ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
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ClinicalTrials.gov ID: NCT00754559

Study Identification

Unique Protocol ID:	ML21469
Brief Title:	A Study to Assess Efficacy With Respect to Clinical Improvement in Disease Activity and Safety of Tocilizumab in Patients Wtih Active Rheumatoid Arthritis.
Official Title:	"Effectiveness After Four and Twentyfour Weeks and Safety of Tocilizumab in Patients With Active RA"
Secondary IDs:	2008-000105-11

Study Status

Record Verification:	January 2016
Overall Status:	Completed
Study Start:	August 2008
Primary Completion:	November 2009 [Actual]
Study Completion:	November 2009 [Actual]

Sponsor/Collaborators

Sponsor:	Hoffmann-La Roche
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	No
IND/IDE Protocol?:	No

Review Board:	Approval Status: Approved Approval Number: ZS EK 13 247 7 08 Board Name: Ethik-Kommission des Landes berlin Board Affiliation: Landesamt fur Gesundheit und Soziales Phone: +49 30 9012 7638 Email: ethik-kommission@lageso.berlin.de
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Germany: Landesamt fur Gesundheit und Soziales

Study Description

Brief Summary:	This single arm study will assess the effectiveness of tocilizumab in combination with traditional DMARDs with regard to the clinical improvement in disease activity (achievement of LDAS) after 24 weeks' treatment in patients with active rheumatoid arthritis (RA) who have had an inadequate response to current traditional DMARD and/or anti-TNF therapy. Patients will receive tocilizumab 8mg/kg iv every 4 weeks, in addition to ongoing DMARDs at the stable pre-entry dose prescribed by the physician, for a total of 6 infusions during the regular treatment period and a further 6 infusions during an optional extension phase. The anticipated time on study treatment is 6 to 12 months, and the target sample size is <500 individuals.
Detailed Description:	

Conditions

Conditions:	Rheumatoid Arthritis
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Single Group Assignment
Number of Arms:	1
Masking:	Open Label
Allocation:	N/A
Endpoint Classification:	Safety/Efficacy Study

Enrollment: 286 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Tocilizumab	Drug: Tocilizumab 8mg/kg iv every 4 weeks

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- adult patients, >=18 years of age;
- rheumatoid arthritis of >=6 months duration diagnosed according to the revised 1987 ACR criteria;
- DAS28 of >3.2;
- At screening either ESR >=28 mm/h or CRP >=1 mg/dL;
- Having received permitted DMARDs, 1 or more; current DMARD therapy must have been at a stable dose for at least 8 weeks prior to baseline.

Exclusion Criteria:

- major surgery (including joint surgery) within 8 weeks prior to screening or planned major surgery within 6 months following screening;
- functional class IV as identified by the ACR classification of functional status in RA;
- rheumatoid autoimmune disease other than RA;
- prior history of or current inflammatory joint disease other than RA.

Contacts/Locations

Study Officials: Clinical Trials
Study Director

Hoffmann-La Roche

Locations: Germany

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Münster, Germany, 48149

Damp, Germany, 24351

Treuenbrietzen, Germany, 14929

Pirna, Germany, 01796

Sendenhorst, Germany, 48324

Heidelberg, Germany, 69120

Halle, Germany, 06120

Erfurt, Germany, 99096

Gommern, Germany, 39245

München, Germany, 80335

Bremen, Germany, 28199

Aachen, Germany, 52064

Frankfurt, Germany, 60596

München, Germany, 81541

Tübingen, Germany, 72076

Hagen, Germany, 58135

Marburg, Germany, 35037

Hofheim, Germany, 65719

Bad Bramstedt, Germany, 24576

Göttingen, Germany, 37075

Bad Nauheim, Germany, 61231

Stuttgart, Germany, 70372

Rostock, Germany, 18059

Donaueschingen, Germany, 78166

Köln, Germany, 50924

Zeven, Germany, 27404

Essen, Germany, 45239

Berlin, Germany, 14163

Hannover, Germany, 30625

Düsseldorf, Germany, 40225

Mainz, Germany, 55131

Dresden, Germany, 01109

Mainz, Germany, 55122

Dresden, Germany, 01067

Hildesheim, Germany, 31134

Homburg/saar, Germany, 66424

ULM, Germany, 89081

Ratingen, Germany, 40882

Erlangen, Germany, 91056

Wiesbaden, Germany, 65189

Berlin, Germany, 13055

Erlangen, Germany, 91054

Hamburg, Germany, 22767

Grafschaft, Germany, 53501

Leipzig, Germany, 04103

Potsdam, Germany, 14469

Neuss, Germany, 41460

Hoyerswerda, Germany, 02977

Berlin, Germany, 12161

Oberammergau, Germany, 82487

Ludwigsfelde, Germany, 14974

Berlin, Germany, 13125

Hamburg, Germany, 22609

Plochingen, Germany, 73207

Köln, Germany, 50679

Berlin, Germany, 14109

Lüneburg, Germany, 21335

Bayreuth, Germany, 95445

München, Germany, 81925

Goslar, Germany, 38642

Berlin, Germany, 12161

Bad Abbach, Germany, 93077

Hamburg, Germany, 22147

Düsseldorf, Germany, 40217

Hamburg, Germany, 22081

Muenchen, Germany, 80336

Berlin, Germany, 12435

Nürnberg, Germany, 90402

Halle, Germany, 06108

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 milligrams/kilogram (mg/kg) intravenously (iv) every 4 weeks for a total of 6 infusions.

Overall Study

	Tocilizumab
Started	286
Completed	239
Not Completed	47
Adverse Event	15
Protocol Violation	11
Lack of Efficacy	10
Lost to Follow-up	2
Administrative reason	1
Unknown	5
Withdrawal by Subject	3

Baseline Characteristics

Analysis Population Description

All treated participants were included in the safety population as well as the intent to-treat (ITT) population.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks for a total of 6 infusions.

Baseline Measures

	Tocilizumab
Number of Participants	286
Age, Continuous [units: years] Mean (Standard Deviation)	54.9 (12.2)
Gender, Male/Female [units: participants]	
Female	216
Male	70

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With Low Disease Activity Score at Week 24
Measure Description	Low Disease Activity Score (LDAS) is defined as Disease Activity score less than or equal to (≤) 3.2. Disease activity score 28 (DAS28) was calculated from the number of swollen joints and tender joints using the 28-joint count, the erythrocyte sedimentation rate (ESR) (millimeters per hour [mm/hour]) and global health assessment (participant rated global assessment of disease activity using 100-mm Visual analog scale [VAS]); DAS28 score ranged from 0 to 10, where higher scores correspond to greater disease activity.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Percentage of Participants With Low Disease Activity Score at Week 24 [units: Percentage of Participants] Number (95% Confidence Interval)	57 (51 to 62.8)

Statistical Analysis 1 for Percentage of Participants With Low Disease Activity Score at Week 24

Statistical Analysis Overview	Comparison Groups	Tocilizumab
	Comments	Null hypothesis: Proportion of participants reaching LDAS (≤ 3.2) at Week 24 equals (=) expected proportion of 42%.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Other [Exact Binomial Test]
	Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Absolute Changes in DAS28 From Baseline
Measure Description	DAS28 calculated from the number of swollen joints and tender joints using the 28-joint count, the ESR (mm/hour) and global health assessment (participant rated global assessment of disease activity using 100-mm VAS); DAS28 score ranged from 0 to 10, where higher scores correspond to greater disease activity. DAS28 ≤3.2 = low disease activity, DAS28 greater than (>)3.2 to 5.1 = moderate to high disease activity.
Time Frame	Weeks 1, 2, 4, 8, 12, 16, 20 and 24
Safety Issue?	No

Analysis Population Description

ITT Population; only participants with a DAS28 value at baseline were included in the analysis.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	274
Absolute Changes in DAS28 From Baseline [units: units on a scale] Mean (Standard Deviation)	
Week 1	-1.31 (1.1)
Week 2	-2.1 (1.2)
Week 4	-2.4 (1.2)
Week 8	-2.8 (1.3)
Week 12	-3.2 (1.4)
Week 16	-3.2 (1.4)

	Tocilizumab
Week 20	-3.3 (1.4)
Week 24	-3.4 (1.4)

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a Response at Week 24 by European League Against Rheumatism (EULAR) Category
Measure Description	The DAS28-based EULAR response criteria were used to measure individual response as none, good, and moderate, depending on the extent of change from baseline and the level of disease activity reached. Good responders: change from baseline >1.2 with DAS28 ≤3.2; moderate responders: change from baseline >1.2 with DAS28 >3.2 to ≤5.1 or change from baseline >0.6 to ≤1.2 with DAS28 ≤5.1; non-responders: change from baseline ≤ 0.6 or change from baseline >0.6 and ≤1.2 with DAS28 >5.1.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Percentage of Participants With a Response at Week 24 by European League Against Rheumatism (EULAR) Category [units: Percentage of Participants]	
Good	54.9
Moderate	20.3
None	24.8

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a DAS28 Response at Weeks 4 and 24
Measure Description	DAS28 calculated from the number of swollen joints and painful joints using the 28-joint count, the ESR and participant's global assessment (PGA) of disease activity (participant rated arthritis activity assessment using VAS) with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity. DAS28 ≤3.2 = low disease activity, DAS28 <2.6 = remission and a clinically significant (CS) reduction was defined as ≥1.2.
Time Frame	Weeks 4 and 24
Safety Issue?	No

Analysis Population Description

ITT Population;

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Percentage of Participants With a DAS28 Response at Weeks 4 and 24 [units: percentage of participants] Number (95% Confidence Interval)	
Week 4, CS reduction	75.2 (69.7 to 80.1)
Week 4, Remission	23.1 (18.3 to 28.4)
Week 4, CS reduction or remission	76.6 (71.2 to 81.4)
Week 4, LDAS	40.9 (35.2 to 46.9)
Week 24, CS reduction	74.5 (69.0 to 79.4)
Week 24, Remission	47.6 (41.6 to 53.5)
Week 24, CS reduction or remission	76.6 (71.2 to 81.4)
Week 24, LDAS	57.0 (51.0 to 62.8)

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants With an American College of Rheumatology 20%, 50%, or 70% (ACR20/ACR50/ACR70) Response
Measure Description	ACR20/50/70 response: ≥20%, 50%, or 70% improvement, respectively, in swollen and tender joint count; and ≥20% improvement in at least 3 of 5 remaining ACR core measures: participant assessment of pain; participant global assessment of disease activity; physician global assessment of disease activity; self-assessed disability (disability index of the Health Assessment Questionnaire [HAQ-DI]); and C-Reactive Protein (CRP).
Time Frame	Weeks 1, 2, 4, 8, 12, 16, 20 and 24
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Percentage of Participants With an American College of Rheumatology 20%, 50%, or 70% (ACR20/ACR50/ACR70) Response [units: percentage of participants] Number (95% Confidence Interval)	
Week 1 ACR20	25.2 (20.3 to 30.6)
Week 1 ACR50	7.0 (4.3 to 10.6)
Week 1 ACR70	2.4 (1.0 to 5.0)
Week 2 ACR20	41.3 (35.5 to 47.2)
Week 2 ACR50	14.7 (10.8 to 19.3)
Week 2 ACR70	4.9 (2.7 to 8.1)
Week 4 ACR20	50.0 (44.1 to 55.9)
Week 4 ACR50	25.5 (20.6 to 31.0)
Week 4 ACR70	12.2 (8.7 to 16.6)

	Tocilizumab
Week 8 ACR20	64.3 (58.5 to 69.9)
Week 8 ACR50	37.4 (31.8 to 43.3)
Week 8 ACR70	17.1 (13.0 to 22.0)
Week 12 ACR20	69.6 (63.9 to 74.9)
Week 12 ACR50	48.6 (42.7 to 54.6)
Week 12 ACR70	26.2 (21.2 to 31.7)
Week 16 ACR20	67.5 (61.7 to 72.9)
Week 16 ACR50	49.0 (43.0 to 54.9)
Week 16 ACR70	29.4 (24.2 to 35.0)
Week 20 ACR20	67.8 (62.1 to 73.2)
Week 20 ACR50	49.7 (43.7 to 55.6)
Week 20 ACR70	33.9 (28.4 to 39.7)
Week 24 ACR20	65.0 (59.2 to 70.6)
Week 24 ACR50	50.7 (44.7 to 56.6)
Week 24 ACR70	33.9 (28.4 to 39.7)

6. Secondary Outcome Measure:

Measure Title	Change From Baseline in Swollen and Tender Joint Counts at Week 24
Measure Description	Swollen joint count: 66 joints were assessed for swelling and joints were classified as swollen/not swollen giving a total possible swollen joint count score of 0 to 66. Tender joint counts: 68 joints were assessed for tenderness and joints were classified as tender/not tender giving a total possible tender joint count score of 0 to 68.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT Population; missing data were imputed using last observation carried forward (LOCF).

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks up to week 20 for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Change From Baseline in Swollen and Tender Joint Counts at Week 24 [units: Joints] Mean (95% Confidence Interval)	
Number of swollen joints	-9.6 (-10.4 to -8.7)
Number of tender joints	-13.4 (-14.7 to -12.1)

7. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Levels of C-Reactive Protein at Week 24
Measure Description	The serum concentration of CRP is measured in mg/L. A reduction in the level was considered an improvement.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT Population; missing data were imputed using LOCF.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks up to week 20 for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Change From Baseline in the Levels of C-Reactive Protein at Week 24 [units: mg/L] Mean (95% Confidence Interval)	-20.1 (-23.7 to -16.6)

8. Secondary Outcome Measure:

Measure Title	Change From Baseline in Participant's Global Assessment of Pain (VAS) at Week 24
Measure Description	Participant's global assessment of pain was assessed using a 100-mm horizontal VAS (0 to 100 mm) with 0=pain absent and 100=unbearable pain. Participants responded by placing a mark on the line to indicate their current level of pain.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT Population; missing data were imputed using LOCF.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks up to week 20 for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Change From Baseline in Participant's Global Assessment of Pain (VAS) at Week 24 [units: mm] Mean (95% Confidence Interval)	-36.2 (-39.6 to -32.7)

9. Secondary Outcome Measure:

Measure Title	Change From Baseline in Participant and Physician Assessment of Global Disease Activity (VAS) at Week 24
Measure Description	Participant’s global assessment of disease activity was an overall assessment of their current disease activity on a 100-mm horizontal VAS scale (left-hand extreme: “no disease activity”; right-hand extreme: “maximum disease activity”). Physician’s global assessment of disease activity was measured as participant’s current disease activity on a 100-mm horizontal VAS scale (left hand extreme: “no disease activity”; right-hand extreme: “maximum disease activity”).
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT Population; missing data were imputed using LOCF.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks up to week 20 for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Change From Baseline in Participant and Physician Assessment of Global Disease Activity (VAS) at Week 24 [units: mm] Mean (95% Confidence Interval)	
Participant's assessment	-35.9 (-39.5 to -32.4)
Physician's assessment	-44.9 (-47.7 to -42.1)

10. Secondary Outcome Measure:

Measure Title	Change From Baseline in Clinical Disease Activity Index (CDAI) Score
Measure Description	CDAI was calculated according to the following formula: CDAI = Number of swollen joints (plus) + Number of tender joints + VAS disease activity participant assessment + VAS disease activity investigator assessment. The maximum score was 334 (66 joints + 68 joints + 100 mm + 100 mm); higher scores indicated higher disease activity.
Time Frame	Weeks 1, 2, 4, 8, 12, 16, 20 and 24
Safety Issue?	No

Analysis Population Description

ITT population; only participants with values for CDAI at baseline and the respective visit were included in the analysis.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Change From Baseline in Clinical Disease Activity Index (CDAI) Score [units: units on a scale] Mean (Standard Deviation)	
Week 1	-8.4 (12.1)
Week 2	-13.3 (12.4)
Week 4	-15.6 (13.4)
Week 8	-19.7 (13.2)
Week 12	-22.4 (13.4)
Week 16	-22.4 (13.8)
Week 20	-22.7 (13.3)
Week 24	-24.2 (12.9)

11. Secondary Outcome Measure:

Measure Title	Change From Baseline in HAQ-DI at Week 24
Measure Description	HAQ-DI: participant-reported assessment of ability to perform tasks in 8 categories of daily living activities: dress/ groom; arise; eat; walk; reach; grip; hygiene; and common activities over past week. Each item scored on 4-point scale from 0 to 3: 0=no difficulty; 1=some difficulty; 2=much difficulty; 3=unable to do. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible score range 0-3 where 0 = least difficulty and 3 = extreme difficulty.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT Population; Missing data were imputed using LOCF.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks up to week 20 for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Change From Baseline in HAQ-DI at Week 24 [units: units on a scale] Mean (Standard Deviation)	-0.48 (0.60)

12. Secondary Outcome Measure:

Measure Title	Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Score at Week 24
Measure Description	FACIT-F is a 13-item questionnaire. Participants scored each item on a 5-point scale: 0 (Not at all) to 4 (Very much). The larger the participant's response to the questions (with the exception of 2 negatively stated), the greater the participant's fatigue. For all questions, except for the 2 negatively stated ones, the code was reversed and a new score was calculated as (4 minus the participant's response). The sum of all responses resulted in the FACIT-Fatigue score for a total possible score of 0 (worse score) to 52 (better score). A higher score reflects an improvement in the participant's health status.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT Population; Missing data were imputed using LOCF.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks up to week 20 for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Score at Week 24 [units: units on a scale] Mean (Standard Deviation)	8.6 (11.1)

13. Secondary Outcome Measure:

Measure Title	Change From Baseline in Short Form-36 (SF-36) Score at Week 24
Measure Description	SF-36 is a standardized survey evaluating 8 aspects of functional health and well being: physical and social functioning, physical and emotional role limitations, bodily pain, general health, vitality, mental health. The score for a section is an average of the individual question scores, which are scaled 0-100 (100=highest level of functioning). Absolute change was defined as the change from baseline to Week 24.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT Population; Missing data were imputed using LOCF.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8mg/kg iv every 4 weeks up to week 20 for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Change From Baseline in Short Form-36 (SF-36) Score at Week 24 [units: units on a scale] Mean (Standard Deviation)	
Physical functioning	18.4 (24.6)
Role physical	16.5 (21.6)
Bodily pain	25.0 (22.3)
General health perception	11.9 (18.7)
Vitality	18.0 (20.2)
Social functioning	13.8 (27.2)
Role emotional	13.9 (50.1)
Mental health	10.3 (19.1)

14. Secondary Outcome Measure:

Measure Title	Participant's Global Assessment of Pain as Assessed by Patient Take Home Form (PTHF)
Measure Description	Participant's were asked to state the worst level of pain felt in the past 24 hours using a 100-mm horizontal VAS (0 to 100 mm) with 0=no pain and 100=unbearable pain. Participants responded by placing a mark on the line to indicate their level of pain. Participants were asked to document their response during the first 4 treatment weeks at approximately the same time every day.
Time Frame	Baseline and Weeks 1, 2, and 4
Safety Issue?	No

Analysis Population Description

ITT Population; Missing data were imputed using LOCF.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Participant's Global Assessment of Pain as Assessed by Patient Take Home Form (PTHF) [units: mm] Mean (Standard Deviation)	
Baseline	60.7 (23.1)
Week 1	48.6 (25.2)
Week 2	41.9 (25.4)
Week 4	36.3 (26.7)
Change at Week 1	-12.0 (22.3)
Change at Week 2	-18.7 (24.9)
Change at Week 4	-24.4 (27.4)

15. Secondary Outcome Measure:

Measure Title	Duration of Morning Stiffness as Assessed Using PTHF

Measure Description	Duration of morning stiffness: participants were asked 'how long did your morning stiffness last from the time you woke up yesterday' and the response was provided in minutes and hours. Participants were asked to document their response during the first 4 treatment weeks at approximately the same time every day.
Time Frame	Baseline, Weeks 1, 2, and 4
Safety Issue?	No

Analysis Population Description

ITT Population; Missing data were imputed using LOCF.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Duration of Morning Stiffness as Assessed Using PTHF [units: hours] Mean (Standard Deviation)	
Baseline	2.4 (2.8)
Week 1	1.8 (2.3)
Week 2	1.5 (1.8)
Week 4	1.2 (1.5)
Change at Week 1	-0.6 (1.8)
Change at Week 2	-0.9 (2.1)
Change at Week 4	-1.2 (2.3)

16. Secondary Outcome Measure:

Measure Title	Participant Assessment of Fatigue/Tiredness as Assessed Using PTHF

Measure Description	Participants were asked to assess their overall level of fatigue/tiredness during the previous 24 hours using a 100-mm horizontal VAS with 0=none and 100=very severe. Participants responded by placing a mark on the line to indicate their current level of fatigue. Participants were asked to document their response during the first 4 treatment weeks at approximately the same time every day.
Time Frame	Baseline and Weeks 1, 2 and 4
Safety Issue?	No

Analysis Population Description

ITT Population; Missing data were imputed using LOCF.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Participant Assessment of Fatigue/Tiredness as Assessed Using PTHF [units: mm] Mean (Standard Deviation)	
Baseline	52.9 (26.9)
Week 1	42.2 (26.2)
Week 2	36.3 (26.5)
Week 4	30.6 (26.0)
Change at Week 1	-10.6 (22.0)
Change at Week 2	-16.6 (24.1)
Change at Week 4	-22.2 (26.5)

17. Secondary Outcome Measure:

Measure Title	Treatment Satisfaction Questionnaire for Medication (TSQM) Score

Measure Description	The TSQM is a general measure of participants treatment satisfaction and consists of 14 questions that result in 4 subscales: “effectiveness”, “side-effects”, “convenience” and “global satisfaction”. All subscale scores range from 0 to 100%, with 100% being the best possible result.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description
ITT Population

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Treatment Satisfaction Questionnaire for Medication (TSQM) Score [units: units on a scale] Mean (Standard Deviation)	
Percent Effectiveness	69.4 (28.3)
Percent Side-effects	88.7 (21.7)
Percent Convenience	72.4 (20.8)
Percent Global satisfaction	74.7 (25.9)

18. Secondary Outcome Measure:

Measure Title	Changes in Hemoglobin
Measure Description	Hemoglobin levels were determined as a hematology parameter to measure changes in disease related anemia.
Time Frame	Baseline, Weeks 1, 2, 4 and 24
Safety Issue?	No

Analysis Population Description
ITT Population.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks up to week 20 for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Changes in Hemoglobin [units: g/dL] Mean (Standard Deviation)	
Baseline	128.6 (13.1)
Week 1	132.2 (13.4)
Week 2	133.5 (13.1)
Week 4	133.5 (13.6)
Week 24	136.1 (13.7)
Change at Week 1	3.5 (6.8)
Change at Week 2	4.8 (6.5)
Change at Week 4	4.3 (8.0)
Change at Week 24	7.5 (9.7)

19. Secondary Outcome Measure:

Measure Title	Changes in C-Reactive Protein
Measure Description	CRP is an acute phase inflammatory marker used as a measure of inflammation. A reduction in CRP is considered to be an improvement.
Time Frame	Baseline, Weeks 1, 2 ,4 and 24
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Changes in C-Reactive Protein [units: mg/L] Mean (Standard Deviation)	
Baseline	23.1 (30.7)
Week 1	3.5 (6.6)
Week 2	2.4 (4.4)
Week 4	5.5 (14.8)
Week 24	3.0 (7.7)
Change at Week 1	-19.6 (29.4)
Change at Week 2	-20.7 (29.8)
Change at Week 4	-17.5 (27.7)
Change at Week 24	-20.1 (29.9)

20. Secondary Outcome Measure:

Measure Title	Changes in Erythrocyte Sedimentation Rate (ESR)
Measure Description	ESR is an inflammation marker used to determine acute phase response.
Time Frame	Baseline, Weeks 1, 2, 4 and 24
Safety Issue?	No

Analysis Population Description

ITT Population.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	286
Changes in Erythrocyte Sedimentation Rate (ESR) [units: mm/h] Mean (Standard Deviation)	
Baseline	37.4 (22.1)
Week 1	16.7 (14.2)
Week 2	10.6 (11.0)
Week 4	10.3 (13.5)
Week 24	7.1 (9.5)
Change at Week 1	-20.6 (17.9)
Change at Week 2	-26.7 (19.0)
Change at Week 4	-27.2 (18.6)
Change at Week 24	-30.3 (21.7)

21. Secondary Outcome Measure:

Measure Title	Percentage of Participants Withdrawing From Study Treatment Because of Insufficient Therapeutic Response
Measure Description	Participants who withdrew from study drug due to other reasons were not taken into account.
Time Frame	Weeks 1, 2, 4, 8, 12, 16, 20 and 24
Safety Issue?	No

Analysis Population Description

ITT Population; participants who withdrew from study drug due to other reaasons were not included in the analysis.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8mg /kg iv every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab
Number of Participants Analyzed	249
Percentage of Participants Withdrawing From Study Treatment Because of Insufficient Therapeutic Response [units: percentage of participants] Number (95% Confidence Interval)	4.0 (1.9 to 7.3)

Reported Adverse Events

Time Frame	Adverse events were reported throughout the study including any reactions that occurred within 24 hours after infusion.
Additional Description	An adverse event is defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv every 4 weeks for a total of 6 infusions.

Serious Adverse Events

	Tocilizumab
	Affected/At Risk (%)
Total	32/286 (11.19%)
Ear and labyrinth disorders	
Vertigo [A] *	1/286 (0.35%)
Endocrine disorders	

	Tocilizumab
	Affected/At Risk (%)
Hypothyroidism [A] *	1/286 (0.35%)
Gastrointestinal disorders	
Periodontitis [A] †	1/286 (0.35%)
Vomiting [A] †	1/286 (0.35%)
General disorders	
Chest pain [A] *	1/286 (0.35%)
General physical health deterioration [A] †	1/286 (0.35%)
Infections and infestations	
Abscess jaw [A] †	1/286 (0.35%)
Bronchopneumonia [A] †	1/286 (0.35%)
Herpes zoster [A] †	1/286 (0.35%)
Osteomyelitis [A] †	1/286 (0.35%)
Pharyngeal abscess [A] †	1/286 (0.35%)
Pneumonia [A] †	2/286 (0.7%)
Postoperative wound infection [A] †	1/286 (0.35%)
Septic shock [A] †	1/286 (0.35%)
Injury, poisoning and procedural complications	
Lower limb fracture [A] *	1/286 (0.35%)
Overdose [A] *	8/286 (2.8%)
Investigations	
Alanine aminotransferase increased [A] *	1/286 (0.35%)
Aspartate aminotransferase increased [A] *	1/286 (0.35%)
Low density lipoprotein increased [A] †	1/286 (0.35%)

	Tocilizumab
	Affected/At Risk (%)
Musculoskeletal and connective tissue disorders	
Back pain [A] *	1/286 (0.35%)
Bursitis [A] †	1/286 (0.35%)
Rheumatoid arthritis [A] *	1/286 (0.35%)
Tendonitis [A] †	1/286 (0.35%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Bladder transitional cell carcinoma [A] *	1/286 (0.35%)
Non-Hodgkin's lymphoma [A] †	1/286 (0.35%)
Nervous system disorders	
Headache [A] *	1/286 (0.35%)
Multiple sclerosis relapse [A] †	1/286 (0.35%)
Pregnancy, puerperium and perinatal conditions	
Abortion [A] *	1/286 (0.35%)
Psychiatric disorders	
Post-traumatic stress disorder [A] *	1/286 (0.35%)
Renal and urinary disorders	
Renal failure acute [A] †	1/286 (0.35%)
Respiratory, thoracic and mediastinal disorders	
Interstitial lung disease [A] †	1/286 (0.35%)

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	Tocilizumab
	Affected/At Risk (%)
Total	242/286 (84.62%)
Blood and lymphatic system disorders	
Eosinophilia [A] †	1/286 (0.35%)
Haemolysis [A] *	2/286 (0.7%)
Intravascular haemolysis [A] *	2/286 (0.7%)
Leukopenia [A] *	19/286 (6.64%)
Neutropenia [A] *	5/286 (1.75%)
Thrombocytopenia [A] *	5/286 (1.75%)
Cardiac disorders	
Extrasystoles [A] *	1/286 (0.35%)
Palpitations [A] *	2/286 (0.7%)
Tachyarrhythmia [A] *	1/286 (0.35%)
Ear and labyrinth disorders	
Ear pain [A] *	1/286 (0.35%)
Tinnitus [A] *	2/286 (0.7%)
Vertigo [A] *	4/286 (1.4%)
Endocrine disorders	
Cushingoid [A] *	1/286 (0.35%)
Goitre [A] *	2/286 (0.7%)
Hypothyroidism [A] *	1/286 (0.35%)
Eye disorders	
Conjunctival haemorrhage [A] *	2/286 (0.7%)

	Tocilizumab
	Affected/At Risk (%)
Conjunctivitis [A] *	6/286 (2.1%)
Dry eye [A] *	1/286 (0.35%)
Eye inflammation [A] *	1/286 (0.35%)
Eyelid oedema [A] *	1/286 (0.35%)
Visual acuity reduced [A] *	1/286 (0.35%)
Gastrointestinal disorders	
Abdominal discomfort [A] *	1/286 (0.35%)
Abdominal distension [A] *	1/286 (0.35%)
Abdominal pain [A] *	2/286 (0.7%)
Abdominal pain upper [A] *	4/286 (1.4%)
Aphthous stomatitis [A] *	3/286 (1.05%)
Constipation [A] *	2/286 (0.7%)
Dental caries [A] *	2/286 (0.7%)
Diarrhoea [A] *	16/286 (5.59%)
Diarrhoea haemorrhagic [A] *	1/286 (0.35%)
Dry mouth [A] *	1/286 (0.35%)
Dyspepsia [A] *	4/286 (1.4%)
Enteritis [A] *	2/286 (0.7%)
Eructation [A] *	1/286 (0.35%)
Flatulence [A] *	1/286 (0.35%)
Gastric ulcer [A] *	1/286 (0.35%)
Gastritis [A] *	2/286 (0.7%)

	Tocilizumab
	Affected/At Risk (%)
Gastrooesophageal reflux disease [A] *	1/286 (0.35%)
Gingival bleeding [A] *	1/286 (0.35%)
Gingival erythema [A] *	1/286 (0.35%)
Loose tooth [A] †	1/286 (0.35%)
Nausea [A] *	9/286 (3.15%)
Periodontitis [A] *	5/286 (1.75%)
Stomatitis [A] *	3/286 (1.05%)
Toothache [A] *	1/286 (0.35%)
Vomiting [A] *	5/286 (1.75%)
General disorders	
Chest pain [A] *	2/286 (0.7%)
Chills [A] *	2/286 (0.7%)
Discomfort [A] *	3/286 (1.05%)
Drug intolerance [A] *	3/286 (1.05%)
Fatigue [A] *	13/286 (4.55%)
General physical health deterioration [A] *	1/286 (0.35%)
Local swelling [A] *	1/286 (0.35%)
Malaise [A] *	1/286 (0.35%)
Mucosal inflammation [A] *	1/286 (0.35%)
Oedema [A] *	1/286 (0.35%)
Oedema peripheral [A] *	6/286 (2.1%)
Pitting oedema [A] *	1/286 (0.35%)

	Tocilizumab
	Affected/At Risk (%)
Thirst [A] *	1/286 (0.35%)
Hepatobiliary disorders	
Hepatotoxicity [A] *	1/286 (0.35%)
Immune system disorders	
Food allergy [A] *	1/286 (0.35%)
Hypersensitivity [A] *	5/286 (1.75%)
Seasonal allergy [A] *	2/286 (0.7%)
Infections and infestations	
Abscess jaw [A] *	1/286 (0.35%)
Abscess limb [A] *	1/286 (0.35%)
Acute tonsillitis [A] *	1/286 (0.35%)
Anal abscess [A] *	1/286 (0.35%)
Bacterial disease carrier [A] *	1/286 (0.35%)
Bacteriuria [A] *	1/286 (0.35%)
Bronchitis [A] *	16/286 (5.59%)
Bronchopneumonia [A] *	2/286 (0.7%)
Cellulitis [A] *	1/286 (0.35%)
Cystitis [A] *	5/286 (1.75%)
Eyelid infection [A] *	1/286 (0.35%)
Folliculitis [A] *	3/286 (1.05%)
Fungal skin infection [A] *	1/286 (0.35%)
Furuncle [A] *	1/286 (0.35%)

	Tocilizumab
	Affected/At Risk (%)
Gastroenteritis [A] *	5/286 (1.75%)
Gastrointestinal infection [A] *	1/286 (0.35%)
Herpes simplex [A] *	1/286 (0.35%)
Herpes virus infection [A] †	1/286 (0.35%)
Herpes zoster [A] *	2/286 (0.7%)
Herpes zoster ophthalmic [A] *	1/286 (0.35%)
Influenza [A] *	3/286 (1.05%)
Lower respiratory tract infection viral [A] *	1/286 (0.35%)
Nasopharyngitis [A] *	54/286 (18.88%)
Onychomycosis [A] *	2/286 (0.7%)
Oral herpes [A] *	6/286 (2.1%)
Osteomyelitis [A] *	1/286 (0.35%)
Otitis media [A] *	3/286 (1.05%)
Paronychia [A] *	1/286 (0.35%)
Parotitis [A] *	1/286 (0.35%)
Peritonsillar abscess [A] *	1/286 (0.35%)
Pharyngeal abscess [A] *	1/286 (0.35%)
Pharyngitis [A] *	4/286 (1.4%)
Pneumonia [A] *	2/286 (0.7%)
Post procedural infection [A] *	1/286 (0.35%)
Postoperative wound infection [A] *	1/286 (0.35%)
Prostate infection [A] *	1/286 (0.35%)

	Tocilizumab
	Affected/At Risk (%)
Pulpitis dental [A] *	2/286 (0.7%)
Respiratory tract infection [A] *	4/286 (1.4%)
Rhinitis [A] *	15/286 (5.24%)
Septic shock [A] *	1/286 (0.35%)
Sinobronchitis [A] *	1/286 (0.35%)
Sinusitis [A] *	8/286 (2.8%)
Skin bacterial infection [A] *	1/286 (0.35%)
Tinea pedis [A] *	1/286 (0.35%)
Tinea versicolour [A] *	1/286 (0.35%)
Tonsillitis [A] *	1/286 (0.35%)
Tooth abscess [A] *	2/286 (0.7%)
Tooth infection [A] *	1/286 (0.35%)
Tracheobronchitis [A] *	2/286 (0.7%)
Upper respiratory tract infection [A] *	9/286 (3.15%)
Upper respiratory tract infection bacterial [A] *	1/286 (0.35%)
Urethritis [A] *	1/286 (0.35%)
Urinary tract infection [A] *	15/286 (5.24%)
Urinary tract infection bacterial [A] *	1/286 (0.35%)
Vaginal infection [A] *	1/286 (0.35%)
Viral infection [A] *	4/286 (1.4%)
Vulvitis [A] *	1/286 (0.35%)
Vulvovaginal mycotic infection [A] †	3/286 (1.05%)

	Tocilizumab
	Affected/At Risk (%)
Injury, poisoning and procedural complications	
Contusion [A] *	2/286 (0.7%)
Excoriation [A] *	1/286 (0.35%)
Fall [A] *	1/286 (0.35%)
Foot fracture [A] *	2/286 (0.7%)
Humerus fracture [A] *	1/286 (0.35%)
Joint sprain [A] *	2/286 (0.7%)
Lower limb fracture [A] *	1/286 (0.35%)
Meniscus lesion [A] *	1/286 (0.35%)
Nail injury [A] *	1/286 (0.35%)
Overdose [A] *	8/286 (2.8%)
Radius fracture [A] *	1/286 (0.35%)
Skeletal injury [A] *	1/286 (0.35%)
Tendon rupture [A] *	1/286 (0.35%)
Wound [A] *	1/286 (0.35%)
Wrist fracture [A] *	1/286 (0.35%)
Investigations	
Alanine aminotransferase increased [A] *	24/286 (8.39%)
Aspartate aminotransferase increased [A] *	14/286 (4.9%)
Basophil count increased [A] *	1/286 (0.35%)
Blood bilirubin increased [A] *	4/286 (1.4%)
Blood cholesterol increased [A] *	5/286 (1.75%)

	Tocilizumab
	Affected/At Risk (%)
Blood creatinine increased [A] *	1/286 (0.35%)
Blood lactate dehydrogenase increased [A] *	2/286 (0.7%)
Blood triglycerides increased [A] *	2/286 (0.7%)
Blood uric acid increased [A] *	2/286 (0.7%)
Body temperature increased [A] *	2/286 (0.7%)
Haematocrit increased [A] *	1/286 (0.35%)
Haemoglobin increased [A] *	1/286 (0.35%)
Hepatic enzyme increased [A] *	2/286 (0.7%)
Low density lipoprotein increased [A] *	79/286 (27.62%)
Lymphocyte count increased [A] *	1/286 (0.35%)
Neutrophil count decreased [A] *	4/286 (1.4%)
Transaminases increased [A] *	2/286 (0.7%)
Weight decreased [A] *	1/286 (0.35%)
Weight increased [A] *	7/286 (2.45%)
Metabolism and nutrition disorders	
Anorexia [A] *	1/286 (0.35%)
Hypercholesterolaemia [A] *	5/286 (1.75%)
Hyperglycaemia [A] *	1/286 (0.35%)
Hyperlipidaemia [A] *	6/286 (2.1%)
Hyperureicaemia [A] *	1/286 (0.35%)
Hypokalaemia [A] †	1/286 (0.35%)
Musculoskeletal and connective tissue disorders	

	Tocilizumab
	Affected/At Risk (%)
Arthralgia [A] *	8/286 (2.8%)
Arthritis [A] *	1/286 (0.35%)
Back pain [A] *	9/286 (3.15%)
Bursitis [A] *	2/286 (0.7%)
Facit joint syndrome [A] *	1/286 (0.35%)
Groin pain [A] *	1/286 (0.35%)
Haemarthrosis [A] *	1/286 (0.35%)
Intervertebral disc protrusion [A] *	1/286 (0.35%)
Jaw cyst [A] *	1/286 (0.35%)
Joint range of motion decreased [A] *	1/286 (0.35%)
Ligament disorder [A] *	1/286 (0.35%)
Muscle spasms [A] *	1/286 (0.35%)
Muscle tightness [A] *	2/286 (0.7%)
Musculoskeletal chest pain [A] *	1/286 (0.35%)
Musculoskeletal pain [A] *	2/286 (0.7%)
Myalgia [A] *	2/286 (0.7%)
Osteoarthritis [A] *	1/286 (0.35%)
Osteoporosis [A] *	1/286 (0.35%)
Pain in extremity [A] *	2/286 (0.7%)
Rheumatoid arthritis [A] *	25/286 (8.74%)
Sacroiliitis [A] *	1/286 (0.35%)
Synovial cyst [A] *	1/286 (0.35%)

	Tocilizumab
	Affected/At Risk (%)
Tendonitis [A] *	1/286 (0.35%)
Tenosynovitis [A] *	2/286 (0.7%)
Tenosynovitis stenosans [A] *	1/286 (0.35%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Benign bone neoplasm [A] *	1/286 (0.35%)
Bladder transitional cell carcinoma [A] *	1/286 (0.35%)
Non-Hodgkin's lymphoma [A] *	1/286 (0.35%)
Uterine leiomyoma [A] *	1/286 (0.35%)
Nervous system disorders	
Aphasia [A] †	1/286 (0.35%)
Carpal tunnel syndrome [A] *	1/286 (0.35%)
Cervicobrachial syndrome [A] *	1/286 (0.35%)
Dizziness [A] *	3/286 (1.05%)
Dysaesthesia [A] *	1/286 (0.35%)
Dysgeusia [A] *	1/286 (0.35%)
Facial neuralgia [A] *	1/286 (0.35%)
Headache [A] *	27/286 (9.44%)
Migraine [A] *	4/286 (1.4%)
Multiple sclerosis relapse [A] *	1/286 (0.35%)
Paraesthesia [A] †	1/286 (0.35%)
Restless legs syndrome [A] *	2/286 (0.7%)
Sciatica [A] *	3/286 (1.05%)

	Tocilizumab
	Affected/At Risk (%)
Somnolence [A] *	1/286 (0.35%)
Synope [A] *	1/286 (0.35%)
Tremor [A] *	1/286 (0.35%)
Pregnancy, puerperium and perinatal conditions	
Abortion [A] *	1/286 (0.35%)
Psychiatric disorders	
Depression [A] *	2/286 (0.7%)
Food aversion [A] *	1/286 (0.35%)
Insomnia [A] *	2/286 (0.7%)
Mood altered [A] *	1/286 (0.35%)
Post-traumatic stress disorder [A] *	1/286 (0.35%)
Sleep disorder [A] *	3/286 (1.05%)
Renal and urinary disorders	
Haematuria [A] *	3/286 (1.05%)
Leukocyturia [A] *	2/286 (0.7%)
Nocturia [A] †	1/286 (0.35%)
Renal failure acute [A] *	1/286 (0.35%)
Urethral stenosis [A] *	1/286 (0.35%)
Reproductive system and breast disorders	
Breast disorder [A] *	1/286 (0.35%)
Breast pain [A] *	1/286 (0.35%)
Genital cyst [A] *	1/286 (0.35%)
Menopausal symptoms [A] *	2/286 (0.7%)

	Tocilizumab
	Affected/At Risk (%)
Vulvovaginal dryness [A] *	1/286 (0.35%)
Respiratory, thoracic and mediastinal disorders	
Allergic cough [A] *	1/286 (0.35%)
Asthma [A] *	2/286 (0.7%)
Cough [A] †	9/286 (3.15%)
Dysphonia [A] *	2/286 (0.7%)
Dyspnoea [A] *	3/286 (1.05%)
Dyspnoea exertional [A] *	1/286 (0.35%)
Epistaxis [A] †	3/286 (1.05%)
Interstitial lung disease [A] *	1/286 (0.35%)
Nasal dryness [A] *	1/286 (0.35%)
Nasal mucosal disorder [A] *	1/286 (0.35%)
Oropharyngeal blistering [A] *	1/286 (0.35%)
Oropharyngeal pain [A] *	3/286 (1.05%)
Pleurisy [A] *	2/286 (0.7%)
Rales [A] *	1/286 (0.35%)
Rhinitis allergic [A] *	2/286 (0.7%)
Rhinorrhoea [A] *	1/286 (0.35%)
Skin and subcutaneous tissue disorders	
Acne [A] *	2/286 (0.7%)
Alopecia [A] †	5/286 (1.75%)
Blister [A] *	1/286 (0.35%)

	Tocilizumab
	Affected/At Risk (%)
Dermatitis allergic [A] *	1/286 (0.35%)
Drug eruption [A] *	1/286 (0.35%)
Dry skin [A] *	1/286 (0.35%)
Eczema [A] *	8/286 (2.8%)
Erythema [A] *	1/286 (0.35%)
Hyperhidrosis [A] *	3/286 (1.05%)
Pruritus [A] *	7/286 (2.45%)
Pruritus generalised [A] *	1/286 (0.35%)
Psoriasis [A] *	2/286 (0.7%)
Rash [A] *	3/286 (1.05%)
Rash macular [A] *	1/286 (0.35%)
Rash pruritic [A] *	1/286 (0.35%)
Skin chapped [A] *	1/286 (0.35%)
Skin exfoliation [A] *	1/286 (0.35%)
Skin fissures [A] *	1/286 (0.35%)
Skin irritation [A] *	2/286 (0.7%)
Skin reaction [A] *	1/286 (0.35%)
Skin ulcer [A] *	1/286 (0.35%)
Urticaria [A] *	2/286 (0.7%)
Vascular disorders	
Haematoma [A] *	2/286 (0.7%)
Hypertension [A] *	16/286 (5.59%)

	Tocilizumab
	Affected/At Risk (%)
Lymphoedema [A] *	1/286 (0.35%)
Thrombosis [A] *	1/286 (0.35%)

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA

Limitations and Caveats

Nonserious adverse events presented in this record include all adverse events reported during the study, not just nonserious events.

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The study being conducted under this agreement is part of the overall study. Investigator is free to publish in reputable journals or to present at professional conferences the results of the study, but after the first publication or presentation that involves the overall study. Sponsor may request that confidential information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights

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