Synopsis (C0524T08 GO-REVEAL)

Name of Sponsor/Company: Centocor, Inc	**Associated with Module 5.3 of the Dossier**	
Name of Finished Product: CNTO 148 (golimumab)		
Name of Active Ingredient: CNTO 148 (golimumab)		
Protocol: C0524T08	**EudraCT No.: 2004-003298-10**	
Title of the study: A Multicenter, Randomized, Double-blind, Placebo-controlled Trial of Golimumab, a Fully Human Anti-TNFα Monoclonal Antibody, Administered Subcutaneously in Subjects with Active Psoriatic Arthritis: 24-Week Report		
Principal/Coordinating Investigator(s): [redacted] MD, [redacted] US		
Study Center(s): Subjects were enrolled at 58 centers: 36 in North America (18 in the US and 18 in Canada) and 22 in Europe (5 in Belgium, 10 in Poland, 3 in Spain, and 4 in the UK)		
Publication (reference): None		
Studied Period: 12 Dec 2005/14 May 2007	**Phase of Development:** 3	
Objectives: The primary objective of this trial was to evaluate the efficacy of SC injections of golimumab in subjects with active psoriatic arthritis (PsA) by assessing reduction in signs and symptoms of PsA and inhibition of progression of structural damage. Inhibition of progression of structural damage will be addressed in a later report. The major secondary objectives of this trial were to evaluate the efficacy of golimumab in: 1) achieving sustained arthritis response, 2) improving psoriatic skin lesions, 3) improving physical function, and 4) improving quality of life; and to assess the safety of golimumab in subjects with active PsA.		
Methodology: This was a multicenter, randomized, double-blind, placebo-controlled (through Week 24) study designed to assess the efficacy, safety, and clinical pharmacology of golimumab 50 mg or 100 mg administered as SC injections q4 weeks in adult subjects with active PsA. Subjects are to be treated through Week 48 and followed for routine efficacy and safety assessments through Week 52. The long-term extension of the study starts with the Week 52 study agent injection and ends when the last subject enrolled completes the Week 268 visit. This 24-week report describes the placebo-controlled portion of the study (Weeks 0 to 24).		
Number of Subjects (Planned and Analyzed): Subjects were randomly assigned in a 1:1.3:1.3 ratio to 1 of 3 treatment groups: placebo (n = 110 planned; 113 actual), golimumab 50 mg (n = 143 planned; 146 actual), golimumab 100 mg (n = 143 planned; 146 actual). All 405 subjects were analyzed for safety, efficacy, and health economics, and 154 (of 150 planned) were analyzed for biomarkers.		
Diagnosis and Main Criteria for Inclusion: Subjects eligible for this study were men and women with a diagnosis of PsA for at least 6 months prior to first study agent administration who had active PsA despite current or previous disease-modifying antirheumatic drug (DMARD) or nonsteroidal anti-inflammatory drug (NSAID) therapy, and who had not previously been treated with anti-tumor necrosis factor (TNF) α therapy.		
Test Product, Dose and Mode of Administration, Batch Number: Golimumab was supplied as a sterile liquid for SC injection at a volume of 0.5 mL or 1.0 mL in 2 mL single-use glass vials (lot numbers: D05PJ7456, 6ES39, 6ES3C, D05PJ7455, and 6HS3R). Each vial contained 50 or 100 mg golimumab in an aqueous medium of histidine, sorbitol, and polysorbate 80 at pH 5.5.		
Duration of Treatment: Study agent administered through Week 20		

Synopsis (C0524T08 GO-REVEAL)

Name of Sponsor/Company: Centocor, Inc	**Associated with Module 5.3 of the Dossier**	
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Name of Active Ingredient: CNTO 148 (golimumab)		

Reference Therapy, Dose and Mode of Administration, Batch Number: Placebo, consisting of an aqueous medium of histidine, sorbitol, and polysorbate 80 at pH 5.5, was also supplied as a sterile liquid for SC injection at a volume of 0.5 mL or 1.0 mL in single-use 2 mL glass vials (lot numbers: 6ES14, 6HS2J, 6ES15, D05PJ7457, and D05PJ7458).

Criteria for Evaluation: All efficacy analyses were based on randomized subjects; ie, the intent-to-treat population. Clinical pharmacology and safety analyses were based on subjects who received at least 1 study agent administration.

Pharmacokinetics/Pharmacodynamics: Golimumab pharmacokinetics were evaluated by summarizing serum golimumab concentrations over time, trough golimumab levels in the presence or absence of methotrexate (MTX), and the proportion of subjects with undetectable golimumab concentrations over time. Antibody to golimumab status was reported according to treatment group, including induced antibody titers, the relationship to trough golimumab concentrations, and comparisons with selected efficacy and safety parameters. The effects of golimumab treatment on serum biomarkers relating to inflammation and bone/cartilage metabolism were assessed and correlated with change from baseline in Disease Activity Score (DAS) 28 (using C-reactive protein [CRP]) at Week 14.

Efficacy: The 24-week primary endpoint was American College of Rheumatology (ACR) 20 response at Week 14. Major secondary analyses included ACR 20 response at Week 24, Psoriasis Area and Severity Index (PASI) 75 response at Week 14 in a subset of subjects with ≥ 3% body surface area (BSA) psoriasis skin involvement at baseline, improvement from baseline in HAQ scores at Week 24, and change from baseline in the physical component summary score of the SF 36 at Week 14. In addition, other secondary endpoints related to the signs and symptoms of arthritis, psoriasis, physical function, and quality of life were evaluated. Data for the coprimary endpoint of change from baseline in PsA modified van der Heijde-Sharp (vdH-S) score at Week 24 will be presented in a separate report.

Safety: Safety was assessed by evaluating the incidence and type of adverse events (AEs), including serious AEs (SAEs), reasonably related, severe, or clinically significant AEs, and discontinuations due to AEs; routine clinical laboratory values; the relationship of antibodies to golimumab to selected safety measures; and the development of antinuclear antibodies or anti-double-stranded DNA antibodies.

Health Economics: Resource utilization was evaluated through Week 24.

Statistical Methods: Descriptive statistics, such as the mean, median, standard deviation (SD), range, and the interquartile range for continuous variables, and counts and percentages for categorical variables were used to summarize most data. Pearson's chi-square test was used to compare binary categorical data, and the Cochran-Mantel-Haenszel (CMH) chi square test to compare binary categorical data with stratification (stratified by baseline MTX usage [yes/no]). Analysis of variance (ANOVA) on van der Waerden normal scores (Conover, 1980) with treatment and subject's baseline MTX usage as factors in the model was used to compare continuous data, unless otherwise specified. In the analyses of efficacy endpoints, the first test compared golimumab at any dose (golimumab 50 mg and 100 mg combined) versus placebo. If the results were significant, then pairwise comparisons of golimumab 50 mg versus placebo and golimumab 100 mg versus placebo were made. All statistical testing was 2-tailed, at a significance level of 0.05.

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Name of Sponsor/Company: Centocor, Inc	**Associated with Module 5.3 of the Dossier**	
Name of Finished Product: CNTO 148 (golimumab)		
Name of Active Ingredient: CNTO 148 (golimumab)		

SUMMARY – CONCLUSIONS

Study Population Results: Baseline characteristics were generally well balanced across treatment groups. The majority of subjects were men (60.2%), most were Caucasian (97.0%), with a median age of 47.0 years. Approximately half of the subjects in each treatment group were receiving MTX at baseline. Baseline clinical characteristics were similar across the treatment groups and indicative of subjects with PsA of moderate to severe activity.

Pharmacokinetic/Pharmacodynamic Results:

- **Pharmacokinetics:** Serum golimumab concentrations were detectable throughout treatment in the majority of subjects and proportional to dose. Concentrations achieved steady state by Week 12, with median trough concentrations of 0.4 μg/mL (50 mg only group) and 0.9 μg/mL (100 mg group). Subjects in the 50 mg, but not in the 100 mg treatment group, had generally higher serum golimumab concentrations if receiving MTX than if not receiving MTX at baseline.
- **Antibodies to golimumab**: Antibodies to golimumab were detected in < 5% of subjects receiving golimumab, none of whom were receiving MTX at baseline. Serum golimumab concentrations were greater in those subjects with undetectable antibody status than in either antibody-negative or antibody-positive subjects. Concentrations in antibody-negative subjects were similar to those in antibody-positive subjects. No apparent relationships were noted between the development of antibodies to golimumab and either safety (injection-site reactions) or efficacy.
- **Pharmacodynamics:** Significant decreases in MMP-3, intercellular adhesion molecule1 (ICAM-1), IL-6, vascular endothelial growth factor (VEGF), and IL-8 levels (serum inflammatory markers) were observed 4 weeks after treatment with golimumab. Of these, IL-6, VEGF and IL-8 remained below baseline levels through Week 24. Significant increases in osteocalcin and N-terminal propeptide of Type I procollagen (PINP) and significant decreases in deoxypyridinoline (DPD) levels (serum bone and cartilage markers) were observed 4 weeks after treatment with golimumab, and DPD levels were below baseline levels at Week 24.

Efficacy Results:

- **Primary Endpoint:** The proportion of subjects achieving an ACR 20 response at Week 14 was significantly greater in the combined golimumab group than in the placebo group (47.9% vs 8.8%; $p < 0.001$). Benefit was seen for both the golimumab 50 mg and 100 mg dose, with no evidence of increased benefit at the higher dose and no effect of concomitant MTX use. Efficacy was consistently demonstrated in virtually all baseline demographic, disease characteristic, and medication subgroup analyses.
- **Major Secondary and Other Efficacy Endpoints**: All major secondary endpoints were met for both the golimumab 50 mg and 100 mg groups.

<u>Arthritis evaluations</u>

- ACR 20 response at Week 24 (a major secondary endpoint) was achieved in a significantly greater proportion of subjects in the combined golimumab group (and in each golimumab dose group) than in the placebo group at Week 24 (56.5% vs 12.4%; $p < 0.001$). ACR 20 response with golimumab treatment was noted as early as Week 4.
- ACR 50 and ACR 70 response, Psoriatic Arthritis Response Criteria (PsARC), and Disease Activity Score (DAS) 28 response were achieved in a significantly greater proportion of subjects in the combined golimumab group (and in each golimumab dose group) than in the placebo group at both Week 14 and at Week 24 ($p < 0.001$ for all comparisons).

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- For subjects with dactylitis at baseline, dactylitis severity was significantly improved in subjects in the combined golimumab group compared with subjects in the placebo group at both Week 14 and at Week 24 ($p = 0.010$ and $p = 0.002$, respectively). Subjects with enthesitis in the combined golimumab group (and in each golimumab dose group) also experienced significant improvements in enthesitis score compared with subjects treated with placebo at both Week 14 and at Week 24 ($p < 0.001$ for both comparisons).

Skin and nail evaluations

- PASI 75 was achieved at Week 14 (a major secondary efficacy endpoint) in a significantly greater proportion of subjects with ≥ 3% BSA involvement at baseline in the combined golimumab group (and in each golimumab dose group) than in the placebo group (49.3% vs 2.5%; $p < 0.001$) and maintained through Week 24.
- Nail Psoriasis Severity Index (NAPSI) improvement and improvement in Nail Physician Global Assessment (PGA) were achieved in a significantly greater proportion of subjects with fingernail involvement at baseline in the combined golimumab group (and in each golimumab dose group) than in the placebo group at both Week 14 and at Week 24 ($p < 0.001$ for all comparisons).
- Psoriatic target skin lesion score improvement was achieved in a significantly greater proportion of subjects in the combined golimumab group (and in each golimumab dose group) than in the placebo group at both Week 14 and at Week 24 ($p < 0.001$ for all comparisons).

Impact of Baseline MTX Use

No effect of baseline MTX use on efficacy was seen as measured by the proportions of subjects achieving a ACR 20, ACR 50, or ACR 70 response or the proportions of subjects achieving a PASI 50, PASI 75, or PASI 90 response through Week 24.

Improvement in Physical Function

- HAQ score improvement (and proportions of subjects with meaningful improvement) was significantly greater in the combined golimumab group (and in each golimumab dose group) than in the placebo group at Week 14 and this difference was maintained through Week 24 (a major secondary endpoint; $p < 0.001$ for all comparisons).
- HAQ score improvement was evident as early as the first evaluation at Week 4, with a mean ± SD improvement from baseline of 0.231 ± 0.450 for subjects in the combined golimumab group versus 0.046 ± 0.382 in the placebo group.

Improvement in Quality of Life

- SF-36 Physical Component Summary (PCS) score improvement was significantly greater in the combined golimumab group (and in each golimumab dose group) than in the placebo group at Week 14 (a major secondary endpoint), and this difference was sustained through Week 24 ($p < 0.001$ for all comparisons).
- SF-36 Mental Component Summary (MCS) score improvement was significantly greater in the combined golimumab group (and in each golimumab dose group) than in the placebo group at Week 14, and this difference was sustained through Week 24 ($p = 0.019$ and $p < 0.001$, respectively).

Safety Results:

- **Adverse Events:** Proportions of subjects experiencing at least 1 AE were similar in the golimumab and placebo groups (57.2% and 55.8%) through Week 16, and were also similar through Week 24 despite longer duration of follow-up for golimumab subjects than for placebo subjects. The system-organ class with the highest incidence of AEs was Infections and infestations, with URI, nasopharyngitis and headache as the most frequently reported AEs in the golimumab groups through Week 24. The proportion of golimumab-treated subjects experiencing AEs was not increased by MTX use.

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- **Serious Adverse Events**: The proportions of subjects experiencing SAEs were low overall and lower in the golimumab groups than in the placebo group (1.7% vs 5.3% through Week 16 and 2.0% vs 6.2% through Week 24). The incidence and type of SAEs reported were as expected in this study population and did not differ by MTX use in the golimumab groups. Four subjects in the placebo group and 2 subjects in the golimumab group had serious infections.
- **Deaths:** There were no deaths.
- **Malignancies**: Malignancies were reported for 3 subjects (2 with basal cell carcinoma and 1 with prostate cancer) all in the golimumab 100 mg group.
- **Study Agent Discontinuations**: A greater proportion of subjects in the placebo group than in the golimumab groups discontinued study agent due to AEs.
- I**njection-site Reactions:** Injection-site reactions consisted primarily of injection-site erythema, and occurred with approximately 1% of study agent injections regardless of treatment administered. None was severe or serious, and none led to discontinuation of study agent administration. No relationship between development of antibodies to golimumab and injection-site reactions was noted.
- **Infections**: Similar proportions of subjects (approximately 25%) in each treatment group experienced infections through Week 16. Through Week 24, somewhat greater proportions of subjects in the golimumab group than in the placebo group, and in the 100 mg group than in the 50 mg group reported infections. Greater proportions of subjects not receiving MTX at baseline than those receiving MTX at baseline reported infections.
- **Laboratory assessments:** Laboratory safety assessments did not identify any unanticipated safety issues. Among both subjects who received treatment for latent tuberculosis and those who did not, subjects treated with golimumab were more likely to develop abnormal ALT than those who received placebo. In addition, abnormal ALT values were noted more frequently in subjects who received treatment for latent tuberculosis than in those who did not, regardless of study treatment administered. For markedly abnormal liver function tests, ALT and AST elevations were seen more commonly among subjects treated with placebo than subjects treated with golimumab, while elevations in total bilirubin levels occurred in similar proportions of subjects receiving placebo or golimumab.
- **TB:** No cases of latent or active TB were diagnosed during the study. Overall, approximately 11% of subjects required treatment for latent TB at study entry, most of whom were treated with isoniaside (INH). In general, more subjects treated for latent TB had transaminase abnormalities compared with subjects not receiving this treatment; but for the most part, observed elevations were transient and mild to moderate. There was no suggestion that treatment with golimumab and INH increased the risk of serious liver function test abnormalities.
- **Vaccine Response:** There was no significant difference between the placebo and golimumab groups in the proportion of subjects who responded to pneumococcal vaccination. However, numerically fewer subjects receiving MTX at baseline across all treatment groups were classified as responders to pneumococcal vaccine.

Synopsis (C0524T08 GO-REVEAL)

Name of Sponsor/Company: Centocor, Inc	**Associated with Module 5.3 of the Dossier**	
Name of Finished Product: CNTO 148 (golimumab)		
Name of Active Ingredient: CNTO 148 (golimumab)		

Conclusions:

Golimumab 50 mg or 100 mg administered subcutaneously every 4 weeks:

- Provides substantial benefit to subjects with PsA by reducing clinical signs and symptoms of arthritis, decreasing the severity of dactylitis and enthesitis, improving psoriatic skin and nail lesions, and by improving physical function and quality of life.
- Is generally well tolerated with similar proportions of subjects with AEs in placebo and golimumab groups. The incidence of SAEs and other significant AEs was comparable between subjects treated with golimumab and placebo. With or without MTX use at baseline, demonstrated a safety profile similar to other anti-TNF agents.
- With or without MTX use at baseline, demonstrated significant efficacy that was comparable between golimumab dose groups, except for psoriasis-related endpoints where numerically greater improvements were seen with golimumab 100 mg than with 50 mg.

Date of Report: 16 Oct 2007

Synopsis (C0524T08 GO-REVEAL)

Name of Sponsor/Company: Centocor R&D, Inc	**Associated with Module 5.3 of the Dossier**	
Name of Finished Product: SIMPONI™ (golimumab)		
Name of Active Ingredient: CNTO 148 (golimumab)		

Protocol: C0524T08	**EudraCT No.: 2004-003298-10**

Title of the study: A Multicenter, Randomized, Double-blind, Placebo-controlled Trial of Golimumab, a Fully Human Anti-TNFα Monoclonal Antibody, Administered Subcutaneously in Subjects with Active Psoriatic Arthritis

Principal/Coordinating Investigator(s): [redacted] MD, [redacted] US

Study Center(s): Subjects were enrolled at 58 centers: The number of enrolling sites by geographic location was as follows: 36 in North America (18 in the US and 18 in Canada) and 22 in Europe (5 in Belgium, 10 in Poland, 3 in Spain, and 4 in the UK)

Publication (reference): Kavanaugh A, McInnes I, Mease P, et al. Golimumab, a new human tumor necrosis factor alpha antibody, administered every four weeks as a subcutaneous injection in psoriatic arthritis: Twenty-four-week efficacy and safety results of a randomized, placebo-controlled study. *Arthritis Rheum.* 2009;60(4):976-986.

Studied Period: 12 Dec 2005/15 Nov 2007	**Phase of Development:** 3

Objectives: The primary objective of this study was to evaluate the efficacy of subcutaneous (SC) injections of golimumab in subjects with active psoriatic arthritis (PsA) by the following:

- Reduction in signs and symptoms of PsA
- Inhibition of progression of structural damage

The major secondary objectives of this study were to evaluate the efficacy of golimumab in: 1) achieving sustained arthritis response, 2) improving psoriatic skin lesions, 3) improving physical function, and 4) improving quality of life; and to assess the safety of golimumab in subjects with active PsA.

Methodology: This was a multicenter, randomized, double-blind, placebo-controlled study designed to assess the efficacy, safety, and clinical pharmacology of golimumab 50 mg or 100 mg administered as SC injections every 4 weeks in adult subjects with active PsA. All subjects were on active (ie, golimumab) treatment beginning at Week 24. Dose remained blinded through the 52-week database lock. The long term extension began with the Week 52 study agent injection and ends when the last subject enrolled completes the Week 268 visit.
This report presents data through Week 52 with the last injection received at Week 48.

Number of Subjects (Planned and Analyzed): Subjects were randomly assigned in a 1:1.3:1.3 ratio to 1 of 3 treatment groups: golimumab 50 mg (n = 143 planned; 146 actual), golimumab 100 mg (n = 143 planned; 146 actual), placebo (n = 110 planned; 113 actual). All 405 subjects were analyzed for safety, efficacy, and health economics (HEcon).

Diagnosis and Main Criteria for Inclusion: Subjects eligible for this study were men and women 18 years of age or older with a diagnosis of PsA for at least 6 months prior to first study agent administration who had active PsA despite current or previous disease-modifying antirheumatic drug (DMARD) or NSAID therapy, and who had not previously been treated with anti-tumor necrosis factor alpha (TNFα) therapy.

Synopsis (C0524T08 GO-REVEAL)

Name of Sponsor/Company: Centocor R&D, Inc	**Associated with Module 5.3 of the Dossier**	
Name of Finished Product: SIMPONI™ (golimumab)		
Name of Active Ingredient: CNTO 148 (golimumab)		

Test Product, Dose and Mode of Administration, Batch Number: Golimumab supplied as a sterile liquid for SC injection at a volume of 0.5 mL or 1.0 mL in 2 mL single-use glass vials containing 50 or 100 mg golimumab. No preservatives were present. Lot numbers were as follows: D05PJ7456, 6ES39, 6ES3C, D05PJ7455, 6HS3U, 6HS3R, 6KS1K, and 6KS1P.

Duration of Treatment: Duration of treatment for this report was through Week 52.

Reference Therapy, Dose and Mode of Administration, Batch Number: Placebo, consisting of an aqueous medium of histidine, sorbitol, and polysorbate 80 at pH 5.5, was supplied as a sterile liquid for SC injection at a volume of 0.5 mL or 1.0 mL in single-use 2 mL glass vials. Lot numbers were as follows: 6ES14, 6HS2J, 6HS1W, 6ES15, D05PJ7457, and D05PJ7458.

Criteria for Evaluation: Efficacy analyses were based on randomized groups for selected radiographic parameters, while other efficacy analyses were based on early escape and crossover treatment status. Clinical pharmacology and safety analyses were based on subjects who received at least 1 study agent administration.

Pharmacokinetics: Golimumab pharmacokinetics were evaluated by summarizing serum golimumab concentrations over time, trough golimumab levels in the presence or absence of methotrexate (MTX), and the proportion of subjects with undetectable golimumab concentrations over time. Antibody to golimumab status was reported according to treatment group, including induced antibody titers, the relationship to trough golimumab concentrations, and comparisons with selected efficacy and safety parameters.

Efficacy: The coprimary endpoints were American College of Rheumatology (ACR) 20 response at Week 14 that was previously reported, and the change from baseline in PsA modified van der Heijde-Sharp (vdH-S) score at Week 24 that evaluated the inhibition of progression of structural damage of arthritis. In addition, other secondary endpoints related to the signs and symptoms of arthritis, psoriasis, physical function, quality of life, and structural damage were evaluated.

Safety: Safety was assessed for golimumab-treated subjects by evaluating the incidence and type of AEs, including SAEs, reasonably related, severe, or clinically significant AEs, and discontinuations due to AEs; routine clinical laboratory values; the relationship of antibodies to golimumab to selected safety measures; and the development of antinuclear antibodies (ANA) or anti-double-stranded DNA antibodies.
Health Economics: Resource utilization was evaluated at Week 52.

Statistical Methods: Descriptive statistics, such as the mean, median, SD, range, and the interquartile range for continuous variables, and counts and percentages for categorical variables were used to summarize most data. The majority of the Week 52 analyses were based on observed data. The Cochran-Mantel-Haenszel (CMH) chi square test was used to compare binary categorical data with stratification (stratified by baseline MTX usage [yes/no]). Analysis of variance (ANOVA) on van der Waerden normal scores (Conover, 1980) with treatment and subject's baseline MTX usage as factors in the model was used to compare continuous data, unless otherwise specified. In addition to statistical analyses, graphical data displays (eg, line plots) and subject listings were also used to summarize or present the data.

Synopsis (C0524T08 GO-REVEAL)

Name of Sponsor/Company: Centocor R&D, Inc	**Associated with Module 5.3 of the Dossier**	
Name of Finished Product: SIMPONI™ (golimumab)		
Name of Active Ingredient: CNTO 148 (golimumab)		

SUMMARY – CONCLUSIONS

Study Population Results: Study population results were previously reported. Baseline characteristics were generally well balanced across treatment groups. The majority of subjects was men (60.2%); most were Caucasian (97.0%), with a median age of 47.0 years. Approximately half of the subjects in each treatment group were receiving MTX at baseline. Baseline clinical characteristics were similar across the treatment groups and indicative of subjects with PsA of moderate to severe activity.

Pharmacokinetic/Pharmacodynamic Results:

- **Pharmacokinetics:** Serum golimumab concentrations were dose proportional and were maintained through Week 52 in both the golimumab 50 mg and golimumab 100 mg groups, with the majority of subjects having detectable trough serum golimumab concentrations.
- **Antibodies to golimumab:** The overall incidence of antibodies to golimumab through Week 52 (4.9%) was consistent with that through Week 24, and all subjects with positive antibodies to golimumab status had neutralizing antibodies. Among subjects receiving MTX at baseline, the proportion of subjects who developed antibodies to golimumab was lower (0.5%) than among subjects not receiving MTX at baseline (9.1%).

Efficacy Results:

Coprimary Endpoints

The first coprimary endpoint for ACR 20 response at Week 14 was statistically significant in favor of the golimumab 50 mg dose as compared with the placebo group.

The coprimary analysis presented in this report, change from baseline in total modified vdH-S score at Week 24, demonstrated significant inhibition of progression of structural damage in favor of the golimumab 50 mg subjects compared with placebo subjects, with the mean change in total modified vdH-S score of -0.09 ($p = 0.015$) and -0.16 ($p = 0.011$) in the golimumab 50 mg group compared with 0.27 in the placebo group. A negative mean change from baseline in total modified vdH-S score was also observed in the golimumab 100 mg group (-0.02) compared with the placebo group (0.27), suggesting less progression of structural damage in the 100 mg group, but this change did not reach statistical significance ($p = 0.086$). Multiple sensitivity analyses confirmed the robustness of the results. Additional supportive analyses are summarized below for the golimumab 50 mg and 100 mg groups at Week 24.

Analyses Supportive of Inhibiting Progression of Structural Damage at Week 24

The following statistically significant differences in favor of both the golimumab 50 mg and 100 mg dose groups compared with the placebo group for the following analyses:

- Less change in hand ($p = 0.039$ and $p = 0.015$) and feet ($p = 0.004$ and $p = 0.008$) erosion scores in the golimumab 50 mg and golimumab 100 mg groups, respectively.
- Fewer joints with new erosions ($p = 0.003$ and $p < 0.001$) and new joint space narrowing (JSN) ($p = 0.009$ and $p = 0.011$) in the golimumab 50 mg and golimumab 100 mg groups, respectively.
- Greater number of subjects with no new erosions ($p = 0.003$ and $p < 0.001$) and no new JSN ($p = 0.008$ and $p = 0.013$) in the golimumab 50 mg and golimumab 100 mg groups, respectively.
- Greater number of subjects ($p = 0.007$ and $p = 0.020$) with a change in total modified vdH-S score ≤ 0 (no radiographic progression) in the golimumab 50 mg and golimumab 100 mg groups, respectively.
- Significantly fewer subjects with radiographic progression (defined as change in a total modified vdH-S score greater than the smallest detectable change [SDC]) in the golimumab 50 mg group ($p = 0.030$) compared with the placebo group.

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Endpoints Related to Inhibiting Progression of Structural Damage Through Week 52

Although there were no statistical comparisons performed, secondary radiographic analyses through Week 52 showed the maintenance of radiographic benefit in golimumab-treated subjects, and some improvement in total modified vdH-S score in subjects who either early escaped or crossed over from placebo to active treatment at Week 16 and Week 24, respectively. The subjects that were randomized to the placebo group had more structural damage at Week 52 compared with subjects randomized to the golimumab groups. Analyses are summarized below.

- The mean change in total modified vdH-S from baseline to Week 52 was negative in the golimumab 50 mg and golimumab 100 mg groups (-0.22 ± 1.643 and -0.14 ±1.529, respectively), suggesting inhibition of radiographic progression through 52-weeks in both treatment groups. Subjects in the placebo group that had received golimumab since at least Week 24 had less progression (0.22 ± 1.379) through Week 52 than through Week 24 (mean change in total modified vdH-S score 0.27 ± 1.259).
- The mean change in total modified vdH-S from Week 24 to Week 52 was negative or 0 in the golimumab 50 mg group, golimumab 100 mg group, and the group originally randomized to placebo, indicating inhibition of radiographic progression in all 3 groups over this time period.
- At Week 52, the proportion of subjects with no newly eroded joints ranged from 66.7% to 85.1%, and the proportion of subjects with no new JSN ranged from 91.7% to 98.0%. These proportions were similar to those observed at Week 24.
- At Week 52, greater than 60% of subjects across treatment groups had a change from baseline in total modified vdH-S score of ≤ 0 (no progression). The golimumab treatment groups had a higher proportion of subjects with a score ≤ 0 (77.2%, 76.0%, and 73.9% in the golimumab 50 mg only, the golimumab 50 mg early escape, and the golimumab 100 mg groups, respectively) compared with the combined placebo group (66.0%) in which subjects all subjects received golimumab from at least Week 24. These proportions were similar to those observed at Week 24.
- At Week 52, few subjects had radiographic progression (based on change in a total modified vdH-S score greater than the SDC), and no differences were discernable across treatment groups.

Signs and Symptoms of Psoriatic Arthritis at Week 52

For each endpoint, efficacy was maintained in the golimumab 50 mg only and 100 mg only treatment groups after Week 24 through Week 52. Subjects in the placebo → golimumab 50 mg early escape group and in the placebo → golimumab 50 mg crossover group demonstrated similar efficacy over time, after initiation of golimumab 50 mg dosing, to that seen in the golimumab 50 mg only group, who began receiving golimumab at Week 0. In both golimumab early escape groups (golimumab 50 mg → 100 mg and golimumab 100 mg → 100 mg), for most endpoints, efficacy did not appear to be as substantial as in other treatment groups.

The evaluations are summarized below **for the golimumab 50 mg only and 100 mg only groups, respectively, at Week 52.**

Arthritis Evaluations

- ACR 20 response was observed in 78.4% and 80.9% of subjects.
- ACR 50 response was observed in 56.9% and 59.1% of subjects.
- ACR 70 response was observed in 43.1% and 35.7% of subjects.
- ACR 20, ACR 50, and ACR 70 responses were similar regardless of baseline MTX use for both groups.
- The median ACR-N improvement was 56.10% and 56.40%.
- The proportion of subjects with Disease Activity Score including evaluation of 28 joints (DAS28) response (moderate or good) using C-reactive protein (CRP) was 92.8% and 90.9%.

Synopsis (C0524T08 GO-REVEAL)

Name of Sponsor/Company: Centocor R&D, Inc	**Associated with Module 5.3 of the Dossier**	
Name of Finished Product: SIMPONI™ (golimumab)		
Name of Active Ingredient: CNTO 148 (golimumab)		

- The median change from baseline in DAS28 score (using CRP) was -2.135 and -2.110.
- Psoriatic Arthritis Response Criteria (PsARC) was observed in 93.9% and 94.7% of subjects.
- Among subjects with dactylitis, the median improvement from baseline in dactylitis score was 100.0% for both groups.
- Among subjects with enthesitis at baseline, the median improvement in Maastricht AS Enthesitis Score (MASES) enthesitis score was 100.0% for both groups.

Skin and Nail Evaluations

- Psoriasis Area and Severity Index (PASI) 50 response was observed in 83.1% and 87.2% of subjects.
- PASI 75 response was observed in 62.0% and 69.8% of subjects.
- PASI 90 response was observed in 32.4% and 48.8% of subjects.
- PASI 50, PASI 75, and PASI 90 responses were similar regardless of baseline MTX use for both groups.
- The median change from baseline in PASI score was 80.80% and 89.40%.
- The median improvement in target lesion score was 85.7% and 100.0%.
- The median change from baseline in Nail Psoriasis Severity Index (NAPSI) score was 75.0% and 100.0%.
- The proportion of subjects with improvement in Nail Physician Global Assessment (PGA) was 68.3% and 72.9%.

Physical Function

- The median improvement from baseline in HAQ was 0.49 ± 0.54 and 0.50 ± 0.53.
- The proportion of subjects with HAQ improvement from baseline ≥ 0.25 units was 64.0% and 68.1%.
- The proportion of subjects with HAQ improvement from baseline ≥ 0.3 units was 55.0% and 62.8%.

Health Related Quality of Life

- The median change in the SF-36 physical component summary (PCS) score was 11.10 and 9.80.
- The median change in the SF-36 mental component summary (MCS) score was 2.10 and 4.30.

Health Economics

- Improvements from baseline in healthcare utilization were seen in the mean number of physician visits, hospitalizations, number of days spent in the hospital, and employability at Week 52.
- Improvements from baseline in time lost from work for both the caregiver and subject were noted at Week 52.
- Improvement in employabilty was observed at Week 52 in subjects who were not employed at baseline.
- Improvements in productivity over the preceding 4 weeks at work, school, and home were observed at Week 52.

Efficacy and Pharmocokinetics

There were no consistent correlations between steady-state trough serum golimumab concentration and ACR 20 and ACR 50 responses at Week 52.

Efficacy and Antibodies to Golimumab

Overall, the generation of antibodies to golimumab does not appear to preclude a clinically meaningful response. However, the number of subjects with antibodies to golimumab is too small to support definitive conclusions regarding the impact of antibody status on efficacy.

Synopsis (C0524T08 GO-REVEAL)

Name of Sponsor/Company: Centocor R&D, Inc	**Associated with Module 5.3 of the Dossier**	
Name of Finished Product: SIMPONI™ (golimumab)		
Name of Active Ingredient: CNTO 148 (golimumab)		

Safety Results:

The safety profile of golimumab through Week 52 was consistent with the safety profile observed through Week 24. Golimumab administered SC every 4 weeks, with or without MTX, was generally well tolerated in subjects with active PsA. The safety results observed in this study are consistent with the well-known safety profiles of MTX and anti-TNFα agents; no unexpected safety issues were observed on review of safety data.

- **Adverse Events:** The proportion of subjects with 1 or more AEs through Week 52 was 78.2% in golimumab-treated subjects (ranged 58.8% to 80.8% across treatment groups), with generally greater proportions of subjects with AEs in groups with greater durations of follow-up. The 3 system-organ classes with the highest incidence of AEs through Week 52 in golimumab-treated subjects were Infections and infestations (50.3%), GI disorders (22.1%), and Musculoskeletal and connective tissue disorders (20.8%). The most commonly reported AE was upper respiratory tract infection. Regardless of MTX use at baseline, the incidence of AEs was comparable among golimumab-treated subjects. There was no apparent difference between the golimumab 50 mg and 100 mg treatment groups in frequency or type of adverse events.
- **Deaths:** Through Week 52, 2 deaths were reported, 1 subject (golimumab 50 mg) died due to a small cell lung carcinoma with metastases, and 1 subject (golimumab 50 mg) died in an [redacted] Both events occurred after Week 24.
- **Serious Adverse Events:** Through Week 52, the proportion of subjects for whom 1 or more SAEs were reported was 4.6% in golimumab-treated subjects (range 0.0% to 7.1% across treatment groups), with little difference between subjects receiving MTX and subjects not receiving MTX at baseline. Superficial thrombophlebitis was the only SAE reported in more than 1 subject.
- **Study Agent Discontinuations Due to AEs:** Through Week 52, a total of 14 (3.6%) subjects (including 8 reported prior to Week 24) who discontinued study agent because of 1 or more AE.
- **Infections:** The pattern and types of infections observed through Week 52 were similar to those reported through Week 24, with upper respiratory tract infection continuing to be the most frequently reported infection in golimumab-treated subjects (16.5%). This was followed by nasopharyngitis (11.7%), pharyngitis (4.1%), and sinusitis (3.3%) as the most frequent infections reported in the golimumab-treated subjects.
- **Serious Infections:** Through Week 52, 3 subjects had serious infections. Two subjects had events (1 abscess in the golimumab 50 mg group and 1 sepsis and acute cholecystitis in the golimumab 100 mg group) previously reported through Week 24 and 1 subject had superficial thrombophlebitis in the golimumab 50 mg group that was reported after Week 24**.**
- **Tuberculosis and Opportunistic Infections:** No events of TB or opportunistic infections were identified through Week 52.
- **Malignancies**: Through Week 52, 5 subjects had malignancies. Three subjects had malignancies (2 basal cell carcinomas of the skin and 1 prostate cancer, (all in the golimumab 100 mg group) previously reported through Week 24, and 2 subjects had malignancies (colon cancer in a placebo subject after early escape and a fatal small cell lung cancer in the golimumab 50 mg group) that were reported after Week 24.

Synopsis (C0524T08 GO-REVEAL)

Name of Sponsor/Company: Centocor R&D, Inc	**Associated with Module 5.3 of the Dossier**	
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Name of Active Ingredient: CNTO 148 (golimumab)		

- **Injection-site Reactions:** The proportion of subjects with 1 or more injection-site reactions to golimumab injection was 6.3%; 1.1% of golimumab injections resulted in an injection-site reaction. The most commonly reported reactions to golimumab injections were injection-site erythemas. No injection-site reaction was severe, none was serious, and none resulted in permanent discontinuation of study agent.
- **Laboratory assessments: The most common markedly abnormal changes in hematology values were a decrease in neutrophils or lymphocytes or an increase in eosinophils. The most common markedly abnormal changes in chemistry values were an elevation in ALT, AST or bilirubin.** Laboratory safety assessments through Week 52 did not identify any new safety issues not previously reported through Week 24 or reported with other anti-TNFα agents**.**

Conclusions:

Through 24-weeks of treatment:

- Golimumab 50 mg administered subcutaneously every 4 weeks inhibited the progression of structural damage in subjects with moderately to severely active PsA as measured by a change from baseline in total modified vdH-S score (primary radiographic endpoint). The benefit of golimumab 50 mg was observed irrespective of baseline MTX use.
- No significant difference was observed in the change from baseline in total modified vdH-S score (primary radiographic endpoint) between the golimumab 100 mg and the placebo group.
- There were statistically significant differences in favor of both the golimumab 50 mg and 100 mg dose groups compared with the placebo group for multiple supportive radiographic analyses at Week 24.

Through 52-weeks of treatment:

- The radiographic benefit achieved at Week 24 was maintained in the golimumab 50 mg and 100 mg groups.
- Placebo subjects who early escaped or crossed over to active treatment with golimumab 50 mg demonstrated improvement in radiographic scores.
- Both golimumab doses provided benefit to subjects with PsA by reducing clinical signs and symptoms of arthritis, decreasing the severity of dactylitis and enthesitis, improving psoriatic skin and nail lesions, and improving physical function and quality of life.
- Clinical efficacy, as measured by ACR and PASI responses, was observed irrespective of MTX use for the golimumab 50 mg and 100 mg groups.
- Golimumab was generally well tolerated, with similar proportions of subjects and types of AEs observed in the golimumab 50 mg and 100 mg groups.
- The frequency and type of adverse events were similar in golimumab-treated subjects regardless of MTX use at baseline.
- Golimumab showed a safety profile similar to that seen in the 24-week reporting period and consistent with that of other anti-TNFα agents used to treat PsA disease.

Date of Report: 23 Sep 2010

Synopsis (C0524T08 GO-REVEAL)

Name of Sponsor/Company: Centocor, Inc	**Associated with Module 5.3 of the Dossier**	
Name of Finished Product: SIMPONI™ (golimumab)		
Name of Active Ingredient: CNTO 148 (golimumab)		

Protocol: C0524T08	**EudraCT No.: 2004-003298-10**

Title of the study: A Multicenter, Randomized, Double-blind, Placebo-controlled Trial of Golimumab, a Fully Human Anti-TNFα Monoclonal Antibody, Administered Subcutaneously in Subjects with Active Psoriatic Arthritis

Principal/Coordinating Investigator(s): [redacted], MD, [redacted] US

Study Center(s): Subjects were enrolled at 58 centers: The number of enrolling sites by geographic location was as follows: 36 in North America (18 in the US and 18 in Canada) and 22 in Europe (5 in Belgium, 10 in Poland, 3 in Spain, and 4 in the UK).

Publication (reference):
Xu, Z., Vu, T., Lee, H., Hu, C., Ling J., Yan, H., Baker, D., Beutler, A., et al; Population pharmacokinetics of golimumab, an anti-tumor necrosis factor-α human monoclonal antibody, in patients with psoriatic arthritis. J Clin Pharmacol 2009;49:1046-1070.

Kavanaugh, A., Mease, P., Krueger, G.G., Gladman, D., Zrubek, J., Beutler, A., et al; Golimumab, a new, human, TNF alpha antibody, administered subcutaneously every 4 weeks in psoriatic arthritis patients: 104-Week Efficacy and Safety Results of the Randomized, Placebo-Controlled GO-REVEAL Study [abstract]. *Arthritis Rheum* 2009;60 Suppl 10:512.

Studied Period: 12 Dec 2005/18 Nov 2008	**Phase of Development:** 3

Objectives: The primary objective of this study was to evaluate the efficacy of subcutaneous (SC) injections of golimumab in subjects with active psoriatic arthritis (PsA) by the following:

- Reduction in signs and symptoms of PsA
- Inhibition of progression of structural damage

The major secondary objectives of this study were to evaluate the efficacy of golimumab in: 1) achieving sustained arthritis response, 2) improving psoriatic skin lesions, 3) improving physical function, and 4) improving quality of life; and to assess the safety of golimumab in subjects with active PsA.

Methodology: This was a multicenter, randomized, double-blind, placebo-controlled study designed to assess the efficacy, safety, and clinical pharmacology of golimumab 50 mg or 100 mg administered as SC injections every 4 weeks in adult subjects with active PsA. Subjects were randomly assigned and stratified by MTX use to receive placebo, golimumab 50 mg, or golimumab 100 mg SC injections. At Week 16, subjects in any group who had < 10% improvement from baseline in both swollen and tender joint count entered early escape in a double-blinded fashion to receive either golimumab 50 mg or 100 mg every 4 weeks. At Week 24, subjects remaining in the placebo group crossed over to blinded treatment with golimumab 50 mg SC injections every 4 weeks. Subjects in the golimumab treatment groups continued their dosing regimen. All subjects were on active (ie, golimumab) treatment beginning at Week 24. Dose remained blinded through the 52-week database lock. After the Week 52 database lock and at the investigator's discretion, subjects who were receiving 50 mg of golimumab every 4 weeks had the option to increase their golimumab dose to 100 mg. Subjects receiving golimumab 100 mg every 4 weeks have remained on this dose. The long term extension began with the Week 52 study agent injection and ends when the last subject enrolled completes the Week 268 visit.

Synopsis (C0524T08 GO-REVEAL)

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Name of Active Ingredient: CNTO 148 (golimumab)		

This 104-Week report presents data through Week 104.

Number of Subjects (Planned and Analyzed): Subjects were randomly assigned in a 1:1.3:1.3 ratio to 1 of 3 treatment groups: golimumab 50 mg (n = 143 planned; 146 actual), golimumab 100 mg (n = 143 planned; 146 actual), placebo (n = 110 planned; 113 actual).

Diagnosis and Main Criteria for Inclusion: Subjects eligible for this study were men and women 18 years of age or older with a diagnosis of PsA for at least 6 months prior to first study agent administration who had active PsA despite current or previous disease-modifying antirheumatic drug (DMARD) or nonsteroidal anti inflammatory drug (NSAID) therapy, and who had not previously been treated with anti-tumor necrosis factor alpha (TNFα) therapy

Test Product, Dose and Mode of Administration, Batch Number: Through Week 52, golimumab was supplied as a sterile liquid for SC injection at a volume of 0.5 mL or 1.0 mL in 2 mL single-use glass vials. Each glass vial contained golimumab 50 mg or 100 mg in an aqueous medium of histidine, sorbitol, and polysorbate 80 at pH 5.5. No preservatives were present. Lot numbers for liquid in vial were as follows: D05PJ7455, D05PJ7456, 6ES39, 6ES3C, 6HS3R, 6HS3U, 6KS1K, 6KS1P, and 7DS1N. Golimumab was also supplied as a pre-filled syringe (PFS). After the Week 52 DBL (12 Dec 2007), the subject and all study site personnel were unblinded on 18 Jan 2008 to the subject's treatment, and from that point onward, a single injection using a PFS was administered according to the subject's treatment assignment. Each PFS contained golimumab 50 mg or 100 mg in an aqueous medium of histidine, sorbitol, and polysorbate 80 at pH 5.5. Lot numbers for PFS were as follows: 03643.01, 03643.02, 03643.05, 03643.06, 03643.07, 03643.08, V07PH7102, V07PK7146, and V07PK7147.

Duration of Treatment: Duration of treatment for this report was through Week 104.

Reference Therapy, Dose and Mode of Administration, Batch Number: Placebo for golimumab, consisting of an aqueous medium of histidine, sorbitol, and polysorbate 80 at pH 5.5, was also supplied as a sterile liquid for SC injection at a volume of 0.5 mL or 1.0 mL in single-use 2 mL glass vials. Lot numbers for placebo liquid in vial were as follows: 6ES14, 6ES15, 6HS1W, 6HS2J, 7GS47, D05PJ7457, and D05PJ7458.

Criteria for Evaluation: In general, signs and symptoms efficacy analyses were done based on treatment regimen received, and without missing data imputation rules applied. Radiographic analyses were based on randomized treatment groups (ie, placebo, golimumab 50 mg, golimumab 100 mg). For selected radiographic and other efficacy data, the analyses were presented in 2 ways: data columns by randomized treatment group and data columns by treatment regimen received. For selected efficacy measurements, summaries were provided to show the change/percent improvement over time after dose escalation from golimumab 50 mg to 100 mg. Clinical pharmacology and safety analyses were based on subjects who received at least 1 study agent administration.

Pharmacokinetics: Golimumab pharmacokinetics was evaluated by summarizing serum golimumab concentrations over time from Week 0 through Week 100 by methotrexate (MTX) use at baseline. Antibody to golimumab status was reported according to treatment group, including antibody titers, and the relationship to selected safety and efficacy parameters.

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Efficacy: The 24-week coprimary endpoints were American College of Rheumatology (ACR) 20 response at Week 14, and the change from baseline in PsA modified van der Heijde-Sharp (vdH-S) score at Week 24 that evaluated the inhibition of progression of structural damage of arthritis were previously reported. Major secondary endpoints (ie, ACR 20 response at Week 24; PASI 75 at Week 14; Improvement from baseline in HAQ at Week 24; Change from baseline in SF-36 PCS at Week 14) were also previously reported. This report focuses on long term extension endpoints related to the signs and symptoms of arthritis, psoriasis, physical function, quality of life, and structural damage.

Safety: Safety was assessed for golimumab-treated subjects by evaluating the incidence and type of AEs, including SAEs, reasonably related, severe, or clinically significant AEs, and discontinuations due to AEs; routine clinical laboratory values; and the relationship of antibodies to golimumab to selected safety measures.

Statistical Methods: Descriptive statistics, such as the mean, median, SD, range, and the interquartile range for continuous variables, and counts and percentages for categorical variables were used to summarize most data.

SUMMARY – CONCLUSIONS

Study Population Results: Study population results were previously reported. Baseline demographic characteristics were generally well balanced across treatment groups. The majority of subjects were men (60.2%), most were Caucasian (97.0%), with a median age of 47.0 years. Approximately half of the subjects in each treatment group were receiving MTX at baseline. Baseline clinical characteristics were similar across the treatment groups and indicative of subjects with PsA of moderate to severe activity.

Pharmacokinetic/Pharmacodynamic Results:

Pharmacokinetics

Serum trough golimumab concentrations were dose proportional and were generally maintained through Week 100, for the group receiving golimumab 50 mg only (ie, subjects randomized to golimumab 50 mg and not changing treatment to golimumab 100 mg), and golimumab 100 mg only group (ie, subjects randomized to golimumab 100 mg and continuing to receive golimumab 100 mg).

Antibodies to Golimumab

- The overall incidence of antibodies to golimumab through Week 100 (5.4%) was consistent with that through Week 52 (4.9%).
- Among subjects receiving MTX at baseline, the proportion of subjects who developed antibodies to golimumab was lower (1.6%) compared with subjects not receiving MTX at baseline (9.1%).

Efficacy Results:

Overall, the benefit of treatment with golimumab in reducing signs and symptoms of active PsA achieved at Week 52 was maintained through Week 104, as improvements and responses in clinical efficacy measures at Week 104 were numerically similar or greater than those observed at Week 52. In general, subjects who changed the treatment from golimumab 50 mg to 100 mg in early escape or through dose escalation, had lowest responses as reflected by lower ranges described below.

Arthritis Evaluations

- The proportion of subjects with ACR responses was generally maintained within each treatment group after Week 52 through Week 104. At Week 104, between 56.6% and 91.4% achieved an ACR 20 response; between 35.5% and 65.7% achieved an ACR 50 response, and 22.4% and 44.3% achieved an ACR 70 response across all treatment groups.

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- Median percent improvement for swollen and tender joint counts was similar within each treatment group after Week 52 through Week 104. At Week 104, the median improvement from baseline in the number of swollen joints was between 84.25% and 100% across treatment groups. The median percent improvement from baseline in the number of tender joints was between 80% and 100% across treatment groups.
- Median percent improvement in CRP from baseline was similar within each treatment group after Week 52 through Week 104. At Week 104, the median improvement in CRP was between 32.50% and 50% across treatment groups.
- Median improvement in ACR-N index was maintained after Week 52 through Week 104 within each treatment group. At Week 104, the median ACR improvement was between 50% and 61.25% across treatment groups with the exception of the golimumab 50 mg → golimumab 100 mg group that had a median ACR improvement of 25.55%.
- The proportion of DAS28 (using CRP) responders was maintained after Week 52 through Week 104 within each treatment group. At Week 104, the proportion of subjects was between 84.7% and 100.0% across treatment groups. At Week 104, the median change from baseline was between -2.543 and -2.030 across treatment groups.
- Dactylitis and enthesitis improved with golimumab treatment through Week 104. In each treatment group less than 20% of subjects with dactylitis at baseline had 1 or more digits with dactylitis at Week 104. Of the subjects with enthesitis at baseline, approximately 50% of subjects within each treatment group no longer had enthesitis at Week 104.

Psoriasis Evaluations

- The proportion of subjects with PASI responses was generally maintained after Week 52 through Week 104 within each treatment group. At Week 104, between 82.1 and 89.6% achieved PASI 50 response; between 62.5% and 76.0% achieved PASI 75 response, and between 43.8% and 53.5% achieved PASI 90 response across all treatment groups.
- Nail disease improvement with golimumab treatment was maintained through Week 104**.** At Week 104, among subjects with fingernail involvement at baseline, at least 75% of subjects in each treatment group achieved improvement from baseline in Nail PGA.

Radiographic Evaluation

This 104-week CSR describes radiographic results from Reading Session 2 which includes images from baseline, Week 52, and Week 104. The 52-week CSR reported the results from Reading Session 1 which included images from baseline, Week 24, and Week 52. The same readers were employed for Reading Session 1 and Reading Session 2, with the exception that a third reader (the adjudicator) was only used in Reading Session 1. Scores from Reading Session 1 and Reading Session 2 ± were analyzed and reported separately.

The majority of golimumab subjects had an x-ray image and score at baseline (approximately 98%), at Week 52 (approximately 91%), and at Week 104 (approximately 84%).

- At Week 104, the change from baseline in total modified vdH-S scores (with missing data imputation rules applied) were generally similar to values observed at Week 52: 0.22 ± 3.666, 0.19 ± 7.471, and -0.33 ± 2.229 for the placebo, golimumab 50 mg, and golimumab 100 mg groups, respectively.
- The results of the sensitivity analysis of mean change from baseline in total modified vdH-S scores (with no missing data imputation rules applied to Week104) for the placebo, golimumab 50 mg, and golimumab 100 mg groups were 0.08 ± 3.193, -0.39 ± 2.041, and -0.32 ± 1.873, respectively.
- Negative changes were observed from Week 52 to Week 104 for the mean change in total modified vdH-S score in the subjects randomized to placebo and golimumab 50 mg groups (-0.03 ± 1.585 and

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-0.10 ± 0.999, respectively). Minimal to no radiographic progression was observed in the golimumab 100 mg group (0.02 ± 0.706) from Week 52 to Week 104.

Physical Function

- The improvement of physical function observed at Week 52 was maintained at Week 104. There were between 86.8% to 100% subjects who achieved ≥ 0.25 unit improvement in HAQ score at Week 52 in each treatment group that maintained this level of improvement at Week 104. There were between 84.9% to 100% subjects who achieved ≥ 0.3 unit improvement in HAQ score at Week 52 in each treatment group and maintained this level of improvement at Week 104.

Health-related Quality of Life

- Improvements from baseline in SF-36 and in the physical component summary (PCS) and mental component summary (MCS) scores at Week 104 were similar to those observed at Week 52 in all golimumab groups. At Week 104, the median change from baseline in SF-36 PCS ranged from 6.40 to 9.60. At Week 104, the median change from baseline in SF-36 MCS ranged from 1.45 to 4.30.

Dose Escalation

- The following parameters were evaluated for subjects with dose escalation and with at least 12 weeks of follow-up: percent improvement in swollen and tender joint count; percent improvement in CRP; change from baseline in DAS28 (using CRP); percent change in PASI score; and improvement from baseline in HAQ. Efficacy data were available for a total of 33 subjects who dose escalated. Disease activity in these subjects was generally low prior to dose escalation with some benefit from a higher dose.

Efficacy and Antibodies to Golimumab

- The number of subjects positive for antibodies (ie, 21) to golimumab is too small to support definitive conclusions regarding the impact of antibodies to golimumab status on efficacy. For subjects positive for antibodies to golimumab the proportion of subjects with an ACR 20 response at Week 100 was 66.7% (10/15) in the combined golimumab group. For subjects negative for antibodies to golimumab, the proportion of subjects with an ACR 20 response at Week 100 was 73.8% (236/320) in the combined golimumab group.

Health Economics

- For health economics and resource utilization measures, the results at Week 104 showed a consistent trend towards improvements from baseline for all treatment groups. The mean for physician visits, hospitalizations, days spent in the hospital were each lower than at baseline for all treatment groups. Mean paid household assistance visits and emergency room (ER) visits at Week 104 were equal to or lower than baseline values for all treatment groups except the placebo → 50 mg treatment group which showed a 0.1 day increase in the number of paid household assistance visits. At Week 104, the median change from baseline in productivity scores (lower scores indicate better productivity) ranged from -2.35 to -3.10 across treatment groups showing an increase in productivity.

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Name of Active Ingredient: CNTO 148 (golimumab)		

Safety Results:

The safety profile of golimumab through Week 104 was consistent with the safety profile observed through Week 52. Golimumab administered SC every 4 weeks, with or without MTX, was generally well tolerated in subjects with active PsA. The safety results observed in this study were consistent with the safety profiles of other anti-TNFα agents; no unexpected safety issues were observed on review of safety data.

- **Adverse Events:** The proportion of subjects with 1 or more AEs through Week 104 was 78.2% in the group of subjects receiving golimumab 50 mg, and 70.9% in the group receiving golimumab 100 mg. The 3 system-organ classes with the highest incidence of AEs through Week 104 were Infections and infestations (54.8% and 49.3% in the golimumab 50 mg and 100 mg groups, respectively), Musculoskeletal and connective tissue disorders (26.6% and 25.6% in the golimumab 50 mg and 100 mg groups, respectively), and GI disorders (25.0% and 22.5% in the golimumab 50 mg and 100 mg groups, respectively).
- **Deaths:** Through Week 104, there were 2 deaths reported in the golimumab 50 mg group, 1 subject died due to a small cell lung carcinoma with metastases, and 1 subject died in an [redacted]. Both events occurred before Week 52**.** No new deaths were reported after Week 52 through Week 104.
- **Serious Adverse Events:** Through Week 104, the proportion of subjects for whom 1 or more SAEs were reported was 8.6% in golimumab-treated subjects that included 6.5% and 7.9% of subjects in the golimumab 50 mg and 100 mg groups, respectively. The proportions of subjects for whom SAEs were reported were generally similar regardless of golimumab dose or MTX use at baseline.
- **Study Agent Discontinuation Due to AEs:** Through Week 104, the proportion of subjects who discontinued study agent because of 1 or more AEs was 5.8% in golimumab-treated subjects that included 4.4% and 5.3% of subjects in the golimumab 50 mg and 100 mg groups, respectively. There were a total of 23 subjects (including 14 reported prior to Week 52) who discontinued study agent because of 1 or more AEs.
- **Infections:** The pattern and types of infections observed through Week 104 were similar to those reported through Week 52 with upper respiratory tract infection the most frequently reported infection in the golimumab 50 mg (20.6%) and golimumab 100 mg (17.6%) groups, respectively. This was followed in frequency by nasopharyngitis (12.5% and 11.5%), sinusitis (8.1% and 3.5%), bronchitis (5.2% and 5.7%), pharyngitis (4.0% and 4.4%), UTI (3.2% and 5.3%), and influenza (2.4% and 3.5%) for the golimumab 50 mg and golimumab 100 mg groups, respectively.
- **Serious Infections:** Through Week 104, 6 subjects (1.5%) in the combined golimumab group that included 1.2% and 1.3% in the golimumab 50 mg and 100 mg groups, respectively had serious infections. Three subjects had events (1 abscess, 1 sepsis and acute cholecystitis, and 1 superficial thrombophlebitis) previously reported, and 3 subjects had infections (1 cellulitis, 1 abscess, and 1 histoplasmosis) that were reported after Week 52.
- **Tuberculosis and Opportunistic Infections:** Through Week 104, there were no reports of TB; 1 subject in the golimumab 100 mg group had histoplasmosis.
- **Malignancies:** Through Week 104, 8 subjects had malignancies. Five subjects had malignancies (2 basal cell carcinomas of the skin in the golimumab 100 mg group;1 prostate cancer in the golimumab 100 mg group; 1 colon cancer in the placebo → 50 mg early escape group; and 1 fatal small cell lung cancer in the golimumab 50 mg group) previously reported, and 3 subjects had malignancies (2 basal cell carcinomas with 1 each in the golimumab 50 mg and golimumab 100 mg, respectively and 1 small cell lung cancer in the golimumab 100 mg group) that were reported after Week 52.

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- **Injection-site Reactions:** The proportion of subjects with 1 or more injection-site reactions to golimumab injection was 8%; 1% of golimumab injections resulted in an injection-site reactions. The most commonly reported reactions to golimumab injections were injection site erythemas. The majority of the injection site reactions were mild in intensity. No injection site reaction was severe, none was serious, and none resulted in permanent discontinuation of study agent. There were no events of anaphylaxis or serum sickness like reactions.
- **Laboratory Assessments:** Laboratory safety assessments through Week 104 did not identify any new safety issues not previously reported through Week 52 and with other anti-TNFα agents. Through Week 104, neutrophil decreases were reported in 0.8% and 3.8% of subjects in the golimumab 50 mg and golimumab 100 mg groups, respectively. Lymphocyte decreases were reported in 1.6% and 3.8% of subjects in the golimumab 50 mg and golimumab 100 mg groups, respectively. Eosinophil increases were reported in 3.2% and 1.9% of subjects in the golimumab 50 mg and golimumab 100 mg groups, respectively. Through Week 104, elevated ALT values were reported in 2.8% and 1.4% of subjects in the golimumab 50 mg and golimumab 100 mg groups, respectively. Elevated AST values were reported in 1.6% and 1.0% of subjects in the golimumab 50 mg and golimumab 100 mg groups, respectively. Total elevated bilirubin values were reported in 3.6% and 2.4% of subjects in the golimumab 50 mg and golimumab 100 mg groups, respectively.

Conclusions: Through 104 weeks of treatment, golimumab 50 mg and 100 mg administered subcutaneously every 4 weeks:

- Provided benefit to subjects with PsA by reducing clinical signs and symptoms of arthritis, decreasing the severity of dactylitis and enthesitis, improving psoriatic skin and nail lesions, and quality of life.
- Maintained inhibition of progression of structural damage.
- Maintained improvement in physical function.
- With or without MTX use at baseline, demonstrated efficacy in improving arthritis and associated psoriasis that was comparable between golimumab dose groups.
- Is generally well tolerated with similar proportions of subjects with AEs and similar types of AEs in 50 mg and 100 mg golimumab groups.
- Demonstrated a safety profile similar to other anti-TNFα agents
- The cumulative incidence of antibodies to golimumab through Week 100 was low.

Date of Report: 08 Oct 2010

SYNOPSIS

Issue Date: 13 Dec 2012

Name of Sponsor/Company	Janssen Research & Development, LLC
Name of Finished Product	SIMPONI®
Name of Active Ingredient(s)	CNTO 148 (golimumab)

Protocol No.: C0524T08

Title of Study: A Multicenter, Randomized, Double-blind, Placebo-controlled Trial of Golimumab, a Fully Human Anti-TNFα Monoclonal Antibody, Administered Subcutaneously in Subjects with Active Psoriatic Arthritis.

Study Name: GO-REVEAL

EudraCT Number: 2004-003298-10

NCT No.: NCT00265096

Clinical Registry No.: CR006340

Principal/Coordinating Investigator(s): [redacted] MD, [redacted] US

Study Centers: Subjects were enrolled at 58 centers: The number of enrolling sites by geographic location was as follows: 36 in North America (18 in the US and 18 in Canada) and 22 in Europe (5 in Belgium, 10 in Poland, 3 in Spain, and 4 in the UK).

Publication (Reference):

Hsia EC, Cush JJ, Matteson EL, et al. A comprehensive tuberculosis screening program in patients with inflammatory arthritides treated with golimumab, a human anti-TNF antibody, in phase 3 clinical trials. Arthritis Care Res. (Hoboken) 2012 Jul 10. doi: 10.1002/acr.21788. [Epub ahead of print]

Hsia EC, Schluger N, Cush JJ, et al. Interferon-γ release assay versus tuberculin skin test prior to treatment with golimumab, a human anti-tumor necrosis factor antibody, in patients with rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis. Arthritis Rheum. 2012;64:2068-77.

Kavanaugh A, McInnes I, Mease P, et al. Clinical efficacy, radiographic, and safety findings through 2 years of golimumab treatment in patients with active psoriatic arthritis: results from a long-term extension of the randomized, placebo-controlled, GO-REVEAL® study. Ann Rheum Dis. Accepted for publication.

Kavanaugh A, McInnes I, Mease P, et al. Golimumab, a new, human, TNF alpha antibody, administered subcutaneously every 4 weeks in psoriatic arthritis patients: 104-Week Efficacy and Safety Results of the Randomized, Placebo-Controlled GO-REVEAL Study [abstract]. Arthritis Rheum. 2009;60 Suppl 10:512.

Kavanaugh A, van der Heijde D, McInnes IB, et al. Golimumab in psoriatic arthritis: One-year clinical efficacy, radiographic, and safety results from a phase III, randomized, placebo-controlled trial. Arthritis Rheum. 2012:64 (8): 2504-2517.

Wagner CL, Visvanathan S, Elashoff M, et al. Markers of inflammation and bone remodelling associated with improvement in clinical response measures in psoriatic arthritis patients treated with golimumab. Ann Rheum Dis. 2012 Sep 21. [Epub ahead of print]

Xu Z, Vu T, Lee H, et al. Population pharmacokinetics of golimumab, an anti-tumor necrosis factor-α human monoclonal antibody, in patients with psoriatic arthritis. J Clin Pharmacol. 2009;49:1046-1070.

Study Period: 12 December 2005 to 13 January 2012

Phase of Development: 3

Objectives: The primary objective of this trial was to evaluate the efficacy of subcutaneous (SC) injections of golimumab in subjects with active psoriatic arthritis (PsA) by assessing reduction in signs and symptoms of PsA and inhibition of progression of structural damage.

The secondary objectives of this study were to evaluate the efficacy of golimumab in: 1) achieving sustained arthritis response, 2) improving psoriatic skin lesions, 3) improving physical function, and 4) improving quality of life; and to assess the safety of golimumab in subjects with active PsA.

Methodology: This multicenter, randomized, double-blind, placebo-controlled study was designed to assess the efficacy, safety, and clinical pharmacology of golimumab 50 mg or 100 mg administered as SC injections every 4 weeks (q4wks) in adult subjects with active PsA. Subjects were randomly assigned and stratified by methotrexate (MTX) use to receive placebo, golimumab 50 mg, or golimumab 100 mg SC injections. At Week 16, any subject who had < 10% improvement from baseline in both swollen and tender joint count qualified to enter early escape (EE) in a double-blinded fashion to receive either golimumab 50 mg or 100 mg q4wks. At Week 24, subjects remaining in the placebo group crossed over to blinded treatment with golimumab 50 mg SC injections q4wks. Subjects in the golimumab treatment groups continued their dosing regimen. All subjects were on active (ie, golimumab) treatment beginning at Week 24. Dose remained blinded through the 52-week database lock (DBL). The long-term extension (LTE) began with the Week 52 study agent injection. After the Week 52 DBL and at the investigator's discretion, subjects who were receiving 50 mg of golimumab q4wks had the option to increase their golimumab dose to 100 mg. Subjects receiving golimumab 100 mg q4wks continued to receive this dose.

After implementation of amendment 1 (22 December 2009), subjects who were receiving golimumab 100 mg during the LTE had the option of decreasing their golimumab dose to 50 mg q4wks and subjects who were receiving golimumab 50 mg q4wks during the LTE who had never received golimumab 100 mg had the option to increase their golimumab dose to 100 mg q4wks at the investigator's discretion.

This 268-Week report presents efficacy results from Week 104 through Week 256 and safety results through Week 268.

Number of Subjects (planned and analyzed): Subjects were randomly assigned in a 1:1.3:1.3 ratio to 1 of 3 treatment groups: placebo (n = 110 planned; 113 actual), golimumab 50 mg (n = 143 planned; 146 actual), and golimumab 100 mg (n = 143 planned; 146 actual).

Diagnosis and Main Criteria for Inclusion: Subjects eligible for this study were men and women 18 years of age or older with a diagnosis of PsA for at least 6 months prior to first study agent administration who had active PsA despite current or previous disease-modifying antirheumatic drug (DMARD) or nonsteroidal anti-inflammatory drug (NSAID) therapy, and who had not previously been treated with anti-tumor necrosis factor alpha (TNFα) therapy.

Test Product, Dose and Mode of Administration, Batch No.: Through Week 52, golimumab was supplied as a sterile liquid for SC injection at a volume of 0.5 mL or 1.0 mL in 2 mL single-use glass vials. Lot numbers for liquid in vial were as follows: D05PJ7455, D05PJ7456, 6ES39, 6ES3C, 6HS3R, 6HS3U, 6KS1K, 6KS1P, and 7DS1N. Golimumab was also supplied as a prefilled syringe (PFS). After the Week 52 DBL (12 December 2007), the subject and all study site personnel were unblinded on 18 January 2008 to the subject's treatment, and from that point onward, a single injection using a PFS was administered according to the subject's treatment assignment. Each PFS contained golimumab 50 mg or 100 mg in an aqueous medium of histidine, sorbitol, and polysorbate 80 at pH 5.5. Lot numbers for

PFS were as follows: 3643.01, 3643.02, 3643.05, 3643.06, 3643.07, 3643.08, 28197.1, 28197.2, 28197.3, 28947.1, 28947.2, 360268/360501, 360269/360502, 360270/360503, 360271/360504, 361564, 361740, 361905, 361906, 361907, 362749, 362767, 362870, 362871, 08A101, 08A102, B127796, B129448, V07PH7102, V07PK7146, and V07PK7147.

Reference Therapy, Dose and Mode of Administration, Batch No.: Golimumab placebo was supplied as a sterile liquid for SC injection at a volume of 0.5 mL or 1.0 mL in single-use 2 mL glass vials. Lot numbers for placebo liquid in vial were as follows: 6ES14, 6ES15, 6HS1W, 6HS2J, 7GS47, D05PJ7457, and D05PJ7458.

Duration of Treatment: Duration of treatment for this study was through Week 252.

Criteria for Evaluation: Efficacy results (including signs and symptoms of PsA, physical function, health assessment questionnaire [HAQ], and health-related quality of life [HRQoL]) and data related to joint structural damage (radiographic data) from Week 104 through Week 256 were summarized by randomized treatment groups (ie, placebo, golimumab 50 mg, golimumab 100 mg). The efficacy analysis (signs and symptoms of PsA, HAQ, and HRQoL) included subjects who did not discontinue study participation as of Week 104. Efficacy summaries were based on observed data. No treatment failure rules and no imputation rules for missing data were to be applied for the analyses. For radiographic analyses, subjects with baseline, Week 104, and at least 1 post Week 104 score were to be included in the analysis. Missing scores were to be replaced by carrying forward the last non-missing observation. Clinical pharmacology and safety analyses were based on subjects who received at least 1 study agent administration.

Statistical Methods: Descriptive statistics, such as the mean, median, standard deviation (SD), range, and the interquartile range for continuous variables, counts and percentages for categorical variables, graphical data displays, and subject listings were used to summarize data.

RESULTS:

STUDY POPULATION:

Study population results were previously reported. Baseline demographic characteristics were generally well balanced across all treatment groups. The majority of subjects were men (60.2%), most were Caucasian (97.0%), with a median age of 47.0 years. Approximately half of the subjects in each treatment group were receiving MTX at baseline. Baseline clinical characteristics were similar across the treatment groups and indicative of subjects with PsA of moderate to severe activity.

Of the 405 subjects randomized, 47 (11.6%), 91 (22.5%), and 110 (27.2%) subjects terminated study participation as of Week 104, Week 256, and Week 268, respectively.

EFFICACY RESULTS:

The coprimary and major secondary endpoints of the study were met at Week 14 and Week 24. Overall, the benefits of treatment with golimumab in reducing signs and symptoms of active PsA achieved at Week 52 were maintained through Week 104 and Week 256 in subjects remaining in the study.

Arthritis Evaluations

- The proportions of subjects with American College of Rheumatology (ACR) responses were maintained within each treatment group from Week 104 through Week 256. At Week 256, between 76.8% and 78.0% of subjects achieved an ACR 20 response, between 49.4% and 58.9% of subjects achieved an ACR 50 response, and between 36.4% and 41.1% of subjects achieved an ACR 70 response across all randomized treatment groups.

- The mean percent improvement from baseline in ACR components was stable over time from Week 104 through Week 256 with no appreciable difference between treatment groups. At Week 256, the mean percent improvement from baseline in the number of swollen joints was between 81.05% and 86.27%, the mean percent improvement from baseline in the number of tender joints was between 70.49% and 82.50%, and the mean percent improvement from baseline in CRP (C-reactive protein) was between 28.08% and 37.92% across all randomized treatment groups.
- The proportion of disease activity score (DAS) 28 (using CRP) responders was maintained from Week 104 through Week 256. At Week 256, the proportion of subjects with a DAS28 (CRP) response was between 91.3% and 94.5% across all randomized treatment groups.
- There was no appreciable change in the dactylitis score over time from Week 104 through Week 256, except in the golimumab 100 mg group where the mean dactylitis score was reduced to 71.95% at Week 256 from 85.81% at Week 104.
- An improvement was observed in the enthesitis score over time from Week 104 through Week 256. The mean change from baseline was between 42.13% and 65.64% at Week 104 and between 68.30% and 73.66% at Week 256 across all randomized treatment groups.

Psoriasis Evaluations

- The proportions of subjects with psoriasis area and severity index (PASI) responses were maintained from Week 104 through Week 256. At Week 256, between 82.9% and 94.9% of subjects achieved a PASI 50 response, between 68.6% and 78.5% of subjects achieved a PASI 75 response, and between 45.7% and 64.6% of subjects achieved a PASI 90 response across all randomized treatment groups.
- Nail disease improved with golimumab treatment and this improvement was maintained at Week 256. At Week 256, the mean percent change from baseline in nail psoriasis severity index (NAPSI) score was between 75.9% and 79.2% across all randomized treatment groups.

Physical Function

- The improvement in physical function observed at Week 104 was maintained at Week 256. At Week 256, a ≥ 0.25 unit improvement in HAQ score was achieved in 67.6% to 79.2% of subjects and a ≥ 0.30 unit improvement was achieved in 61.0% to 62.5% of subjects across all randomized treatment groups.

Quality of Life

- Improvements from baseline in the SF-36 physical component summary (PCS) and mental component summary (MCS) scores at Week 256 were generally similar to those observed at Week 104. At Week 256, the mean change from baseline in PCS scores was between 9.6 and 10.1 and the mean change from baseline in MCS scores was between 4.4 and 4.9 across all randomized treatment groups.
- The proportion of subjects achieving US population norms on the PCS and MCS SF-36 scales was maintained from Week 104 to Week 256, with a greater number of subjects achieving US population norms on the MCS scores.

Radiographic Evaluations

This 268-week clinical study report (CSR) describes radiographic results from Reading Session 3 (baseline, Week 104, Week 184, and Week 256). Scores from Reading Session 1 (baseline, Week 24, and Week 52) and Reading Session 2 (baseline, Week 52, and Week 104) were analyzed separately and reported in the 52-Week and 104-Week CSRs, respectively.

- Subjects randomized to placebo appeared to have the highest positive changes in van der Heijde-Sharp (vdH-S) scores numerically, followed by the golimumab 50 mg and 100 mg groups; however, the changes are very small. At Week 256, the mean (SD) change from baseline in total modified vdH-S scores was 0.29 (3.700), 0.18 (3.932), and -0.01 (2.596) in the placebo, golimumab 50 mg, and golimumab 100 mg groups, respectively. The results of sensitivity analysis supported the main analysis.
- At Week 184, the mean (SD) change from Week 104 in total modified vdH-S was 0.02 (0.804), 0.40 (1.735), and 0.26 (1.941) in the placebo, golimumab 50 mg, and golimumab 100 mg groups, respectively. At Week 256, the mean (SD) change from Week 104 in total modified vdH-S was 0.24 (1.076), 0.53 (2.579), and 0.44 (1.594) in the placebo, golimumab 50 mg, and golimumab 100 mg groups, respectively. There was no appreciable difference between randomized treatment groups over time.
- Among subjects with baseline erosion or joint space narrowing (JSN) score of 0, the proportions of subjects with no new erosions or JSN decreased slightly over time. At Week 104, the proportion of subjects with no new erosions in joints with a 0 score was 79.0%, 81.1%, and 89.7%, and the proportion of subjects with no new JSN in joints with a 0 score was 88.9%, 91.5%, and 90.6% in the placebo, golimumab 50 mg, and golimumab 100 mg groups, respectively. At Week 256, the proportion of subjects with no new erosions in joints with a 0 score was 65.4%, 64.2%, and 66.7%, and the proportion of subjects with no new JSN in joints with a 0 score was 79.0%, 73.6%, and 70.1% in the placebo, golimumab 50 mg, and golimumab 100 mg groups, respectively.
- The proportions of subjects who maintained a total modified vdH-S score, erosion score, and JSN score of 0 decreased slightly over time. At Week 104, the proportion of subjects with a vdH-S score of 0 was 80.0%, 100.0%, and 94.4%, the proportion of subjects with an erosion score of 0 was 83.3%, 100.0%, and 95.0% in the placebo, golimumab 50 mg, and golimumab 100 mg groups, respectively. The proportion of subjects with a JSN score of 0 was 100% for all randomized treatment group. At Week 256, the proportion of subjects with vdH-S score of 0 was 80.0%, 75.0%, and 93.8%, the proportion of subjects with erosion score of 0 was 81.8%, 85.7%, and 94.1%, and the proportion of subjects with JSN score of 0 was 95.2%, 90.0%, and 93.9% in the placebo, golimumab 50 mg, and golimumab 100 mg groups, respectively.

Health Economics

- Health economics and resource utilization measures showed improvements from baseline at Week 256. The means for hospitalizations and days spent in the hospital were each lower than baseline values for all randomized treatment groups. The mean paid household assistance visits and emergency room (ER) visits were equal to or lower than baseline values for all randomized treatment groups. The mean number of physician visits was equal to or slightly higher than baseline values for all randomized treatment groups.
- Across all randomized treatment groups, the mean change from baseline in impact of disease on productivity scores was between -3.3 and -2.8 at Week 160, between -3.6 and -2.9 at Week 208, and between -3.4 and -2.6 at Week 256.

PHARMACOKINETICS:

- Serum trough golimumab concentrations were approximately dose proportional and were generally maintained through Week 256 for subjects that were randomized to golimumab 50 mg and 100 mg and did not change dose.

Antibodies-to-golimumab:

- The overall incidence of antibodies-to-golimumab was low through Week 256 (6.0%). This was similarly low compared with the overall incidence at Week 100 (5.4%) and at Week 52 (4.0%).

- Subjects who received concomitant MTX at baseline had a lower incidence of antibodies-to-golimumab (1.8%; 3/165) through Week 256 compared with those who did not receive concomitant MTX at baseline (10.0%; 17/170).

SAFETY RESULTS:

The safety profile of golimumab through Week 268 was consistent with the safety profile observed through Week 104; no unexpected safety issues were observed. Golimumab administered SC q4wks was generally well tolerated in subjects with active PsA. Overall, there was no appreciable difference between golimumab groups.

Adverse Events (AEs): The proportion of subjects with 1 or more AEs was 88.1% in the combined golimumab group (87.1%, 91.7%, and 86.3% of subjects in the golimumab 50 mg, golimumab 100 mg, and golimumab 50 mg/100 mg groups, respectively). The 3 system organ classes (SOC) with the highest proportion of subjects with AEs through Week 268 in the combined golimumab group were Infections and infestations, Musculoskeletal and connective tissue disorders, and Gastrointestinal disorders.

Deaths: Through the Week 268 DBL, there were 5 deaths reported (2 subjects in the golimumab 50 mg group and 3 subjects in the golimumab 100 mg group). Two subjects died due to accidents ([redacted] [golimumab 50 mg] and [redacted] [golimumab 100 mg]); 2 subjects died due to carcinomas (small cell lung carcinoma with metastases [golimumab 50 mg] and esophageal cancer [golimumab 100 mg]); and the cause for 1 death is unknown (golimumab 100 mg). Two additional deaths were reported after DBL. One subject died due to colon cancer and another subject died due to small cell lung cancer.

Serious Adverse Events (SAEs): Through Week 268, the proportion of subjects for whom 1 or more SAEs was reported was 21.1% in the combined golimumab group (20.9%, 22.9%, and 19.9% of subjects in the golimumab 50 mg, golimumab 100 mg, and golimumab 50 mg/100 mg groups, respectively). The greatest proportion of SAEs was in the Neoplasms benign, malignant and unspecified (including cysts and polyps) SOC. Approximately, half of the malignancies in this SOC were basal cell carcinomas. There were no lymphomas reported.

Study Agent Discontinuation Due to AEs: Through Week 268, the proportion of subjects who discontinued study agent because of 1 or more AEs was 12.4% in the combined golimumab group (15.1%, 17.4%, and 6.2% of subjects in the golimumab 50 mg, golimumab 100 mg, and golimumab 50 mg/100 mg groups, respectively). The majority of AEs leading to discontinuation were in the Neoplasms benign, malignant and unspecified (including cysts and polyps) SOC.

Infections: The pattern and types of infections observed through Week 268 were similar to those reported through Week 104. The most frequently reported infections were upper respiratory tract infection, nasopharyngitis, sinusitis, and bronchitis, which occurred in 29.9%, 18.5%, 12.2%, and 11.9% of subjects, respectively, in the combined golimumab group. One case of presumed active tuberculosis (pulmonary TB in a subject in Poland), 2 serious opportunistic infections (toxoplasmal eye infection and legionella pneumonia), and 1 non-serious herpes zoster involving the head, face, and right eye were reported.

Serious Infections: Through Week 268, 15 (3.8%) subjects in the combined golimumab group (3.6%, 5.5%, and 2.7% of subjects the golimumab 50 mg, golimumab 100 mg, and golimumab 50 mg/100 mg groups, respectively) had at least 1 infection identified by the investigator that was reported as an SAE. Serious infections reported in more than 1 subject included abscess and cellulitis.

Malignancies: Overall, 21 subjects in the combined golimumab group had 1 or more malignancies (8, 8, and 5 subjects in the golimumab 50 mg, golimumab 100 mg, and golimumab 50 mg/100 mg groups, respectively). There were no subjects with malignancies in the placebo group. There were no subjects with lymphoma in any randomized treatment group.

The incidence per 100 subject-years (95% confidence interval [CI]) for all malignancies was 0.00 (0.00, 7.55), 1.58 (0.68, 3.12), 1.77 (0.77, 3.49), and 0.74 (0.24, 1.72) in the, placebo, golimumab 50 mg, golimumab 100 mg, and golimumab 50 mg/100 mg groups, respectively.

The standard incidence ratio (95% CI) for all malignancies was 0.00 (0.00, 16.10), 1.85 (0.60, 4.32), 1.42 (0.39, 3.64), and 0.57 (0.07, 2.05) in the, placebo, golimumab 50 mg, golimumab 100 mg, and golimumab 50 mg/100 mg groups, respectively.

Injection-site Reactions: Through Week 268, 9.4% of subjects in the combined golimumab group (10.1%, 13.8%, and 5.5% of subjects in the golimumab 50 mg, golimumab 100 mg, and golimumab 50 mg/100 mg groups, respectively) had an injection-site reaction. The most commonly reported injection-site reactions were erythema, haematoma, and swelling. There were no events of anaphylaxis or serum sickness-like reactions. None of the injection-site reactions were severe and none resulted in study agent discontinuation.

Laboratory Assessments: Laboratory safety assessments through Week 256 did not identify safety issues not previously reported through Week 104.

STUDY LIMITATIONS: There are several limitations to the analyses after Week 24. There were no subjects receiving placebo after Week 24, and therefore there are no data for the control group beyond Week 24. The study was open label after the Week 52 DBL. In addition, subjects had an opportunity to change golimumab treatments from 50 mg to 100 mg and from 100 mg to 50 mg during the LTE of the study. A total of 42 subjects dose-escalated from golimumab 50 mg q4wks to golimumab 100 mg q4wks and 37 subjects dose-decreased from golimumab 100 mg q4wks to golimumab 50 mg q4wks between Week 104 and Week 256 based on the investigator's judgment of a subject's clinical status. However, the small number of such subjects limits conclusions regarding the effect of dose change.

CONCLUSIONS:

The long-term safety and efficacy of golimumab 50 mg and 100 mg administered subcutaneously q4wks through 5 years in subjects with active PsA were demonstrated by:

- Reduction in clinical signs and symptoms of arthritis, decrease in the severity of dactylitis and enthesitis, improvement in psoriatic skin and nail lesions, and improvement in quality of life. Efficacy in improving arthritis and associated psoriasis was observed irrespective of baseline MTX use
- Inhibition of progression of structural damage
- Improvement in physical function
- Similar proportions of subjects with AEs and SAEs, and similar types of events in the golimumab 50 mg and 100 mg groups
- Rare occurrence of TB and opportunistic infections
- Maintenance of serum golimumab exposure over time
- Low incidence of antibodies-to-golimumab
- Safety profile similar to other anti-TNFα agents and to golimumab in other rheumatologic indications.