharmacology

Evaluations included serum golimumab concentrations and immunogenicity (antibodies to golimumab including neutralizing antibodies).

Efficacy

Evaluations included the Mayo score and partial Mayo score, endoscopy, C-reactive protein (CRP), fecal lactoferrin, and fecal calprotectin. Patient reported outcomes included the Inflammatory Bowel Disease Questionnaire (IBDQ), 36-item short form health survey (SF-36), and the Euro QOL-5D (EQ-5D). Health economics assessments included employment status, impact of disease on daily productivity, time lost from work by subject and caregivers, healthcare resources utilization, UC-related hospitalizations, and surgeries including colectomy.

Safety

Evaluations included AEs and clinical laboratory data (hematology, blood chemistry, ANA and anti-dsDNA antibodies).

Statistical Methods:**Study Information**

All subjects in this maintenance study entered from an induction study. Demographic and baseline disease characteristics from Week 0 of induction study C0524T16 or C0524T17 were summarized for subjects in the target population (ie, were in clinical response to golimumab at Week 6 of an induction study; randomized subjects) and subjects who were enrolled but not randomized (ie, nonrandomized subjects).

Pharmacology

Golimumab PK and immunogenicity (antibodies to golimumab including neutralizing antibodies) summaries were provided separately for randomized subjects and all treated subjects in this maintenance study.

Efficacy

The primary analysis population was subjects randomized at Week 0 of this maintenance study (ie, subjects in clinical response to golimumab induction at Week 0 of this maintenance study as determined by the IVRS), excluding those from sites [REDACTED] and [REDACTED]. All efficacy analyses are based on the primary analysis population with the exception of selected efficacy summaries in nonrandomized subjects.

Primary Endpoint

The primary endpoint was clinical response through Week 54. Clinical response is defined as a decrease from Week 0 of C0524T16 or C0524T17 in the Mayo score by $\geq 30\%$ and ≥ 3 points, with either a decrease in the rectal bleeding subscore of ≥ 1 or a rectal bleeding subscore of 0 or 1. The proportions of subjects in clinical response through Week 54 were summarized and compared between each of the golimumab groups and the placebo group using the CMH chi-square test stratified by clinical remission status at Week 0 (yes or no) in this study and the induction dose factor. A fixed sequence testing procedure was employed to control the overall Type I error rate at the 0.05 level. In this testing procedure, the comparison between the 100 mg group versus the placebo group was first tested at the 2-sided 0.05 level of significance. Only if this test was positive would the 50 mg group be compared with the placebo group at the 2-sided 0.05 level of significance. The study was considered positive if the test involving the 100 mg group was positive, regardless of the result of the test for the 50 mg group.

Major Secondary Endpoints

The major secondary efficacy analyses were only considered if the test between the high maintenance dose (golimumab 100 mg) and placebo was positive for the primary endpoint of clinical response through Week 54. The major secondary analyses are as follows:

1. The proportions of subjects in clinical remission at both Week 30 and Week 54 were summarized and compared between each of the golimumab groups and the placebo group.
2. The proportions of subjects with mucosal healing at both Week 30 and Week 54 were summarized and compared between each of the golimumab groups and the placebo group.
3. Among subjects who were in clinical remission at Week 0 in this study, the proportions of subjects in clinical remission at both Week 30 and Week 54 were summarized and compared between each of the golimumab groups and the placebo group.
4. Among subjects receiving concomitant corticosteroids at Week 0, the proportions of subjects at Week 54 in clinical remission and not receiving concomitant corticosteroids were summarized and compared between each of the golimumab groups and the placebo group.

With the exception of the third major secondary endpoint, analyses of major secondary endpoints were conducted using the CMH chi-square test stratified by clinical remission status at Week 0 (yes or no) in this study and the induction dose factor. For the third major secondary endpoint, a CMH chi-square test stratified by the induction dose factor was used. To control the Type I error rate at the 0.05 (2-sided) significance level, a fixed-sequence testing procedure was applied within each major secondary endpoint and the major secondary endpoints were tested in a hierarchical manner. In this procedure, the 100 mg

group for a major secondary endpoint was tested if the test between the 100 mg group and the placebo group tested positive for the preceding endpoint, regardless of the result of the test between the 50 mg group and the placebo group for the preceding endpoint. The 50 mg group for a major secondary endpoint could not be tested unless the 100 mg group tested positive for the same endpoint and the 50 mg group was positive for the preceding endpoint.

Other Secondary Efficacy Endpoints

For dichotomous endpoints, unless otherwise specified, analyses were conducted using the CMH chi-square test stratified by clinical remission status at Week 0 (yes or no) in this study and the induction dose factor. For continuous endpoints, analyses were conducted using an analysis of covariance or using an analysis of covariance on the van der Waerden normal scores with the Week 0 value, clinical remission status at Week 0 (yes or no) in this study, the induction dose factor, and treatment group as covariates.

Patient Reported Outcomes

For continuous endpoints, an analysis of covariance on the van der Waerden normal scores was used with the Week 0 value, clinical remission status at Week 0 (yes or no) in this study, the induction dose factor and treatment group as covariates.

Safety

Safety summaries are provided for:

- Randomized subjects (ie, the target population) to provide a balance comparison across treatment groups
- Nonrandomized subjects (ie, placebo induction responders, placebo induction nonresponders, and golimumab induction nonresponders)
- All treated subjects, including both randomized and nonrandomized subjects, to provide overall safety across the placebo, golimumab 50 mg, and golimumab 100 mg groups.

RESULTS:

SUBJECT AND TREATMENT INFORMATION

A total of 1228 subjects were enrolled in C0524T18. Of these, 464 subjects were in the target population, with 154 subjects each randomized to golimumab 50 mg and 100 mg, and 156 subjects randomized to placebo. A total of 764 subjects were enrolled but not randomized (ie, nonrandomized subjects): 129 placebo induction responders, 230 placebo induction nonresponders, and 405 golimumab induction nonresponders. In general, subjects received the treatment to which they were assigned, with the exception of 1 nonrandomized subject who was in clinical response to placebo induction and was assigned placebo on entry into this maintenance study but received golimumab 100 mg instead of placebo at Week 32.

Of 464 subjects in the target population, 28.2% discontinued study agent prior to Week 52, with the proportions similar across treatment groups (27.6% and 28.6% in the placebo and combined golimumab groups, respectively). The most common reasons for discontinuation of study agent in the placebo and combined golimumab groups were unsatisfactory therapeutic effect (12.2% and 12.7%, respectively) and AEs (10.9% and 7.8%, respectively). Among subjects in the target population, 12.3% terminated study participation as of Week 54, with the proportions generally comparable across treatment groups (11.5% and 12.7% in the placebo and combined golimumab groups, respectively). The most common reasons for termination of study participation in the placebo and golimumab groups were “Other” and withdrawal of consent.

Of 764 nonrandomized subjects, greater proportions of subjects who were placebo induction nonresponders and golimumab induction nonresponders discontinued study agent (44.8% and 53.3%, respectively) compared with subjects who were placebo induction responders (31.8%) with the most

common reason as unsatisfactory therapeutic effect. Among nonrandomized subjects, 154 terminated study participation as of Week 54; the most common reasons were “Other” and withdrawal of consent.

Demographics, baseline clinical disease characteristics, and the percentage of subjects receiving concomitant UC medications (including corticosteroids, immunomodulatory drugs, and aminosalicylates) were generally comparable across treatment groups among the target population. Results among nonrandomized subjects were generally consistent with those of the target population with the exceptions of gender (more were male), disease severity (more with severe disease [Mayo score of 11 or 12]), and higher median CRP concentrations.

A total of 37.1% (172) of subjects in the target population had a dose adjustment as follows:

- Among subjects randomized to placebo, 48.7% (76 subjects) had a dose adjustment
 - All subjects increased their dose to 100 mg
- Among subjects randomized to 50 mg, 34.4% (53 subjects) had a dose adjustment
 - 28 subjects remained on 50 mg
 - 25 subjects increased their dose to 100 mg
- Among subjects randomized to 100 mg, 27.9% (43 subjects) had a dose adjustment
 - 29 subjects remained on 100 mg
 - 14 subjects increased their dose to 200 mg (3 of these subjects were still receiving 200 mg and had their dose decreased to 100 mg at the time of implementation of Protocol Amendment 3).

A total of 55 subjects who were placebo induction responders (ie, nonrandomized subjects) at Week 6 in C0524T16 or C0524T17 and who subsequently lost response during this study received golimumab 100 mg q4w.

PHARMACOKINETIC, PHARMACODYNAMIC, AND IMMUNOGENICITY RESULTS

- Following maintenance treatment with golimumab 50 mg or 100 mg SC q4w, steady-state was reached after approximately 8 weeks. From Week 8 onward, the median steady-state trough serum golimumab concentrations were 0.69 to 0.83 µg/mL and 1.33 to 1.58 µg/mL in randomized subjects who received golimumab 50 mg and golimumab 100 mg SC maintenance treatment, respectively.
- Following multiple maintenance doses of golimumab 50 mg or 100 mg SC q4w, serum golimumab concentrations were detectable through Week 54 in almost all subjects and were proportional to dose. A smaller proportion of subjects in the golimumab 100 mg group (0.9%-2.2%) relative to those in the golimumab 50 mg group (4.3%-11.2%) had serum golimumab levels below the limit of quantification at preadministration visits from Week 20 through Week 44.
- Within each maintenance dose group (golimumab 50 mg or golimumab 100 mg), subjects reached similar golimumab concentration levels approximately 8 weeks after starting the SC maintenance regimen despite the administration of different IV or SC golimumab induction doses.
- Median serum golimumab concentrations were slightly higher in randomized subjects who weighed < 75 kg compared with subjects who weighed ≥ 75 kg with the equivalent dose.
- Among 1,103 golimumab-treated subjects with appropriate samples for the assessment of antibodies to golimumab, 32 (2.9%) were positive for antibodies to golimumab through Week 54, the majority with low antibody titers (under 1:640). Of the 31 subjects who were positive for antibodies to golimumab and had appropriate samples for NAb assessment, 21 (67.7%) were positive for NAb.

- Among subjects who did not increase their golimumab dose, the proportions of subjects who were positive for antibodies to golimumab were similar between the 50 mg and 100 mg groups (1.6% and 2.1%, respectively). Among subjects who increased their golimumab dose, none of those randomized to the golimumab 100 mg group were positive for antibodies to golimumab, while 8% of subjects randomized to the golimumab 50 mg group were positive for antibodies to golimumab.
- Median serum golimumab concentrations were lower for subjects who were positive for antibodies to golimumab compared with levels in subjects who were negative for antibodies to golimumab.

EFFICACY RESULTS

Efficacy analyses below are based on the primary analysis population.

The primary endpoint was clinical response through Week 54. The proportions of subjects in the primary analysis population who maintained clinical response through Week 54 were greater in the 100 mg and 50 mg groups (50.6% and 47.1%, respectively) compared with the placebo group (31.4%). The comparison between each of the 2 golimumab groups and the placebo group was statistically significant ($p < 0.001$ and $p = 0.010$ for the 100 mg and 50 mg groups, respectively, versus placebo). This study was considered to be a positive study because the 100 mg group was significantly different from the placebo group. The treatment effect of the 100 mg and 50 mg groups versus placebo across demographic, UC disease characteristics, UC-related medication history, concomitant UC medications, and stratification subgroups were generally consistent with that of the primary analysis population. Results for the primary endpoint analysis were robust across multiple prespecified sensitivity analyses: both the 100 mg and 50 mg groups had significantly greater proportions of subjects in clinical response through Week 54 compared with the placebo group (all $p < 0.001$ for 100 mg versus placebo, and all $p < 0.050$ for 50 mg versus placebo).

Results for the major secondary efficacy analyses were as follows:

- The proportions of subjects in clinical remission at both Week 30 and Week 54 were greater in the 100 mg and 50 mg groups (28.6% and 23.5%, respectively) compared with the placebo group (15.4%). The comparison between the 100 mg group and placebo was significant ($p = 0.003$).
- The proportions of subjects with mucosal healing at both Week 30 and Week 54 were greater in the 100 mg and 50 mg groups (43.5% and 41.8%, respectively) compared with the placebo group (26.9%). The comparison between the 100 mg group and placebo was significant ($p = 0.001$).
- Of the approximately 35% of subjects who were in clinical remission at Week 0 of this maintenance study, the proportions who maintained clinical remission (ie, were in clinical remission at both Week 30 and Week 54) were greater in the 100 mg and 50 mg groups (40.4% and 36.5%, respectively) compared with the placebo group (24.1%).
- Of the approximately 54% of subjects who were receiving concomitant corticosteroids at Week 0 of this maintenance study, the proportion in clinical remission and not receiving concomitant corticosteroids at Week 54 was similar in the 100 mg group (22.9%) and greater in the 50 mg group compared with the placebo group (27.8% versus 18.4%, respectively).

Results for other selected clinical and biomarker endpoints were as follows (Note that the analyses of these other secondary endpoints were not controlled for multiplicity; statements of statistical significance for these endpoints are based on nominal p-values.):

- In a post-hoc analysis, the time to loss of clinical remission was longer in the 100 mg and 50 mg groups compared with the placebo group ($p = 0.013$ and $p = 0.207$, respectively). The median time to loss of clinical remission was greater than 54 weeks in the 100 mg group (ie, more than half of the subjects had not met the criteria for loss of clinical remission by Week 54), 52 weeks in the 50 mg group, and 27 weeks in the placebo group.

- A significantly greater proportion of subjects in the 100 mg group (56.1%) and a greater proportion in the 50 mg group (53.8%) maintained clinical remission through Week 30 compared with those in the placebo group (33.3%, $p = 0.018$ for the 100 mg group versus the placebo group).
- A significantly greater proportion of subjects in the 100 mg group (46.1%) and a greater proportion of subjects in the 50 mg group (46.2%) maintained mucosal healing at both Week 30 and Week 54 compared with those in the placebo group (31.5%, $p = 0.021$ for the 100 mg group versus the placebo group).
- The decrease in the Mayo score obtained at Week 0 of this maintenance study was maintained at Week 30 and at Week 54 in the 100 mg and 50 mg groups compared with the placebo group.
- The decrease in the partial Mayo score obtained at Week 0 of this maintenance study was maintained through Week 54 in the 100 mg and 50 mg groups compared with the placebo group.
- The decrease in CRP concentrations at Week 0 of this maintenance study was maintained in the 100 mg group compared with placebo; a similar effect was not observed in the 50 mg group.
- The decreases in the log transformed fecal lactoferrin and fecal calprotectin at Week 0 of this maintenance study were maintained at Week 30 and at Week 54 in the 100 mg group compared with the placebo group; a similar effect was not observed in the 50 mg group.

Results for health-related quality of life were as follows (Note that these analyses were not controlled for multiplicity; statements of statistical significance for these endpoints are based on nominal p-values.):

- Among subjects with a greater than 20-point improvement in IBDQ at Week 0 of this maintenance study from Week 0 of an induction study, significantly greater proportions of subjects in the 100 mg and 50 mg groups maintained the 20-point improvement in IBDQ through Week 54 (41.5% and 44.5%, respectively) compared with subjects in the placebo group (28.2%; $p = 0.032$ and $p = 0.030$, respectively).
- The physical component summary scores of the SF-36 obtained at Week 0 of this maintenance study in the 100 mg and 50 mg groups were maintained through Week 54.
- The EQ-5D scores and EQ VAS obtained at Week 0 of this maintenance study in the 100 mg and 50 mg groups were generally maintained through Week 54.

Results for efficacy and pharmacology endpoints were as follows:

- Among subjects randomized to golimumab, higher proportions of subjects maintaining clinical response through Week 54 and in clinical remission at both Week 30 and Week 54 was associated with increasing serum golimumab concentrations.
- In subjects randomized to golimumab, there was an apparent trend towards lower clinical response in subjects who were positive for antibodies to golimumab, although the number of subjects who were positive for antibodies was limited and a definitive conclusion cannot be reached about the impact of positive antibodies to golimumab on efficacy.

SAFETY RESULTS

Subcutaneous maintenance regimens of golimumab 50 mg and golimumab 100 mg administered q4w through Week 54 were generally well tolerated.

Among randomized subjects:

- The proportions of subjects with AEs were similar across the golimumab treatment groups but were somewhat higher compared with the placebo group; however, the duration of follow-up in the placebo group was notably shorter due to the randomized withdrawal study design. When the safety data were normalized to 100 years of subject follow-up, the incidence of AEs was comparable across treatment groups.
- Similar trends were observed for infections, serious infections, and AEs leading to discontinuation of study agent.

- The proportion of subjects with 1 or more SAEs was higher in the golimumab 100 mg group compared with the placebo and golimumab 50 mg groups; these differences were less remarkable when corrected for subject years of follow-up.
- Colitis ulcerative was the most frequently reported SAE across treatment groups, and was reported for 1.9%, 1.9%, and 3.9% of subjects in the placebo, golimumab 50 mg, and golimumab 100 mg groups. When summarizing events up to the time of dose adjustment, the incidence of colitis ulcerative was comparable across treatment groups: 1.9%, 0.6%, and 1.9%, respectively.
- The safety profile of golimumab was generally consistent in subjects weighing < 75 kg compared with those weighing ≥ 75 kg.

Among nonrandomized subjects, subjects who entered the study and were not in clinical response accounted for the majority of AEs of UC observed in the population of all treated subjects.

Among all treated subjects, the overall safety profile was consistent with that observed in the randomized population.

- Three deaths were reported through Week 54, all in subjects in the golimumab 100 mg group. Causes of death included malnutrition and sepsis; cardiac failure in a subject with a history of thrombosis; and disseminated TB in a subject who was positive for latent TB and was receiving treatment with INH.
- Four malignancies were reported through Week 54, 3 in the golimumab 100 mg group. Of those, 2 (rectal cancer and thyroid cancer) presented as symptoms while the subjects were receiving placebo during induction and the third (lung adenocarcinoma) occurred in a subject with COPD and a 40-year smoking history. The fourth malignancy (breast cancer) occurred in a subject who had received placebo in both induction and maintenance.
- Four cases of active TB were reported through Week 54, all in subjects who had received golimumab. Three cases were reported as disseminated TB and were serious: 2 in the golimumab 100 mg group (1 fatal), and the third in the placebo group in a subject who had received golimumab induction. The fourth case was pulmonary TB in a subject in the golimumab 100 mg group.
- Two serious opportunistic infections were reported through Week 54, 1 cytomegalovirus in the placebo maintenance group in a subject who received golimumab induction and 1 brain abscess with evidence of *Nocardia* in a golimumab 100 mg maintenance subject.
- A small proportion of treated subjects reported injection-site reactions to golimumab administration, which were mild to moderate in intensity, and no serious injection-site reactions were reported. One nonserious AE of delayed Type IV hypersensitivity of moderate intensity was reported.
- No relationship between the development of antibodies to golimumab and injection site reactions in this study was identified.
- Markedly abnormal changes in hematology and chemistry laboratory values were uncommon, with generally unremarkable differences between treatment groups.

STUDY LIMITATIONS

For less common AEs, the overall safety evaluation in this maintenance study was limited by the imbalance in the total number of subjects exposed to each dose regimen (the ratio of the number of subjects exposed to golimumab 100 mg to the number of subjects exposed to golimumab 50 mg was approximately 6:1 and was approximately 3:1 compared with the placebo group). Furthermore, the overall safety evaluation for all treated subjects was confounded by the diversity of subjects in the golimumab 100 mg group, which included golimumab induction responders who were randomized to golimumab 100 mg (n = 154), placebo induction nonresponders (n = 203), golimumab induction nonresponders (n = 405); and subjects who on loss of response received treatment with golimumab 100 mg (n = 157). In contrast, the golimumab 50 mg group only included 154 golimumab induction responders who were randomized to golimumab 50 mg, and the placebo group included 129 placebo induction responders and 156 golimumab induction responders who were randomized to placebo.

CONCLUSIONS

- The SC maintenance dose regimens of golimumab 100 mg and golimumab 50 mg q4w resulted in maintained improvement in UC disease activity following the attainment of clinical response with golimumab induction therapy. The clinical benefit of golimumab 100 mg q4w was more consistently observed across additional measures of efficacy, including the achievement of long-term clinical remission and mucosal healing, in contrast to golimumab 50 mg.
- SC administered maintenance dose regimens of golimumab q4w demonstrated dose-proportional golimumab serum concentrations consistent with previously identified PK characteristics of golimumab. Higher serum golimumab exposures were associated with greater proportions of subjects maintaining clinical response through Week 54 and achieving long-term clinical remission.
- The safety profile of golimumab in these adult subjects with moderately to severely active UC was consistent with the identified safety profile of golimumab in other indications and with that of other anti-TNF therapies. The safety and efficacy data from this study support a favorable benefit/risk profile for maintenance therapy with SC golimumab in the treatment of adults with moderately to severely active UC who initially achieve clinical response with golimumab induction therapy.