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Trial record **1 of 1** for: CR006331

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A Study of the Safety and Efficacy of Golimumab in Subjects With Rheumatoid Arthritis That Are Methotrexate-naive

This study has been completed.

Sponsor:
Centocor, Inc.

Collaborator:
Schering-Plough

Information provided by (Responsible Party):
Centocor, Inc.

ClinicalTrials.gov Identifier:
NCT00264537

First received: December 11, 2005
Last updated: August 27, 2014
Last verified: August 2014
History of Changes

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Results First Received: May 21, 2009

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Rheumatoid Arthritis
Interventions:	Drug: Placebo injections Drug: Placebo capsules Drug: Methotrexate capsules Biological: Golimumab 50 mg injections Biological: Golimumab 100 mg injections

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
A total of 637 participants were enrolled at 90 centers: 25 sites in Asia, 34 sites in Europe/Australia/New Zealand, 10 sites in Latin America and 21 sites in North America.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Group 1: Placebo + Methotrexate	Placebo subcutaneous injections (SC) every 4 weeks from Week 0 for up to 5 years (unless early escape at week 28); Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years;

	Golimumab - if early escape, 50 mg SC injections every 4 weeks from Week 28 up to 5 years; Golimumab – Dr's discretion after unblinding (in participants receiving methotrexate plus placebo), 50 mg SC injections every 4 weeks up to 5 years; Golimumab- Dr's discretion after unblinding, dose adjusted from 50 to 100 mg and from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 2: Golimumab 100 mg + Placebo	Golimumab 100 mg SC injections every 4 weeks from Week 0 for up to 5 years; placebo capsules weekly from Week 0 for up to 5 years (unless early escape at Week 28); Methotrexate - if early escape, 10 to 20 mg weekly from Week 28 up to 5 years; Methotrexate – Dr's discretion after unblinding (in participants receiving golimumab plus placebo) 10 to 20 mg weekly for up to 5 years; Golimumab - Dr's discretion after unblinding, dose adjusted from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 3: Golimumab 50 mg + Methotrexate	Golimumab 50 mg SC injections every 4 weeks from Week 0 for up to 5 years (unless early escape at week 28); Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - if early escape, 100 mg SC injections every 4 weeks from Week 28 for up to 5 yrs; Golimumab - Dr's discretion after unblinding, dose adjusted from 50 to 100 mg and from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 4: Golimumab 100 mg + Methotrexate	Golimumab 100 mg SC injections every 4 weeks from Week 0 for up to 5 years; Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - Dr's discretion after unblinding, dose adjusted from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.

Participant Flow: Overall Study

	Group 1: Placebo + Methotrexate	Group 2: Golimumab 100 mg + Placebo	Group 3: Golimumab 50 mg + Methotrexate	Group 4: Golimumab 100 mg + Methotrexate
STARTED	160	159	159	159
COMPLETED	110	101	109	99
NOT COMPLETED	50	58	50	60
Death	0	3	3	2
Lost to Follow-up	3	4	7	6
Adverse Event	21	32	24	34
Unsatisfactory therapeutic effect	5	6	5	7
Not specified	21	11	10	11
Not treated	0	2	1	0

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Group 1: Placebo + Methotrexate	Placebo subcutaneous injections (SC) every 4 weeks from Week 0 for up to 5 years (unless early escape at week 28); Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - if early escape, 50 mg SC injections every 4 weeks from Week 28 up to 5 years; Golimumab – Dr's discretion after unblinding (in participants receiving methotrexate plus placebo), 50 mg SC injections every 4 weeks up to 5 years; Golimumab- Dr's discretion after unblinding, dose adjusted from 50 to 100 mg and from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.

Group 2: Golimumab 100 mg + Placebo	Golimumab 100 mg SC injections every 4 weeks from Week 0 for up to 5 years; placebo capsules weekly from Week 0 for up to 5 years (unless early escape at Week 28); Methotrexate - if early escape, 10 to 20 mg weekly from Week 28 up to 5 years; Methotrexate – Dr's discretion after unblinding (in participants receiving golimumab plus placebo) 10 to 20 mg weekly for up to 5 years; Golimumab - Dr's discretion after unblinding, dose adjusted from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 3: Golimumab 50 mg + Methotrexate	Golimumab 50 mg SC injections every 4 weeks from Week 0 for up to 5 years (unless early escape at week 28); Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - if early escape, 100 mg SC injections every 4 weeks from Week 28 for up to 5 yrs; Golimumab - Dr's discretion after unblinding, dose adjusted from 50 to 100 mg and from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 4: Golimumab 100 mg + Methotrexate	Golimumab 100 mg SC injections every 4 weeks from Week 0 for up to 5 years; Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - Dr's discretion after unblinding, dose adjusted from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Total	Total of all reporting groups

Baseline Measures

	Group 1: Placebo + Methotrexate	Group 2: Golimumab 100 mg + Placebo	Group 3: Golimumab 50 mg + Methotrexate	Group 4: Golimumab 100 mg + Methotrexate	Total
Number of Participants [units: participants]	**160**	**159**	**159**	**159**	**637**
Age [units: years] Mean (Standard Deviation)	**48.6 (12.91)**	**48.2 (12.85)**	**50.9 (11.32)**	**50.2 (11.87)**	**49.5 (12.28)**
Gender [units: participants]					
Female	**134**	**134**	**135**	**125**	**528**
Male	**26**	**25**	**24**	**34**	**109**

Outcome Measures

Hide All Outcome Measures

1. Primary: Number of Participants Who Achieved American College of Rheumatology (ACR) 50 Response at Week 24 [Time Frame: Week 24]

Measure Type	Primary
Measure Title	Number of Participants Who Achieved American College of Rheumatology (ACR) 50 Response at Week 24
Measure Description	ACR 50 response is defined as a greater than or equal to 50 percent improvement from baseline in: 1. Swollen joint count (66 joints) and tender joint count (68 joints) 2. greater than or equal to 50 percentage improvement in 3 of the following 5 assessments: a. Patient's assessment of pain by the Visual Analogue Scale (VAS) (0-10 cm) b.Patient's Global Assessment of Disease activity VAS (0-10 cm) c. Physician's Global Assessment of Disease Activity VAS (0-10 cm) d. Patient's assessment of physical function as measured by the Health Assessment Questionnaire (HAQ) e. C reactive protein.
Time Frame	Week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.

All participants randomly assigned to each treatment group. Participants considered non-responders if used any prohibited medications or discontinued subcutaneous study agent due to lack of efficacy. Missing ACR components imputed by Last Observation Carried Forward unless all ACR components were missing; in which case considered non-responders.

Reporting Groups

	Description
Group 1: Placebo + Methotrexate	Placebo subcutaneous injections (SC) every 4 weeks from Week 0 for up to 5 years (unless early escape at week 28); Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - if early escape, 50 mg SC injections every 4 weeks from Week 28 up to 5 years; Golimumab – Dr's discretion after unblinding (in participants receiving methotrexate plus placebo), 50 mg SC injections every 4 weeks up to 5 years; Golimumab- Dr's discretion after unblinding, dose adjusted from 50 to 100 mg and from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 2: Golimumab 100 mg + Placebo	Golimumab 100 mg SC injections every 4 weeks from Week 0 for up to 5 years; placebo capsules weekly from Week 0 for up to 5 years (unless early escape at Week 28); Methotrexate - if early escape, 10 to 20 mg weekly from Week 28 up to 5 years; Methotrexate – Dr's discretion after unblinding (in participants receiving golimumab plus placebo) 10 to 20 mg weekly for up to 5 years; Golimumab - Dr's discretion after unblinding, dose adjusted from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 3: Golimumab 50 mg + Methotrexate	Golimumab 50 mg SC injections every 4 weeks from Week 0 for up to 5 years (unless early escape at week 28); Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - if early escape, 100 mg SC injections every 4 weeks from Week 28 for up to 5 yrs; Golimumab - Dr's discretion after unblinding, dose adjusted from 50 to 100 mg and from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 4: Golimumab 100 mg + Methotrexate	Golimumab 100 mg SC injections every 4 weeks from Week 0 for up to 5 years; Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - Dr's discretion after unblinding, dose adjusted from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Combined Golimumab + Methotrexate	Combines Group 3 (golimumab 50 mg + methotrexate) and Group 4 (golimumab 100 mg + methotrexate)

Measured Values

	Group 1: Placebo + Methotrexate	Group 2: Golimumab 100 mg + Placebo	Group 3: Golimumab 50 mg + Methotrexate	Group 4: Golimumab 100 mg + Methotrexate	Combined Golimumab + Methotrexate
Number of Participants Analyzed [units: participants]	**160**	**159**	**159**	**159**	**318**
Number of Participants Who Achieved American College of Rheumatology (ACR) 50 Response at Week 24 [units: Participants]	**47**	**52**	**64**	**58**	**122**

Statistical Analysis 1 for Number of Participants Who Achieved American College of Rheumatology (ACR) 50 Response at Week 24

Groups [1]	Group 1: Placebo + Methotrexate vs. Combined Golimumab + Methotrexate
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.053

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Null hypothesis: No difference in ACR 50 response comparing Group 1 vs combined Groups 3 and 4. The sample size of 150 patients per treatment group will provide >98% power to detect a difference in ACR 50 response between treatment groups at alpha=0.05, assuming 50% of patients with screening C-reactive protein (CRP)<1.5mg/dL, and the difference in ACR 50 response of 15-20% in patients with screening CRP<1.5mg/dL and 20-25% in subjects with screening CRP>=1.5mg/dL, between Groups 1 vs 3 or 4

[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel (CMH) test stratified by screening CRP (< 1.5 mg/dL; >= 1.5 mg/dL)
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	A positive test is concluded if there is a significant difference between golimumab+MTX and placebo+MTX and at least one of the pair-wise comparisons at a 0.05 level.

Statistical Analysis 2 for Number of Participants Who Achieved American College of Rheumatology (ACR) 50 Response at Week 24

Groups [1]	Group 1: Placebo + Methotrexate vs. Group 3: Golimumab 50 mg + Methotrexate
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.042

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Null hypothesis: No difference in ACR 50 response comparing Groups 1 vs 3.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel (CMH) test stratified by screening C-reactive protein (CRP) (< 1.5 mg/dL; >= 1.5 mg/dL)
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 3 for Number of Participants Who Achieved American College of Rheumatology (ACR) 50 Response at Week 24

Groups [1]	Group 1: Placebo + Methotrexate vs. Group 4: Golimumab 100 mg + Methotrexate
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.177

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Null hypothesis: No difference in ACR 50 response comparing Groups 1 vs 4.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel (CMH) test stratified by screening C-reactive protein (CRP) (< 1.5 mg/dL; >= 1.5 mg/dL)
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 4 for Number of Participants Who Achieved American College of Rheumatology (ACR) 50 Response at Week 24

Groups [1]	Group 1: Placebo + Methotrexate vs. Group 2: Golimumab 100 mg + Placebo
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	Cochran-Mantel-Haenszel
P Value [4]	0.521
Difference in ACR 50 Response Rate(%) [5]	3.3
95% Confidence Interval [6]	-6.8 to N/A

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Null hypothesis: Group 2 is inferior to Group 1. Noninferiority of golimumab will be demonstrated if the lower bound of the 2-sided 95% CI is above -10%. The 10% non-inferiority margin was chosen because this difference is not clinically admissible. Under the

	above noted assumed response rates, this corresponds to preservation of at least 70% [(33% - 10%)/33%*100] of the expected "MTX benefit".
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	This sample size (150 patients per treatment group) will provide approximately 85% power to claim non-inferiority of golimumab alone (Group 2) compared with MTX alone (Group 1) at alpha= 0.05 using a one-sided equivalence test assuming the proportion of golimumab alone (Group 2) treated patients with ACR 50 response is not less than 10% compared with proportion of patients with ACR 50 response in MTX alone (Group 1) treated group.
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel (CMH) test stratified by screening C-reactive protein (CRP) (< 1.5 mg/dL; >= 1.5 mg/dL)
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	The positive difference indicates in favor of golimumab+placebo compared to placebo+MTX; The upper bound of CI is not applicable.
[6]	Confidence interval upper limit not applicable:

2. Primary: Change From Baseline in Total Van Der Heijde Modified Sharp (vdH-S) Score at Week 52 [Time Frame: Baseline and Week 52]

Measure Type	Primary
Measure Title	Change From Baseline in Total Van Der Heijde Modified Sharp (vdH-S) Score at Week 52
Measure Description	The vdH-S score is the sum of the joint erosion score and the joint-space narrowing (JSN) score. The total score ranges from 0 (best) to 448 (worst) with higher scores indicating more joint damage.
Time Frame	Baseline and Week 52
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All participants randomly assigned to each treatment group.

Reporting Groups

	Description
Group 1: Placebo + Methotrexate	Placebo subcutaneous injections (SC) every 4 weeks from Week 0 for up to 5 years (unless early escape at week 28); Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - if early escape, 50 mg SC injections every 4 weeks from Week 28 up to 5 years; Golimumab – Dr's discretion after unblinding (in participants receiving methotrexate plus placebo), 50 mg SC injections every 4 weeks up to 5 years; Golimumab- Dr's discretion after unblinding, dose adjusted from 50 to 100 mg and from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 2: Golimumab 100 mg + Placebo	Golimumab 100 mg SC injections every 4 weeks from Week 0 for up to 5 years; placebo capsules weekly from Week 0 for up to 5 years (unless early escape at Week 28); Methotrexate - if early escape, 10 to 20 mg weekly from Week 28 up to 5 years; Methotrexate – Dr's discretion after unblinding (in participants receiving golimumab plus placebo) 10 to 20 mg weekly for up to 5 years; Golimumab - Dr's discretion after unblinding, dose adjusted from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 3: Golimumab 50 mg + Methotrexate	Golimumab 50 mg SC injections every 4 weeks from Week 0 for up to 5 years (unless early escape at week 28); Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years;

	Golimumab - if early escape, 100 mg SC injections every 4 weeks from Week 28 for up to 5 yrs; Golimumab - Dr's discretion after unblinding, dose adjusted from 50 to 100 mg and from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 4: Golimumab 100 mg + Methotrexate	Golimumab 100 mg SC injections every 4 weeks from Week 0 for up to 5 years; Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - Dr's discretion after unblinding, dose adjusted from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Combined Golimumab + Methotrexate	Combines Group 3 (golimumab 50 mg + methotrexate) and Group 4 (golimumab 100 mg + methotrexate)

Measured Values

	Group 1: Placebo + Methotrexate	Group 2: Golimumab 100 mg + Placebo	Group 3: Golimumab 50 mg + Methotrexate	Group 4: Golimumab 100 mg + Methotrexate	Combined Golimumab + Methotrexate
Number of Participants Analyzed [units: participants]	**160**	**159**	**159**	**159**	**318**
Change From Baseline in Total Van Der Heijde Modified Sharp (vdH-S) Score at Week 52 [units: Scores on a scale] Mean (Standard Deviation)	**1.37 (4.555)**	**1.25 (6.155)**	**0.74 (5.233)**	**0.07 (1.833)**	**0.41 (3.929)**

Statistical Analysis 1 for Change From Baseline in Total Van Der Heijde Modified Sharp (vdH-S) Score at Week 52

Groups [1]	Group 1: Placebo + Methotrexate vs. Combined Golimumab + Methotrexate
Method [2]	ANOVA
P Value [3]	0.006

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Null Hypothesis: No difference in vdH-S score comparing Groups 1 vs Groups 3 and 4 combined. The sample size of 150 subjects in each treatment group (Group 1, Group 3, Group 4) will provide > 95% power to detect a difference in the vdH-S score between treatment groups using a 2-sided t-test on van der Waerden normal scores of change from baseline in vdH-S score at α = 0.05, assuming a mean change from baseline in vdH-S score of 3.5 for the placebo group and 1 for Groups 3 and 4.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	A 2-sided ANOVA on the van der Waerden normal scores with 1 factor: screening CRP (< 1.5 mg/dL; ≥ 1.5 mg/dL)
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	If this test is significant, a pairwise comparison between Group 3 and Group 1, and between Group 4 and Group 1 will be performed

Statistical Analysis 2 for Change From Baseline in Total Van Der Heijde Modified Sharp (vdH-S) Score at Week 52

Groups [1]	Group 1: Placebo + Methotrexate vs. Group 3: Golimumab 50 mg + Methotrexate
Method [2]	ANOVA
P Value [3]	0.015

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Null hypothesis: No difference in vdH-S score comparing Groups 1 vs 3.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	A 2-sided ANOVA on the van der Waerden normal scores with 1 factor: screening CRP (< 1.5 mg/dL; >= 1.5 mg/dL)
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

	No text entered.

Statistical Analysis 3 for Change From Baseline in Total Van Der Heijde Modified Sharp (vdH-S) Score at Week 52

Groups [1]	Group 1: Placebo + Methotrexate vs. Group 4: Golimumab 100 mg + Methotrexate
Method [2]	ANOVA
P Value [3]	0.025

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Null hypothesis: No difference in vdH-S score comparing Groups 1 vs 4.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	A 2-sided ANOVA on the van der Waerden normal scores with 1 factor: screening CRP (< 1.5 mg/dL; >= 1.5 mg/dL)
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

3. Secondary: Number of Participants Who Achieved American College of Rheumatology (ACR) 20 Response at Week 24 [Time Frame: Week 24]

Measure Type	Secondary
Measure Title	Number of Participants Who Achieved American College of Rheumatology (ACR) 20 Response at Week 24
Measure Description	ACR 20 response is defined as a greater than or equal to 20 percent improvement from baseline in: 1. Swollen joint count (66 joints) and tender joint count (68 joints) 2. greater than or equal to 20 percentage improvement in 3 of the following 5 assessments: a. Patient's assessment of pain by the Visual Analogue Scale (VAS) (0-10 cm) b.Patient's Global Assessment of Disease activity VAS (0-10 cm) c. Physician's Global Assessment of Disease Activity VAS (0-10 cm) d. Patient's assessment of physical function as measured by the Health Assessment Questionnaire (HAQ) e. C reactive protein.
Time Frame	Week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All participants randomly assigned to each treatment group. Participants considered non-responders if used any prohibited medications or discontinued subcutaneous study agent due to lack of efficacy. Missing ACR components imputed by Last Observation Carried Forward unless all ACR components were missing; in which case considered non-responders.

Reporting Groups

	Description
Group 1: Placebo + Methotrexate	Placebo subcutaneous injections (SC) every 4 weeks from Week 0 for up to 5 years (unless early escape at week 28); Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - if early escape, 50 mg SC injections every 4 weeks from Week 28 up to 5 years; Golimumab – Dr's discretion after unblinding (in participants receiving methotrexate plus placebo), 50 mg SC injections every 4 weeks up to 5 years; Golimumab- Dr's discretion after unblinding, dose adjusted from 50 to 100 mg and from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 2: Golimumab 100 mg + Placebo	Golimumab 100 mg SC injections every 4 weeks from Week 0 for up to 5 years; placebo capsules weekly from Week 0 for up to 5 years (unless early escape at Week 28); Methotrexate - if early escape, 10 to 20 mg weekly from Week 28 up to 5 years; Methotrexate – Dr's discretion after unblinding (in participants receiving golimumab plus placebo) 10 to 20

	mg weekly for up to 5 years; Golimumab - Dr's discretion after unblinding, dose adjusted from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 3: Golimumab 50 mg + Methotrexate	Golimumab 50 mg SC injections every 4 weeks from Week 0 for up to 5 years (unless early escape at week 28); Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - if early escape, 100 mg SC injections every 4 weeks from Week 28 for up to 5 yrs; Golimumab - Dr's discretion after unblinding, dose adjusted from 50 to 100 mg and from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 4: Golimumab 100 mg + Methotrexate	Golimumab 100 mg SC injections every 4 weeks from Week 0 for up to 5 years; Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - Dr's discretion after unblinding, dose adjusted from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Combined Golimumab + Methotrexate	Combines Group 3 (golimumab 50 mg + methotrexate) and Group 4 (golimumab 100 mg + methotrexate)

Measured Values

	Group 1: Placebo + Methotrexate	Group 2: Golimumab 100 mg + Placebo	Group 3: Golimumab 50 mg + Methotrexate	Group 4: Golimumab 100 mg + Methotrexate	Combined Golimumab + Methotrexate
Number of Participants Analyzed [units: participants]	**160**	**159**	**159**	**159**	**318**
Number of Participants Who Achieved American College of Rheumatology (ACR) 20 Response at Week 24 [units: Participants]	**79**	**82**	**98**	**98**	**196**

Statistical Analysis 1 for Number of Participants Who Achieved American College of Rheumatology (ACR) 20 Response at Week 24

Groups [1]	Group 1: Placebo + Methotrexate vs. Combined Golimumab + Methotrexate
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.011

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel(CMH) test stratified by screening C-reactive protein (CRP) (< 1.5 mg/dL; >= 1.5 mg/dL)
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 2 for Number of Participants Who Achieved American College of Rheumatology (ACR) 20 Response at Week 24

Groups [1]	Group 1: Placebo + Methotrexate vs. Group 3: Golimumab 50 mg + Methotrexate
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.028

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	CMH test stratified by screening CRP (< 1.5 mg/dL; >= 1.5 mg/dL)

[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 3 for Number of Participants Who Achieved American College of Rheumatology (ACR) 20 Response at Week 24

Groups [1]	Group 1: Placebo + Methotrexate vs. Group 4: Golimumab 100 mg + Methotrexate
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.028

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	CMH test stratified by screening CRP (< 1.5 mg/dL; >= 1.5 mg/dL)
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 4 for Number of Participants Who Achieved American College of Rheumatology (ACR) 20 Response at Week 24

Groups [1]	Group 1: Placebo + Methotrexate vs. Group 2: Golimumab 100 mg + Placebo
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.677

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	CMH test stratified by screening CRP (< 1.5 mg/dL; >= 1.5 mg/dL)
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

4. Secondary: Number of Patients With Abnormal Baseline C-reactive Protein (CRP) Who Achieved American College of Rheumatology (ACR) 50 Response at Week 24 [Time Frame: Week 24]

Measure Type	Secondary
Measure Title	Number of Patients With Abnormal Baseline C-reactive Protein (CRP) Who Achieved American College of Rheumatology (ACR) 50 Response at Week 24
Measure Description	ACR 50 response is defined as a greater than or equal to 50 percent improvement from baseline in: 1. Swollen joint count (66 joints) and tender joint count (68 joints) 2. greater than or equal to 50 percentage improvement in 3 of the following 5 assessments: a. Patient's assessment of pain by the Visual Analogue Scale (VAS) (0-10 cm) b.Patient's Global Assessment of Disease activity VAS (0-10 cm) c. Physician's Global Assessment of Disease Activity VAS (0-10 cm) d. Patient's assessment of physical function as measured by the Health Assessment Questionnaire (HAQ) e. C reactive protein.
Time Frame	Week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Randomized participants with abnormal baseline CRP. Participants considered non-responders if used any prohibited medications or discontinued subcutaneous study agent due to lack of efficacy. Missing ACR components imputed by Last Observation Carried Forward unless all ACR components were missing; in which case considered non-responders.

Reporting Groups

	Description
Group 1: Placebo + Methotrexate	Placebo subcutaneous injections (SC) every 4 weeks from Week 0 for up to 5 years (unless early escape at week 28); Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - if early escape, 50 mg SC injections every 4 weeks from Week 28 up to 5 years; Golimumab – Dr's discretion after unblinding (in participants receiving methotrexate plus placebo), 50 mg SC injections every 4 weeks up to 5 years; Golimumab- Dr's discretion after unblinding, dose adjusted from 50 to 100 mg and from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 2: Golimumab 100 mg + Placebo	Golimumab 100 mg SC injections every 4 weeks from Week 0 for up to 5 years; placebo capsules weekly from Week 0 for up to 5 years (unless early escape at Week 28); Methotrexate - if early escape, 10 to 20 mg weekly from Week 28 up to 5 years; Methotrexate – Dr's discretion after unblinding (in participants receiving golimumab plus placebo) 10 to 20 mg weekly for up to 5 years; Golimumab - Dr's discretion after unblinding, dose adjusted from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 3: Golimumab 50 mg + Methotrexate	Golimumab 50 mg SC injections every 4 weeks from Week 0 for up to 5 years (unless early escape at week 28); Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - if early escape, 100 mg SC injections every 4 weeks from Week 28 for up to 5 yrs; Golimumab - Dr's discretion after unblinding, dose adjusted from 50 to 100 mg and from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 4: Golimumab 100 mg + Methotrexate (MTX)	Golimumab 100 mg SC injections every 4 weeks from Week 0 for up to 5 years; Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - Dr's discretion after unblinding, dose adjusted from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Combined Golimumab + Methotrexate	Combines Group 3 (golimumab 50 mg + methotrexate) and Group 4 (golimumab 100 mg + methotrexate)

Measured Values

	Group 1: Placebo + Methotrexate	**Group 2: Golimumab 100 mg + Placebo**	**Group 3: Golimumab 50 mg + Methotrexate**	**Group 4: Golimumab 100 mg + Methotrexate (MTX)**	**Combined Golimumab + Methotrexate**
Number of Participants Analyzed [units: participants]	**95**	**90**	**86**	**83**	**169**
Number of Patients With Abnormal Baseline C-reactive Protein (CRP) Who Achieved American College of Rheumatology (ACR) 50 Response at Week 24 [units: Participants]	**34**	**26**	**38**	**37**	**75**

Statistical Analysis 1 for Number of Patients With Abnormal Baseline C-reactive Protein (CRP) Who Achieved American College of Rheumatology (ACR) 50 Response at Week 24

Groups [1]	Group 1: Placebo + Methotrexate vs. Combined Golimumab + Methotrexate
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.178

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel (CMH) test stratified by screening C-reactive protein (CRP) (< 1.5 mg/dL; >= 1.5 mg/dL)
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 2 for Number of Patients With Abnormal Baseline C-reactive Protein (CRP) Who Achieved American College of Rheumatology (ACR) 50 Response at Week 24

Groups [1]	Group 1: Placebo + Methotrexate vs. Group 3: Golimumab 50 mg + Methotrexate
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.250

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel (CMH) test stratified by screening C-reactive protein (CRP) (< 1.5 mg/dL; >= 1.5 mg/dL)
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 3 for Number of Patients With Abnormal Baseline C-reactive Protein (CRP) Who Achieved American College of Rheumatology (ACR) 50 Response at Week 24

Groups [1]	Group 1: Placebo + Methotrexate vs. Group 4: Golimumab 100 mg + Methotrexate (MTX)
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.240

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Cochran-Mantel-Haenszel(CMH) test stratified by screening C-reactive protein (CRP) (< 1.5 mg/dL; >= 1.5 mg/dL)
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 4 for Number of Patients With Abnormal Baseline C-reactive Protein (CRP) Who Achieved American College of Rheumatology (ACR) 50 Response at Week 24

Groups [1]	Group 1: Placebo + Methotrexate vs. Group 2: Golimumab 100 mg + Placebo
Method [2]	Cochran-Mantel-Haenszel
P Value [3]	0.339

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:

	Cochran-Mantel-Haenszel(CMH) test stratified by screening C-reactive protein (CRP) (< 1.5 mg/dL; >= 1.5 mg/dL)
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

5. Secondary: Change From Baseline in Total Van Der Heijde Modified Sharp (vdH-S) Score at Week 52 in Patients With Abnormal C-reactive Protein (CRP Greater Than 1.0 mg/dL) at Baseline [Time Frame: Baseline and Week 52]

Measure Type	Secondary
Measure Title	Change From Baseline in Total Van Der Heijde Modified Sharp (vdH-S) Score at Week 52 in Patients With Abnormal C-reactive Protein (CRP Greater Than 1.0 mg/dL) at Baseline
Measure Description	The vdH-S score is the sum of the joint erosion score and the joint-space narrowing (JSN) score. The total score ranges from 0 (best) to 448 (worst) with higher scores indicating more joint damage.
Time Frame	Baseline and Week 52
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All participants randomly assigned to each treatment group who had C-reactive protein > 1.0 mg/dl at baseline.

Reporting Groups

	Description
Group 1: Placebo + Methotrexate	Placebo subcutaneous injections (SC) every 4 weeks from Week 0 for up to 5 years (unless early escape at week 28); Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - if early escape, 50 mg SC injections every 4 weeks from Week 28 up to 5 years; Golimumab – Dr's discretion after unblinding (in participants receiving methotrexate plus placebo), 50 mg SC injections every 4 weeks up to 5 years; Golimumab- Dr's discretion after unblinding, dose adjusted from 50 to 100 mg and from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 2: Golimumab 100 mg + Placebo	Golimumab 100 mg SC injections every 4 weeks from Week 0 for up to 5 years; placebo capsules weekly from Week 0 for up to 5 years (unless early escape at Week 28); Methotrexate - if early escape, 10 to 20 mg weekly from Week 28 up to 5 years; Methotrexate – Dr's discretion after unblinding (in participants receiving golimumab plus placebo) 10 to 20 mg weekly for up to 5 years; Golimumab - Dr's discretion after unblinding, dose adjusted from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 3: Golimumab 50 mg + Methotrexate	Golimumab 50 mg SC injections every 4 weeks from Week 0 for up to 5 years (unless early escape at week 28); Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - if early escape, 100 mg SC injections every 4 weeks from Week 28 for up to 5 yrs; Golimumab - Dr's discretion after unblinding, dose adjusted from 50 to 100 mg and from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Group 4: Golimumab 100 mg + Methotrexate	Golimumab 100 mg SC injections every 4 weeks from Week 0 for up to 5 years; Methotrexate - 10 to 20 mg weekly from Week 0 for up to 5 years; Golimumab - Dr's discretion after unblinding, dose adjusted from 100 to 50mg. Duration of the blinded period was until the week-52 database lock.
Combined: Golimumab + Methotrexate	Combines Group 3 (golimumab 50 mg + methotrexate) and Group 4 (golimumab 100 mg + methotrexate)

Measured Values

	Group 1: Placebo +	**Group 2: Golimumab**	**Group 3: Golimumab**	**Group 4: Golimumab**	**Combined: Golimumab +**

	Methotrexate	100 mg + Placebo	50 mg + Methotrexate	100 mg + Methotrexate	Methotrexate
Number of Participants Analyzed [units: participants]	**160**	**159**	**159**	**159**	**318**
Change From Baseline in Total Van Der Heijde Modified Sharp (vdH-S) Score at Week 52 in Patients With Abnormal C-reactive Protein (CRP Greater Than 1.0 mg/dL) at Baseline [units: Scores on a scale] Mean (Standard Deviation)	**2.16 (5.642)**	**2.19 (7.967)**	**1.29 (6.991)**	**0.16 (2.195)**	**0.74 (5.235)**

Statistical Analysis 1 for Change From Baseline in Total Van Der Heijde Modified Sharp (vdH-S) Score at Week 52 in Patients With Abnormal C-reactive Protein (CRP Greater Than 1.0 mg/dL) at Baseline

Groups [1]	Group 1: Placebo + Methotrexate vs. Combined: Golimumab + Methotrexate
Method [2]	ANOVA
P Value [3]	0.003

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	2-sided ANOVA on the van der Waerden normal scores
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 2 for Change From Baseline in Total Van Der Heijde Modified Sharp (vdH-S) Score at Week 52 in Patients With Abnormal C-reactive Protein (CRP Greater Than 1.0 mg/dL) at Baseline

Groups [1]	Group 1: Placebo + Methotrexate vs. Group 3: Golimumab 50 mg + Methotrexate
Method [2]	ANOVA
P Value [3]	0.010

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	2-sided ANOVA on the van der Waerden normal scores
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 3 for Change From Baseline in Total Van Der Heijde Modified Sharp (vdH-S) Score at Week 52 in Patients With Abnormal C-reactive Protein (CRP Greater Than 1.0 mg/dL) at Baseline

Groups [1]	Group 1: Placebo + Methotrexate vs. Group 4: Golimumab 100 mg + Methotrexate
Method [2]	ANOVA
P Value [3]	0.014

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.

[2]	Other relevant method information, such as adjustments or degrees of freedom:
	2-sided ANOVA on the van der Waerden normal scores
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 4 for Change From Baseline in Total Van Der Heijde Modified Sharp (vdH-S) Score at Week 52 in Patients With Abnormal C-reactive Protein (CRP Greater Than 1.0 mg/dL) at Baseline

Groups [1]	Group 1: Placebo + Methotrexate vs. Group 2: Golimumab 100 mg + Placebo
Method [2]	ANOVA
P Value [3]	0.545

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	2-sided ANOVA on the van der Waerden normal scores
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Adverse event data were collected for 5 years
Additional Description	3 of 637 randomized participants did not receive treatment & additional 18 participants did not receive any treatment with golimumab during the study. Thus only 616 participants are included in 5-year safety data. AEs were planned to be reported in relation to the doses of golimumab received throughout the study, rather than the treatment regimen.

Reporting Groups

	Description
Group A: Golimumab 50 mg SC Injections Only	Participants who were treated with golimumab and received golimumab 50 mg injections only during the study. Participants also received methotrexate capsules throughout the study. Participants were included from Group 1 and Group 3, who received only Golimumab 50 mg SC Injections.
Group B: Golimumab 100 mg SC Injections Only	Participants who were treated with golimumab and received golimumab 100 mg injections only during the study. Participants also received either methotrexate or placebo capsules throughout the study. Participants were included from Group 1, Group 2 and Group 4, who received only Golimumab 100 mg SC Injections.
Group C: Golimumab 50 and 100 mg SC Injections	Participants who were treated with golimumab and received at least one injection of both golimumab 50 mg and golimumab 100 mg during the study. Participants also received either methotrexate or placebo capsules throughout the study. Participants were included from Group 1, Group 2, Group 3 and Group 4, who received Golimumab 50 mg and 100 mg SC Injections.

Serious Adverse Events

	Group A: Golimumab 50 mg SC Injections Only	**Group B: Golimumab 100 mg SC Injections Only**	**Group C: Golimumab 50 and 100 mg SC Injections**
Total, serious adverse events			

# participants affected / at risk	55/172 (31.98%)	94/243 (38.68%)	55/201 (27.36%)
Blood and lymphatic system disorders			
Anaemia † 1			
# participants affected / at risk	0/172 (0.00%)	2/243 (0.82%)	0/201 (0.00%)
Febrile Neutropenia † 1			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)
Pancytopenia † 1			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)
Cardiac disorders			
Acute Coronary Syndrome † 1			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)
Angina Unstable † 1			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)
Cardiac Arrest † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Cardio-Respiratory Arrest † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Coronary Artery Occlusion † 1			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)
Coronary Artery Stenosis † 1			
# participants affected / at risk	0/172 (0.00%)	0/243 (0.00%)	1/201 (0.50%)
Mitral Valve Incompetence † 1			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)
Myocardial Infarction † 1			
# participants affected / at risk	1/172 (0.58%)	2/243 (0.82%)	1/201 (0.50%)
Pericarditis † 1			
# participants affected / at risk	0/172 (0.00%)	0/243 (0.00%)	1/201 (0.50%)
Supraventricular Tachycardia † 1			
# participants affected / at risk	2/172 (1.16%)	1/243 (0.41%)	0/201 (0.00%)
Endocrine disorders			
Addison's Disease † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Eye disorders			
Cataract † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Retinal Artery Embolism † 1			
# participants affected / at risk	0/172 (0.00%)	0/243 (0.00%)	1/201 (0.50%)
Gastrointestinal disorders			
Abdominal Hernia † 1			
# participants affected / at risk	2/172 (1.16%)	0/243 (0.00%)	0/201 (0.00%)
Abdominal Pain † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	1/201 (0.50%)
Colitis † 1			
# participants affected / at risk	0/172 (0.00%)	0/243 (0.00%)	1/201 (0.50%)

Colitis Ischaemic † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Diarrhoea † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Duodenal Ulcer † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Gastric Ulcer † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Gastritis † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Gastritis Haemorrhagic † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Gastrointestinal Ulcer Haemorrhage † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Gastrooesophageal Reflux Disease † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Haematemesis † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Haematochezia † 1			
# participants affected / at risk	**1/172 (0.58%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Intestinal Obstruction † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Irritable Bowel Syndrome † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Mouth Ulceration † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Pancreatitis † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Umbilical Hernia † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
General disorders			
Chest Pain † 1			
# participants affected / at risk	**1/172 (0.58%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Injection Site Erythema † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Pyrexia † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Sudden Death † 1			
# participants affected / at risk	**1/172 (0.58%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Hepatobiliary disorders			
Cholecystitis Chronic † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Cholelithiasis † 1			
# participants affected / at risk	**1/172 (0.58%)**	**3/243 (1.23%)**	**1/201 (0.50%)**

Cholestasis of Pregnancy † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Hepatitis Toxic † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Hepatomegaly † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Infections and infestations			
Abscess Limb † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Acute Sinusitis † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**2/201 (1.00%)**
Appendicitis † 1			
# participants affected / at risk	**1/172 (0.58%)**	**1/243 (0.41%)**	**2/201 (1.00%)**
Arthritis Bacterial † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Bone Tuberculosis † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Breast Abscess † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Bronchitis † 1			
# participants affected / at risk	**1/172 (0.58%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Bronchopneumonia † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Bursitis Infective † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Cellulitis † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Chronic Tonsillitis † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Cystitis † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Dengue Fever † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Empyema † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Encephalitis Viral † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Enteritis Infectious † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Gastroenteritis † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Gastroenteritis Viral † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
H1n1 Influenza † 1			

# participants affected / at risk	0/172 (0.00%)	0/243 (0.00%)	1/201 (0.50%)
Hepatitis B † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Herpes Zoster † 1			
# participants affected / at risk	0/172 (0.00%)	2/243 (0.82%)	3/201 (1.49%)
Intervertebral Discitis † 1			
# participants affected / at risk	0/172 (0.00%)	0/243 (0.00%)	1/201 (0.50%)
Lung Infection † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Necrotising Fasciitis † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Orchitis † 1			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)
Osteomyelitis † 1			
# participants affected / at risk	0/172 (0.00%)	2/243 (0.82%)	0/201 (0.00%)
Otitis Media † 1			
# participants affected / at risk	0/172 (0.00%)	0/243 (0.00%)	1/201 (0.50%)
Pelvic Inflammatory Disease † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Peritoneal Tuberculosis † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Peritonitis † 1			
# participants affected / at risk	1/172 (0.58%)	1/243 (0.41%)	0/201 (0.00%)
Pharyngitis † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Pneumocystis JiroveCI Pneumonia † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Pneumonia † 1			
# participants affected / at risk	5/172 (2.91%)	4/243 (1.65%)	5/201 (2.49%)
Pneumonia Legionella † 1			
# participants affected / at risk	0/172 (0.00%)	0/243 (0.00%)	1/201 (0.50%)
Pulmonary Tuberculosis † 1			
# participants affected / at risk	1/172 (0.58%)	4/243 (1.65%)	1/201 (0.50%)
Pyelonephritis † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	1/201 (0.50%)
Pyelonephritis Acute † 1			
# participants affected / at risk	0/172 (0.00%)	0/243 (0.00%)	2/201 (1.00%)
Respiratory Tract Infection † 1			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)
Salpingitis † 1			
# participants affected / at risk	0/172 (0.00%)	0/243 (0.00%)	1/201 (0.50%)
Sepsis † 1			
# participants affected / at risk	0/172 (0.00%)	3/243 (1.23%)	1/201 (0.50%)
Septic Shock † 1			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)

Sialoadenitis † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Sinusitis † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Subcutaneous Abscess † 1			
# participants affected / at risk	**0/172 (0.00%)**	**2/243 (0.82%)**	**0/201 (0.00%)**
Tuberculosis † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**1/201 (0.50%)**
Tuberculosis Gastrointestinal † 1			
# participants affected / at risk	**0/172 (0.00%)**	**2/243 (0.82%)**	**0/201 (0.00%)**
Tuberculous Pleurisy † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**1/201 (0.50%)**
Upper Respiratory Tract Infection † 1			
# participants affected / at risk	**1/172 (0.58%)**	**2/243 (0.82%)**	**0/201 (0.00%)**
Urinary Tract Infection † 1			
# participants affected / at risk	**1/172 (0.58%)**	**1/243 (0.41%)**	**2/201 (1.00%)**
Vulval Abscess † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Injury, poisoning and procedural complications			
Ankle Fracture † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Concussion † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Face Injury † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Fall † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Femoral Neck Fracture † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Femur Fracture † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Forearm Fracture † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Fracture † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Hip Fracture † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Humerus Fracture † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Joint Dislocation † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Ligament Rupture † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**

Ligament Sprain † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Meniscus Lesion † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Open Fracture † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Overdose † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Post Lumbar Puncture Syndrome † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Post Procedural Complication † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Radius Fracture † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Spinal Compression Fracture † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Spinal Fracture † [1]			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Sternal Fracture † [1]			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Synovial Rupture † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Tendon Rupture † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Thermal Burn † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Tibia Fracture † [1]			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Wound † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Investigations			
General Physical Condition Abnormal † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Weight Increased † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Metabolism and nutrition disorders			
Electrolyte Imbalance † [1]			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Obesity † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Musculoskeletal and connective tissue disorders			
Arthralgia † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**1/201 (0.50%)**

Arthritis † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**2/243 (0.82%)**	**0/201 (0.00%)**
Back Pain † [1]			
# participants affected / at risk	**2/172 (1.16%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Dupuytren's Contracture † [1]			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Foot Deformity † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**2/201 (1.00%)**
Intervertebral Disc Protrusion † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**2/243 (0.82%)**	**0/201 (0.00%)**
Lumbar Spinal Stenosis † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Osteoarthritis † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**2/201 (1.00%)**
Osteochondrosis † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Osteonecrosis † [1]			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Rhabdomyolysis † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Rheumatoid Arthritis † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**6/243 (2.47%)**	**1/201 (0.50%)**
Spondylolisthesis † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**1/201 (0.50%)**
Synovitis † [1]			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Vertebral Foraminal Stenosis † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Adenoma Benign † [1]			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Anogenital Warts † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Basal Cell Carcinoma † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**2/201 (1.00%)**
Bowen's Disease † [1]			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Breast Cancer † [1]			
# participants affected / at risk	**1/172 (0.58%)**	**3/243 (1.23%)**	**0/201 (0.00%)**
Breast Cancer in Situ † [1]			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**

Cervix Carcinoma † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Colon Cancer † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Hodgkin's Disease † 1			
# participants affected / at risk	**0/172 (0.00%)**	**2/243 (0.82%)**	**0/201 (0.00%)**
Lung Neoplasm † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Lung Neoplasm Malignant † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Malignant Melanoma in Situ † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Neoplasm † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Non-Small Cell Lung Cancer † 1			
# participants affected / at risk	**2/172 (1.16%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Rectal Cancer † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Renal Cell Carcinoma † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Salivary Gland Adenoma † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Squamous Cell Carcinoma of Skin † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Thyroid Neoplasm † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Uterine Leiomyoma † 1			
# participants affected / at risk	**1/172 (0.58%)**	**1/243 (0.41%)**	**2/201 (1.00%)**
Nervous system disorders			
Carotid Artery Stenosis † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Carpal Tunnel Syndrome † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Cerebral Haemorrhage † 1			
# participants affected / at risk	**0/172 (0.00%)**	**2/243 (0.82%)**	**0/201 (0.00%)**
Cerebral Infarction † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Cerebrovascular Accident † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Demyelination † 1			
# participants affected / at risk	**0/172 (0.00%)**	**2/243 (0.82%)**	**0/201 (0.00%)**
Dysarthria † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Hypoglycaemic Coma † 1			

# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)
Hypotonia † [1]			
# participants affected / at risk	0/172 (0.00%)	0/243 (0.00%)	1/201 (0.50%)
Intracranial Aneurysm † [1]			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Migraine † [1]			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)
Multiple Sclerosis † [1]			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Radiculopathy † [1]			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Vocal Cord Paralysis † [1]			
# participants affected / at risk	0/172 (0.00%)	0/243 (0.00%)	1/201 (0.50%)
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous † [1]			
# participants affected / at risk	1/172 (0.58%)	4/243 (1.65%)	0/201 (0.00%)
Psychiatric disorders			
Bipolar Disorder † [1]			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)
Bipolar I Disorder † [1]			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)
Completed Suicide † [1]			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)
Delusional Disorder, Unspecified Type † [1]			
# participants affected / at risk	0/172 (0.00%)	0/243 (0.00%)	1/201 (0.50%)
Depression † [1]			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	1/201 (0.50%)
Major Depression † [1]			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Mania † [1]			
# participants affected / at risk	0/172 (0.00%)	0/243 (0.00%)	1/201 (0.50%)
Renal and urinary disorders			
Bladder Prolapse † [1]			
# participants affected / at risk	1/172 (0.58%)	1/243 (0.41%)	0/201 (0.00%)
Nephrolithiasis † [1]			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	1/201 (0.50%)
Stress Urinary Incontinence † [1]			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Urethral Disorder † [1]			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)
Urinary Incontinence † [1]			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)
Reproductive system and breast disorders			

Breast Calcifications † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Breast Inflammation † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Fibrocystic Breast Disease † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Metrorrhagia † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Uterine Cervical Squamous Metaplasia † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Uterine Polyp † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Uterine Prolapse † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Failure † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Alveolitis Fibrosing † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Asthma † 1			
# participants affected / at risk	**0/172 (0.00%)**	**0/243 (0.00%)**	**1/201 (0.50%)**
Chronic Obstructive Pulmonary Disease † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Epiglottic Cyst † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Interstitial Lung Disease † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Lung Disorder † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Pneumonitis † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Respiratory Failure † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Rheumatoid Lung † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Skin and subcutaneous tissue disorders			
Cutaneous Lupus Erythematosus † 1			
# participants affected / at risk	**0/172 (0.00%)**	**1/243 (0.41%)**	**0/201 (0.00%)**
Erythema Nodosum † 1			
# participants affected / at risk	**1/172 (0.58%)**	**0/243 (0.00%)**	**0/201 (0.00%)**
Generalised Erythema † 1			

# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)
Panniculitis † 1			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)
Pustular Psoriasis † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Vascular disorders			
Arterial Stenosis † 1			
# participants affected / at risk	1/172 (0.58%)	0/243 (0.00%)	0/201 (0.00%)
Deep Vein Thrombosis † 1			
# participants affected / at risk	0/172 (0.00%)	0/243 (0.00%)	1/201 (0.50%)
Femoral Arterial Stenosis † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Haematoma † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Haemorrhage † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Hypertension † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	1/201 (0.50%)
Hypertensive Crisis † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Hypotension † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Iliac Artery Stenosis † 1			
# participants affected / at risk	0/172 (0.00%)	1/243 (0.41%)	0/201 (0.00%)
Varicose Ulceration † 1			
# participants affected / at risk	0/172 (0.00%)	0/243 (0.00%)	1/201 (0.50%)
Venous Thrombosis † 1			
# participants affected / at risk	0/172 (0.00%)	0/243 (0.00%)	1/201 (0.50%)

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA Version 15.0

Other Adverse Events

Hide Other Adverse Events

Time Frame	Adverse event data were collected for 5 years
Additional Description	3 of 637 randomized participants did not receive treatment & additional 18 participants did not receive any treatment with golimumab during the study. Thus only 616 participants are included in 5-year safety data. AEs were planned to be reported in relation to the doses of golimumab received throughout the study, rather than the treatment regimen.

Frequency Threshold

Threshold above which other adverse events are reported	5

Reporting Groups

	Description
Group A: Golimumab 50 mg SC Injections Only	Participants who were treated with golimumab and received golimumab 50 mg injections

	only during the study. Participants also received methotrexate capsules throughout the study. Participants were included from Group 1 and Group 3, who received only Golimumab 50 mg SC Injections.
Group B: Golimumab 100 mg SC Injections Only	Participants who were treated with golimumab and received golimumab 100 mg injections only during the study. Participants also received either methotrexate or placebo capsules throughout the study. Participants were included from Group 1, Group 2 and Group 4, who received only Golimumab 100 mg SC Injections.
Group C: Golimumab 50 and 100 mg SC Injections	Participants who were treated with golimumab and received at least one injection of both golimumab 50 mg and golimumab 100 mg during the study. Participants also received either methotrexate or placebo capsules throughout the study. Participants were included from Group 1, Group 2, Group 3 and Group 4, who received Golimumab 50 mg and 100 mg SC Injections.

Other Adverse Events

	Group A: Golimumab 50 mg SC Injections Only	Group B: Golimumab 100 mg SC Injections Only	Group C: Golimumab 50 and 100 mg SC Injections
Total, other (not including serious) adverse events			
# participants affected / at risk	**139/172 (80.81%)**	**215/243 (88.48%)**	**174/201 (86.57%)**
Blood and lymphatic system disorders			
Anaemia † [1]			
# participants affected / at risk	**5/172 (2.91%)**	**9/243 (3.70%)**	**11/201 (5.47%)**
Gastrointestinal disorders			
Abdominal Pain † [1]			
# participants affected / at risk	**10/172 (5.81%)**	**11/243 (4.53%)**	**7/201 (3.48%)**
Abdominal Pain Upper † [1]			
# participants affected / at risk	**8/172 (4.65%)**	**20/243 (8.23%)**	**17/201 (8.46%)**
Diarrhoea † [1]			
# participants affected / at risk	**15/172 (8.72%)**	**17/243 (7.00%)**	**17/201 (8.46%)**
Dyspepsia † [1]			
# participants affected / at risk	**18/172 (10.47%)**	**17/243 (7.00%)**	**21/201 (10.45%)**
Gastritis † [1]			
# participants affected / at risk	**7/172 (4.07%)**	**16/243 (6.58%)**	**10/201 (4.98%)**
Nausea † [1]			
# participants affected / at risk	**22/172 (12.79%)**	**55/243 (22.63%)**	**44/201 (21.89%)**
Vomiting † [1]			
# participants affected / at risk	**8/172 (4.65%)**	**17/243 (7.00%)**	**18/201 (8.96%)**
General disorders			
Fatigue † [1]			
# participants affected / at risk	**7/172 (4.07%)**	**21/243 (8.64%)**	**10/201 (4.98%)**
Injection Site Erythema † [1]			

# participants affected / at risk	10/172 (5.81%)	28/243 (11.52%)	12/201 (5.97%)
Pyrexia † 1			
# participants affected / at risk	4/172 (2.33%)	13/243 (5.35%)	14/201 (6.97%)
Infections and infestations			
Bronchitis † 1			
# participants affected / at risk	26/172 (15.12%)	40/243 (16.46%)	34/201 (16.92%)
Gastroenteritis † 1			
# participants affected / at risk	9/172 (5.23%)	11/243 (4.53%)	13/201 (6.47%)
Influenza † 1			
# participants affected / at risk	12/172 (6.98%)	17/243 (7.00%)	16/201 (7.96%)
Nasopharyngitis † 1			
# participants affected / at risk	20/172 (11.63%)	31/243 (12.76%)	33/201 (16.42%)
Oral Herpes † 1			
# participants affected / at risk	7/172 (4.07%)	2/243 (0.82%)	12/201 (5.97%)
Pharyngitis † 1			
# participants affected / at risk	16/172 (9.30%)	27/243 (11.11%)	20/201 (9.95%)
Respiratory Tract Infection † 1			
# participants affected / at risk	9/172 (5.23%)	11/243 (4.53%)	5/201 (2.49%)
Sinusitis † 1			
# participants affected / at risk	26/172 (15.12%)	19/243 (7.82%)	24/201 (11.94%)
Upper Respiratory Tract Infection † 1			
# participants affected / at risk	45/172 (26.16%)	62/243 (25.51%)	72/201 (35.82%)
Urinary Tract Infection † 1			
# participants affected / at risk	15/172 (8.72%)	28/243 (11.52%)	16/201 (7.96%)
Investigations			
Alanine Aminotransferase Increased † 1			
# participants affected / at risk	31/172 (18.02%)	36/243 (14.81%)	32/201 (15.92%)
Aspartate Aminotransferase Increased † 1			
# participants affected / at risk	21/172 (12.21%)	21/243 (8.64%)	24/201 (11.94%)
Musculoskeletal and connective tissue disorders			
Arthralgia † 1			
# participants affected / at risk	8/172 (4.65%)	21/243 (8.64%)	17/201 (8.46%)

Back Pain † 1			
# participants affected / at risk	**17/172 (9.88%)**	**23/243 (9.47%)**	**22/201 (10.95%)**
Rheumatoid Arthritis † 1			
# participants affected / at risk	**3/172 (1.74%)**	**19/243 (7.82%)**	**11/201 (5.47%)**
Nervous system disorders			
Dizziness † 1			
# participants affected / at risk	**6/172 (3.49%)**	**15/243 (6.17%)**	**8/201 (3.98%)**
Headache † 1			
# participants affected / at risk	**14/172 (8.14%)**	**33/243 (13.58%)**	**16/201 (7.96%)**
Paraesthesia † 1			
# participants affected / at risk	**4/172 (2.33%)**	**7/243 (2.88%)**	**11/201 (5.47%)**
Psychiatric disorders			
Depression † 1			
# participants affected / at risk	**16/172 (9.30%)**	**10/243 (4.12%)**	**21/201 (10.45%)**
Insomnia † 1			
# participants affected / at risk	**4/172 (2.33%)**	**17/243 (7.00%)**	**9/201 (4.48%)**
Respiratory, thoracic and mediastinal disorders			
Cough † 1			
# participants affected / at risk	**19/172 (11.05%)**	**37/243 (15.23%)**	**29/201 (14.43%)**
Oropharyngeal Pain † 1			
# participants affected / at risk	**7/172 (4.07%)**	**12/243 (4.94%)**	**16/201 (7.96%)**
Skin and subcutaneous tissue disorders			
Alopecia † 1			
# participants affected / at risk	**6/172 (3.49%)**	**12/243 (4.94%)**	**14/201 (6.97%)**
Rash † 1			
# participants affected / at risk	**9/172 (5.23%)**	**18/243 (7.41%)**	**15/201 (7.46%)**
Vascular disorders			
Hypertension † 1			
# participants affected / at risk	**19/172 (11.05%)**	**25/243 (10.29%)**	**23/201 (11.44%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA Version 15.0

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
The count of patients with any nonserious adverse events (NAE) excludes patients who only had NAE that occurred in less than or equal to 5% of patients. This information may vary from existing approved labeling and publications.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.
There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.
The agreement is: ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed. ☑ **Restriction Description:** Generally, the only disclosure restriction on the PI is that the sponsor has 60 days to review results communications prior to public release and can embargo communications regarding trial results for a period that does not exceed 180 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

Results Point of Contact:

Name/Title: Director Clinical Research
Organization: Centocor Research & Development, Inc.
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Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Emery P, Fleischmann RM, Hsia EC, Xu S, Zhou Y, Baker D. Efficacy of golimumab plus methotrexate in methotrexate-naïve patients with severe active rheumatoid arthritis. Clin Rheumatol. 2014 Sep;33(9):1239-46. doi: 10.1007/s10067-014-2731-y. Epub 2014 Jul 9.

Emery P, Fleischmann RM, Doyle MK, Strusberg I, Durez P, Nash P, Amante E, Churchill M, Park W, Pons-Estel B, Xu W, Xu S, Wu Z, Hsia EC. Golimumab, a human anti–tumor necrosis factor monoclonal antibody, injected subcutaneously every 4 weeks in patients with active rheumatoid arthritis who had never taken methotrexate: 1-year and 2-year clinical, radiologic, and physical function findings of a phase III, multicenter, randomized, double-blind, placebo-controlled study. Arthritis Care Res (Hoboken). 2013 Nov;65(11):1732-42.

Østergaard M, Emery P, Conaghan PG, Fleischmann R, Hsia EC, Xu W, Rahman MU. Significant improvement in synovitis, osteitis, and bone erosion following golimumab and methotrexate combination therapy as compared with methotrexate alone: a magnetic resonance imaging study of 318 methotrexate-naive rheumatoid arthritis patients. Arthritis Rheum. 2011 Dec;63(12):3712-22. doi: 10.1002/art.30592.

Responsible Party:	Centocor, Inc.
ClinicalTrials.gov Identifier:	NCT00264537 History of Changes
Other Study ID Numbers:	**CR006331** GO-BEFORE C0524T05
Study First Received:	December 11, 2005
Results First Received:	May 21, 2009
Last Updated:	August 27, 2014
Health Authority:	United States: Food and Drug Administration

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