ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 07/15/2014

An Exploratory Study of Tocilizumab in Patients With Active Rheumatoid Arthritis (RA) and an Inadequate Response to Current Non-Biologic DMARDs and/or Anti-TNF Therapy.

This study has been completed.

Sponsor:	Hoffmann-La Roche
Collaborators:	
Information provided by (Responsible Party):	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT00750880

Purpose

This open-label, single arm study will investigate the safety, tolerability and efficacy of tocilizumab monotherapy, or combination therapy with non-biologic disease modifying antirheumatic drugs (DMARDs), in patients with severe active RA. Patients will receive tocilizumab 8mg/kg iv as a 60 minute infusion every 4 weeks for a total of 6 infusions. The anticipated time on study treatment is 3-12 months, and the target sample size is >500 individuals.

Condition	Intervention	Phase
Rheumatoid Arthritis	Drug: tocilizumab [RoActemra/Actemra]	Phase 3

Study Type: Interventional
Study Design: Treatment, Single Group Assignment, Open Label, Non-Randomized, Safety/Efficacy Study
Official Title: International Multi-Center Open Label Study to Evaluate the Safety, Tolerability and Efficacy of Tocilizumab in Patients With Active Rheumatoid Arthritis on Background Non-biologic DMARDs Who Have An Inadequate Response to Current Non-Biologic DMARD or Anti-TNF Therapy.

Further study details as provided by Hoffmann-La Roche:
Primary Outcome Measure:
- Percentage of Participants With Adverse Events (AEs): Overall Summary [Time Frame: Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: Yes]

Percentage of participants with AEs, serious AEs (SAEs), related AEs, related SAEs, severe AEs, with AEs leading to withdrawal or dose modification, with infection, serious infection, infusion reactions, infusion reactions during an infusion, infusion reactions within 24 hours of an infusion, major adverse cardiac event (MACE), or death.

Secondary Outcome Measures:

- Percentage of Participants Who Achieved Low Disease Activity or Remission Based on Disease Activity Score Based on 28-Joints Count (DAS28) by Visit [Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]
  DAS28 calculated from the number of swollen joints and tender joints using the 28 joints count, the erythrocyte sedimentation rate (ESR) (millimeters per hour [mm/hr]) and Patient's Global Assessment of Disease Activity (participant-rated arthritis activity assessment) with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity. Low disease activity was defined as DAS28 less than or equal to (≤)3.2 and remission was defined as DAS28 less than (<)2.6.
- Time to Low Disease Activity or Remission Based on DAS28 - Number of Participants With an Event [Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]
  DAS28 calculated from the number of swollen joints and tender joints using the 28 joints count, the ESR (mm/hr) and Patient's Global Assessment of Disease Activity (participant-rated arthritis activity assessment) with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity. Low disease activity was defined as DAS28 ≤3.2 and remission was defined as DAS28 <2.6.
- Time to Low Disease Activity and Remission Based on DAS28 Score - Time to Event [Time Frame: Baseline,Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]
  The time to low disease activity or remission was calculated as the number of days from study Day 1 to the first occurrence of low disease activity or remission. Participants who did not achieve low disease activity on or before Week 24 or who withdrew from the study prior to achieving low disease activity were considered censored. DAS28 calculated from the number of swollen joints and tender joints using the 28 joints count, the ESR (mm/hr) and Patient's Global Assessment of Disease Activity (participant-rated arthritis activity assessment) with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity. Low disease activity defined as DAS28 ≤3.2 and remission defined as DAS28 <2.6.
- Percentage of Participants Achieving a Response by European League Against Rheumatism (EULAR) Response Category and Visit [Time Frame: Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]
  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. If the EULAR response could not be determined, it was set to 'No response'.
- DAS28 Scores by Visit [Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]
  DAS28 calculated from the number of swollen joints and tender joints using the 28 joints count, the ESR (mm/hr) and Patient's Global Assessment of Disease Activity (participant-rated arthritis activity assessment) with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity. A negative change from baseline indicates improvement.
- Percentage of Participants Achieving an American College of Rheumatology 20 Percent (%), 50%, 70%, or 90% Improvement (ACR20/ACR50/ACR70/ACR90) by Visit [Time Frame: Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]
  ACR20, ACR50, ACR70, and ACR90 are defined as ≥20%, ≥50%, ≥70%, or ≥90% improvement, respectively, in: swollen joint count (SJC; 66 joints) and tender joint count (TJC; 68 joints) and ≥20%, ≥50%, ≥70%, or ≥90% improvement, respectively, in 3 of following 5 assessments: Patient's Global Assessment of Pain (visual analog scale [VAS]); Patient's Global Assessment of Disease Activity (VAS); Investigator/Physician's Global Assessment of Disease Activity (VAS); participant's assessment of disability measured by the Health Assessment Questionnaire Disability Index (HAQ-DI); or acute phase reactant (ESR or C-reactive protein [CRP]). Participants who did not have the required data to assess ACR status at a given visit were classified as non-responders.
- Time to Achieve ACR20, ACR50, ACR70 and ACR90 Response - Number of Participants With an Event [Time Frame: Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]
  ACR20, ACR50, ACR70, and ACR90 are defined as ≥20%, ≥50%, ≥70%, or ≥90% improvement, respectively, in: swollen joint count (SJC; 66 joints) and tender joint count (TJC; 68 joints) and ≥20%, ≥50%, ≥70%, or ≥90% improvement, respectively, in 3 of following 5 assessments: Patient's Global

Assessment of Pain (VAS); Patient's Global Assessment of Disease Activity (VAS); Investigator/Physician's Global Assessment of Disease Activity (VAS); participant's assessment of disability measured by the HAQ-DI; or acute phase reactant (ESR or CRP).

- Time to Achieve ACR20, ACR50, ACR70 and ACR90 Response [Time Frame: Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]
  ACR20, ACR50, ACR70, and ACR90 are defined as ≥20%, ≥50%, ≥70%, or ≥90% improvement, respectively, in: swollen joint count (SJC; 66 joints) and tender joint count (TJC; 68 joints) and ≥20%, ≥50%, ≥70%, or ≥90% improvement, respectively, in 3 of following 5 assessments: Patient's Global Assessment of Pain (VAS); Patient's Global Assessment of Disease Activity (VAS); Investigator/Physician's Global Assessment of Disease Activity (VAS); participant's assessment of disability measured by the HAQ-DI; or acute phase reactant (ESR or CRP). Time to ACR response was calculated as the number of days from day 1 of study to the date of first achievement of ACR response. Data represent median time for responders only.
- Swollen Joint Count by Visit [Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]
  Number of swollen joints was determined by examination of 66 joints and identifying when swelling was present. The number of swollen joints was recorded on the joint assessment form at each visit, no swelling = 0, swelling =1; total was calculated by adding all the joints for a maximum score of 66. A negative change from baseline indicates improvement.
- Tender Joint Count by Visit [Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]
  Number of tender joints was determined by examining 68 joints and identified the joints that were painful under pressure or to passive motion. The number of tender joints was recorded on the joint assessment form at each visit, no tenderness = 0, tenderness = 1; total was calculated by adding all the joints for a maximum score of 68. A negative change from baseline indicates improvement.
- Patient's Global Assessment of Disease Activity by Visit [Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]
  The participant's global assessment of disease activity is assessed on a 0 to 100 mm horizontal VAS by the participant. The left-hand extreme of the line=0 mm, and is described as "no disease activity" (symptom-free and no arthritis symptoms) and the right-hand extreme=100 mm, as "maximum disease activity" (maximum arthritis disease activity). The line was marked by the participant and the distance from the left edge was recorded. A negative change from baseline indicated improvement.
- Physician's Global Assessment of Disease Activity by Visit [Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]
  The physician's global assessment of disease activity is assessed on a 0 to 100 mm horizontal VAS by the physician. The left-hand extreme of the line=0 mm, and is described as "no disease activity" (symptom-free and no arthritis symptoms) and the right-hand extreme=100 mm as "maximum disease activity" (maximum arthritis disease activity). The physician marked the line and the distance from the left edge was recorded. A negative change from baseline indicated improvement.
- Patient's Global Assessment of Pain by Visit [Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]
  The participants assessed their pain using a 0 to 100 mm horizontal VAS. The left-hand extreme of the line=0 mm, and is described as "no pain" and the right-hand extreme=100 mm as "unbearable pain". The participant marked the line and the distance from the left edge was recorded. A negative change from baseline indicated improvement.
- C-Reactive Protein by Visit [Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]
  The test for CRP (mg per deciliter [mg/dL]) is a laboratory measurement for evaluation of an acute phase reactant of inflammation through the use of an ultrasensitive assay. A decrease in the level of CRP indicates reduction in inflammation and therefore improvement.
- Erythrocyte Sedimentation Rate by Visit [Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]
  ESR (mm/hr) is a blood test used to monitor therapy in inflammatory diseases such as rheumatoid arthritis (RA) and reflects acute phase reactant levels. Active disease in RA is defined by an ESR greater than 30 mm/hr. Change from baseline is computed as the value at each week minus the baseline value. A negative value in change from baseline indicates an improvement.
- HAQ-DI Scores by Visit [Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]
  HAQ-DI includes 20 questions concerning participant's activities of daily life, grouped in 8 scales of 2 to 3 questions for each activity. To respond to each question, a four-level response (score of 0 to 3 points), with higher scores showing larger functional limitations, was chosen. Scoring was as follows with respect to performance of participant's everyday activities: 0 (equals)=without difficulties; 1=with some difficulties; 2=with great difficulties; and 3=unable to perform these actions at all. Minimum score was 0, maximum score was 3.
- Short Form-36 (SF-36) Physical Functioning Domain Scores by Visit [Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]

The SF-36 covers 8 health dimensions including 4 physical subscales (physical function, role-physical, bodily pain, and general health) and 4 mental subscales (vitality, social function, role-emotional, and mental health). The scores range from a minimum of 0 to a maximum of 100, with a higher score indicating better quality of life. Improvements of >3 points were considered clinically meaningful.

- Percentage of Participants With HAQ-DI Clinical Remission and Clinically Meaningful Improvement By Visit [Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]

  The HAQ-DI scale ranges from 0 to 3, where higher scores represent higher disease activity. A score of <0.5 represents clinical remission. A participant achieves a clinically meaningful improvement in HAQ-DI if they had a reduction from baseline of ≥0.22.
- Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-Fatigue) Score by Visit [Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, and 24] [Designated as safety issue: No]

  FACIT-Fatigue 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. 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.

Enrollment: 1681
Study Start Date: September 2008
Primary Completion Date: July 2011
Study Completion Date: July 2011

Arms	Assigned Interventions
Experimental: 1	Drug: tocilizumab [RoActemra/Actemra] 8mg/kg iv (60 minute infusion)

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- male and non-pregnant or nursing female patients >=18 years of age;
- body weight <=150kg;
- moderate to severe active RA (DAS28 >=3.2) of >=6 months duration;
- on >=1 non-biologic DMARDs at a stable dose for a period of >= 8 weeks prior to start of treatment;
- inadequate clinical response to a stable dose of non-biologic DMARD or anti-TNF therapy;
- if receiving oral corticosteroids, the dose must have been stable for at least 25 of 28 days prior to start of treatment.

Exclusion Criteria:

- major surgery (including joint surgery) within 8 weeks prior to screening or planned major surgery within 6 months following enrollment;
- rheumatic autoimmune disease other than RA;
- prior history of, or current inflammatory joint disease other than RA;

- functional class IV as defined by the ACR Classification of Functional Status in RA.

Contacts and Locations

Locations

Australia, Australian Capital Territory

Canberra, Australian Capital Territory, Australia, 2601

Australia, New South Wales

Coffs Harbour, New South Wales, Australia, 2450
Kogarah, New South Wales, Australia, 2217
Parramatta Park, New South Wales, Australia, 4870

Australia, South Australia

Adelaide, South Australia, Australia, 5041

Australia, Victoria

Fitzroy, Victoria, Australia, 3065
Geelong, Victoria, Australia, 3220
Melbourne, Victoria, Australia, 3168

Austria

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Graz-Eggenberg, Austria, 8020
Innsbruck, Austria, 6020
Linz, Austria, 4020
Salzburg, Austria, 5020
Stockerau, Austria, 2000
Wien, Austria, 1130
Wien, Austria, 1160
Wien, Austria, 1100

Belgium

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Bruxelles, Belgium, 1200
Bruxelles, Belgium, 1070
Bruxelles, Belgium, 1020
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- Toronto, Ontario, Canada, M5G 1X5
- Toronto, Ontario, Canada, M4K 1N2
- Toronto, Ontario, Canada, M5T 2S8
- Windsor, Ontario, Canada, N8X 5A6

Canada, Quebec
- Laval, Quebec, Canada, H7G 2E6
- Montreal, Quebec, Canada, H2L 4M1
- Montreal, Quebec, Canada, H2L 1S6
- Quebec City, Quebec, Canada, G1V 3M7
- Rimouski, Quebec, Canada, G5L 8W1
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- Caen, France, 14033
- Cahors, France, 46005
- Colmar, France, 68024
- Corbeil-essonnes, France, 91106
- Dijon, France, 21000
- La Rochelle, France, 17019
- Lievin, France, 62806
- Lomme, France, 59462
- Lyon, France, 69437
- Lyon, France, 69365
- Marseille, France, 13385
- Montivilliers, France, 76290
- Montpellier, France, 34295
- Montpellier, France, 34295
- Mulhouse, France, 68070
- Paris, France, 75674
- Paris, France, 75475
- Pau, France, 64046
- Poitiers, France, 86021
- Reims, France, 51092
- Roubaix, France, 59056
- St Brieuc, France, 22027
- Strasbourg, France, 67098
- Toulouse, France, 31059
- Valence, France, 26000
- Valenciennes, France, 59322

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- Bielefeld, Germany, 33611
- Freiburg, Germany, 79098
- Greifswald, Germany, 17489
- Hamburg, Germany, 22081
- Jena, Germany, 07747
- Kiel, Germany, 24116
- Rostock, Germany, 18059
- Saarbruecken, Germany, 66111
- Wuerzburg, Germany, 97080

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Heraklion, Greece, 711 10
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Patras, Greece, 265 04
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Bangalore, India, 560003
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Kolkata, India, 700 072
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Dublin, Ireland, 15
Dublin, Ireland, 7
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- Aviles, Avila, Spain, 33400
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- Madrid, Madrid, Spain, 28006
- Malaga, Malaga, Spain, 29010
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- Basel, Switzerland, 4055
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Investigators

Study Director:	Clinical Trials	Hoffmann-La Roche

More Information

Responsible Party:	Hoffmann-La Roche
Study ID Numbers:	MA21573 2008-000587-17
Health Authority:	Canada: Health Canada

Study Results

Participant Flow

Reporting Groups

	Description
Tocilizumab (TCZ) 8 Milligrams Per Kilogram (mg/kg)	Participants received tocilizumab 8 mg/kg intravenously (IV) once every 4 weeks for 20 weeks (total of 6 infusions).

Overall Study

	Tocilizumab (TCZ) 8 Milligrams Per Kilogram (mg/kg)
Started	1681
Completed	1466
Not Completed	215
Adverse Event	76

	Tocilizumab (TCZ) 8 Milligrams Per Kilogram (mg/kg)
Death	4
Lack of Efficacy	46
Lost to Follow-up	10
Protocol Violation	15
Withdrawal by Subject	33
Physician Decision	20
Administrative	11

Baseline Characteristics

Analysis Population Description

Inten-to-Treat (ITT) population: all participants included in the study who received at least 1 dose of study medication.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Baseline Measures

	Tocilizumab 8 mg/kg
Number of Participants	1681
Age, Continuous [units: years] Mean (Standard Deviation)	53.5 (12.34)
Gender, Male/Female [units: participants]	
Female	1356
Male	325

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With Adverse Events (AEs): Overall Summary

Measure Description	Percentage of participants with AEs, serious AEs (SAEs), related AEs, related SAEs, severe AEs, with AEs leading to withdrawal or dose modification, with infection, serious infection, infusion reactions, infusion reactions during an infusion, infusion reactions within 24 hours of an infusion, major adverse cardiac event (MACE), or death.
Time Frame	Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	Yes

Analysis Population Description

Safety population: all participants included in the study who received at least 1 dose of study medication and who had at least 1 postbaseline assessment of safety (post-baseline laboratory data, vital signs, or adverse events). number (n) equals (=) number of participants analyzed for the parameter within the specific population.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	1681
Percentage of Participants With Adverse Events (AEs): Overall Summary [units: percentage of participants]	
Any AE	77.4
Related AE	58.4
Severe AE	7.8
SAE	7.8
Related SAE	3.5
AE leading to withdrawal	5.1
AE leading to dose modification	10.8
Infection	35.3
Serious infection	2.1
Any infusion reaction (during or within 24 hours)	17.3
Infusion reaction during infusion	6.7
Infusion reaction within 24 hours of infusion	12.6

	Tocilizumab 8 mg/kg
MACE	0.4
Death	0.2

2. Secondary Outcome Measure:

Measure Title	Percentage of Participants Who Achieved Low Disease Activity or Remission Based on Disease Activity Score Based on 28-Joints Count (DAS28) by Visit
Measure Description	DAS28 calculated from the number of swollen joints and tender joints using the 28 joints count, the erythrocyte sedimentation rate (ESR) (millimeters per hour [mm/hr]) and Patient's Global Assessment of Disease Activity (participant-rated arthritis activity assessment) with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity. Low disease activity was defined as DAS28 less than or equal to (≤)3.2 and remission was defined as DAS28 less than (<)2.6.
Time Frame	Baseline, Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population; no imputation of missing data was performed for this analysis.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv infusions every 4 weeks for 24 weeks.

Measured Values

	Tocilizumab
Number of Participants Analyzed	1681
Percentage of Participants Who Achieved Low Disease Activity or Remission Based on Disease Activity Score Based on 28-Joints Count (DAS28) by Visit [units: percentage of participants]	
Baseline, low disease activity (n=1677)	1.1
Baseline, DAS28 <2.6 (n=1677)	0.2
Week 4, low disease activity (n=1635)	27.6

	Tocilizumab
Week 4, DAS28 <2.6 (n=1635)	14.9
Week 8, low disease activity (n=1594)	49.2
Week 8, DAS28 <2.6 (n=1594)	32.6
Week 12, low disease activity (n=1556)	57.3
Week 12, DAS28 <2.6 (n=1556)	40.0
Week 16, low disease activity (n=1509)	64.7
Week 16, DAS28 <2.6 (n=1509)	48.4
Week 20, low disease activity (n=1467)	69.3
Week 20, DAS28 <2.6 (n=1467)	54.9
Week 24, low disease activity (n=1455)	69.9
Week 24, DAS28 <2.6 (n=1455)	56.8

3. Secondary Outcome Measure:

Measure Title	Time to Low Disease Activity or Remission Based on DAS28 - Number of Participants With an Event
Measure Description	DAS28 calculated from the number of swollen joints and tender joints using the 28 joints count, the ESR (mm/hr) and Patient's Global Assessment of Disease Activity (participant-rated arthritis activity assessment) with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity. Low disease activity was defined as DAS28 ≤3.2 and remission was defined as DAS28 <2.6.
Time Frame	Baseline, Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	1665
Time to Low Disease Activity or Remission Based on DAS28 - Number of Participants With an Event [units: participants]	
Low disease activity	1320
DAS28 <2.6	1127

4. Secondary Outcome Measure:

Measure Title	Time to Low Disease Activity and Remission Based on DAS28 Score - Time to Event
Measure Description	The time to low disease activity or remission was calculated as the number of days from study Day 1 to the first occurrence of low disease activity or remission. Participants who did not achieve low disease activity on or before Week 24 or who withdrew from the study prior to achieving low disease activity were considered censored. DAS28 calculated from the number of swollen joints and tender joints using the 28 joints count, the ESR (mm/hr) and Patient's Global Assessment of Disease Activity (participant-rated arthritis activity assessment) with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity. Low disease activity defined as DAS28 ≤3.2 and remission defined as DAS28 <2.6.
Time Frame	Baseline,Weeks 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 infusions every 4 weeks for 24 weeks.

Measured Values

	Tocilizumab
Number of Participants Analyzed	1320
Time to Low Disease Activity and Remission Based on DAS28 Score - Time to Event [units: days] Median (Full Range)	

	Tocilizumab
Low disease activity (n=1320)	63.0 (60.0 to 80.0)
Remission (n=1127)	112.0 (97.0 to 113.0)

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving a Response by European League Against Rheumatism (EULAR) Response Category and Visit
Measure Description	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. If the EULAR response could not be determined, it was set to 'No response'.
Time Frame	Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	1681
Percentage of Participants Achieving a Response by European League Against Rheumatism (EULAR) Response Category and Visit [units: percentage of participants]	
Week 4, Good Response	24.7
Week 4, Moderate Response	52.6
Week 4, No Response	22.7
Week 8, Good Response	44.7

	Tocilizumab 8 mg/kg
Week 8, Moderate Response	40.8
Week 8, No Response	14.5
Week 12, Good Response	51.3
Week 12, Moderate Response	34.9
Week 12, No Response	13.7
Week 16, Good Response	57.0
Week 16, Moderate Response	27.5
Week 16, No Response	15.5
Week 20, Good Response	59.3
Week 20, Moderate Response	23.7
Week 20, No Response	17.0
Week 24, Good Response	59.6
Week 24, Moderate Response	23.8
Week 24, No Response	16.6

6. Secondary Outcome Measure:

Measure Title	DAS28 Scores by Visit
Measure Description	DAS28 calculated from the number of swollen joints and tender joints using the 28 joints count, the ESR (mm/hr) and Patient's Global Assessment of Disease Activity (participant-rated arthritis activity assessment) with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity. A negative change from baseline indicates improvement.
Time Frame	Baseline, Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg iv infusions every 4 weeks for 24 weeks.

Measured Values

	Tocilizumab
Number of Participants Analyzed	1681
DAS28 Scores by Visit [units: units on a scale] Mean (Standard Deviation)	
Baseline (n=1677)	5.96 (1.201)
Week 4 (n=1635)	4.12 (1.451)
Change at Week 4 (n=1631)	-1.84 (1.165)
Week 8 (n=1594)	3.35 (1.442)
Change at Week 8 (n=1590)	-2.60 (1.336)
Week 12 (n=1556)	3.03 (1.431)
Change at Week 12 (n=1552)	-2.92 (1.429)
Week 16 (n=1509)	2.80 (1.459)
Change at Week 16 (n=1506)	-3.14 (1.464)
Week 20 (n=1467)	2.63 (1.428)
Change at Week 20 (n=1463)	-3.14 (1.488)
Week 24 (n=1455)	2.52 (1.378)
Change at Week 24 (n=1451)	-3.42 (1.438)

7. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving an American College of Rheumatology 20 Percent (%), 50%, 70%, or 90% Improvement (ACR20/ACR50/ACR70/ACR90) by Visit

Measure Description	ACR20, ACR50, ACR70, and ACR90 are defined as ≥20%, ≥50%, ≥70%, or ≥90% improvement, respectively, in: swollen joint count (SJC; 66 joints) and tender joint count (TJC; 68 joints) and ≥20%, ≥50%, ≥70%, or ≥90% improvement, respectively, in 3 of following 5 assessments: Patient's Global Assessment of Pain (visual analog scale [VAS]); Patient's Global Assessment of Disease Activity (VAS); Investigator/Physician's Global Assessment of Disease Activity (VAS); participant's assessment of disability measured by the Health Assessment Questionnaire Disability Index (HAQ-DI); or acute phase reactant (ESR or C-reactive protein [CRP]). Participants who did not have the required data to assess ACR status at a given visit were classified as non-responders.
Time Frame	Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	1681
Percentage of Participants Achieving an American College of Rheumatology 20 Percent (%), 50%, 70%, or 90% Improvement (ACR20/ACR50/ACR70/ACR90) by Visit [units: percentage of participants]	
Week 4, ACR20	36.5
Week 4, ACR50	10.5
Week 4, ACR70	2.7
Week 4, ACR90	0.3
Week 8, ACR20	55.6
Week 8, ACR50	26.9
Week 8, ACR70	10.7
Week 8, ACR90	2.2
Week 12, ACR20	61.0
Week 12, ACR50	36.3

	Tocilizumab 8 mg/kg
Week 12, ACR70	17.5
Week 12, ACR90	4.8
Week 16, ACR20	64.1
Week 16, ACR50	40.2
Week 16, ACR70	21.1
Week 16, ACR90	5.8
Week 20, ACR20	65.0
Week 20, ACR50	44.4
Week 20, ACR70	22.4
Week 20, ACR90	6.7
Week 24, ACR20	66.9
Week 24, ACR50	46.6
Week 24, ACR70	26.4
Week 24, ACR90	8.7

8. Secondary Outcome Measure:

Measure Title	Time to Achieve ACR20, ACR50, ACR70 and ACR90 Response - Number of Participants With an Event
Measure Description	ACR20, ACR50, ACR70, and ACR90 are defined as ≥20%, ≥50%, ≥70%, or ≥90% improvement, respectively, in: swollen joint count (SJC; 66 joints) and tender joint count (TJC; 68 joints) and ≥20%, ≥50%, ≥70%, or ≥90% improvement, respectively, in 3 of following 5 assessments: Patient's Global Assessment of Pain (VAS); Patient's Global Assessment of Disease Activity (VAS); Investigator/Physician's Global Assessment of Disease Activity (VAS); participant's assessment of disability measured by the HAQ-DI; or acute phase reactant (ESR or CRP).
Time Frame	Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	1681
Time to Achieve ACR20, ACR50, ACR70 and ACR90 Response - Number of Participants With an Event [units: participants]	
ACR20	1431
ACR50	1075
ACR70	659
ACR90	232

9. Secondary Outcome Measure:

Measure Title	Time to Achieve ACR20, ACR50, ACR70 and ACR90 Response
Measure Description	ACR20, ACR50, ACR70, and ACR90 are defined as ≥20%, ≥50%, ≥70%, or ≥90% improvement, respectively, in: swollen joint count (SJC; 66 joints) and tender joint count (TJC; 68 joints) and ≥20%, ≥50%, ≥70%, or ≥90% improvement, respectively, in 3 of following 5 assessments: Patient's Global Assessment of Pain (VAS); Patient's Global Assessment of Disease Activity (VAS); Investigator/Physician's Global Assessment of Disease Activity (VAS); participant's assessment of disability measured by the HAQ-DI; or acute phase reactant (ESR or CRP). Time to ACR response was calculated as the number of days from day 1 of study to the date of first achievement of ACR response. Data represent median time for responders only.
Time Frame	Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population; only participants with a response (ACR20/ACR50/ACR70/ACR90) were included in the analysis. n=number of participants with a response for the specified parameter

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	1681
Time to Achieve ACR20, ACR50, ACR70 and ACR90 Response [units: days] Median (95% Confidence Interval)	
ACR20 (n=1431)	57.0 (22 to 197)
ACR50 (n=1075)	84.0 (23 to 243)
ACR70 (n=659)	90.0 (25 to 238)
ACR90 (n=232)	113.0 (27 to 197)

10. Secondary Outcome Measure:

Measure Title	Swollen Joint Count by Visit
Measure Description	Number of swollen joints was determined by examination of 66 joints and identifying when swelling was present. The number of swollen joints was recorded on the joint assessment form at each visit, no swelling = 0, swelling =1; total was calculated by adding all the joints for a maximum score of 66. A negative change from baseline indicates improvement.
Time Frame	Baseline, Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population; missing data were handled using the LOCF approach.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	1681
Swollen Joint Count by Visit [units: swollen joints] Mean (Standard Deviation)	

	Tocilizumab 8 mg/kg
Baseline	12.76 (9.183)
Week 4	9.24 (10.371)
Change at Week 4	-3.52 (10.882)
Week 8	6.56 (8.799)
Change at Week 8	-6.20 (10.597)
Week 12	5.62 (8.324)
Change at Week 12	-7.14 (10.737)
Week 16	5.24 (8.441)
Change at Week 16	-7.52 (11.114)
Week 20	4.77 (8.150)
Change at Week 20	-7.99 (11.130)
Week 24	4.60 (8.216)
Change at Week 24	-8.16 (11.179)

11. Secondary Outcome Measure:

Measure Title	Tender Joint Count by Visit
Measure Description	Number of tender joints was determined by examining 68 joints and identified the joints that were painful under pressure or to passive motion. The number of tender joints was recorded on the joint assessment form at each visit, no tenderness = 0, tenderness = 1; total was calculated by adding all the joints for a maximum score of 68. A negative change from baseline indicates improvement.
Time Frame	Baseline, Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population; missing data were handled using the last observation carried forward (LOCF) approach.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	1681
Tender Joint Count by Visit [units: tender joints] Mean (Standard Deviation)	
Baseline	22.82 (15.019)
Week 4	16.55 (15.024)
Change at Week 4	-6.27 (13.384)
Week 8	12.21 (13.227)
Change at Week 8	-10.61 (13.960)
Week 12	10.47 (12.831)
Change at Week 12	-12.35 (14.611)
Week 16	9.75 (12.372)
Change at Week 16	-13.06 (14.876)
Week 20	9.31 (12.326)
Change at Week 20	-13.51 (15.312)
Week 24	8.74 (12.115)
Change at Week 24	-14.08 (15.520)

12. Secondary Outcome Measure:

Measure Title	Patient's Global Assessment of Disease Activity by Visit
Measure Description	The participant's global assessment of disease activity is assessed on a 0 to 100 mm horizontal VAS by the participant. The left-hand extreme of the line=0 mm, and is described as “no disease activity” (symptom-free and no arthritis symptoms) and the right-hand extreme=100 mm, as “maximum disease activity” (maximum arthritis disease activity). The line was marked by the participant and the distance from the left edge was recorded. A negative change from baseline indicated improvement.
Time Frame	Baseline, Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	1681
Patient's Global Assessment of Disease Activity by Visit [units: mm] Mean (Standard Deviation)	
Baseline (n=1677)	62.52 (21.192)
Week 4 (n=1653)	47.20 (23.945)
Change at Week 4 (n=1649)	-15.32 (23.852)
Week 8 (n=1610)	37.95 (24.377)
Change at Week 8 (n=1606)	-24.52 (25.972)
Week 12 (n=1569)	33.27 (23.474)
Change at Week 12 (n=1565)	-28.98 (25.885)
Week 16 (n=1525)	30.92 (23.720)
Change at Week 16 (n=1522)	-31.42 (26.213)
Week 20 (n=1488)	28.74 (22.948)
Change at Week 20 (n=1484)	-33.42 (26.160)
Week 24 (n=1472)	26.68 (22.070)
Change at Week 24 (n=1468)	-35.53 (25.558)

13. Secondary Outcome Measure:

Measure Title	Physician's Global Assessment of Disease Activity by Visit

Measure Description	The physician's global assessment of disease activity is assessed on a 0 to 100 mm horizontal VAS by the physician. The left-hand extreme of the line=0 mm, and is described as "no disease activity" (symptom-free and no arthritis symptoms) and the right-hand extreme=100 mm as "maximum disease activity" (maximum arthritis disease activity). The physician marked the line and the distance from the left edge was recorded. A negative change from baseline indicated improvement.
Time Frame	Baseline, Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	1681
Physician's Global Assessment of Disease Activity by Visit [units: mm] Mean (Standard Deviation)	
Baseline (n=1675)	58.82 (17.886)
Week 4 (n=1645)	39.79 (19.858)
Change at Week 4 (n=1640)	-18.93 (20.126)
Week 8 (n=1605)	30.01 (18.671)
Change at Week 8 (n=1601)	-28.65 (21.190)
Week 12 (n=1567)	25.71 (18.217)
Change at Week 12 (n=1563)	-32.72 (21.295)
Week 16 (n=1525)	23.17 (17.646)
Change at Week 16 (n=1521)	-35.49 (21.636)
Week 20 (n=1482)	21.18 (17.064)
Change at Week 20 (n=1478)	-37.33 (21.855)
Week 24 (n=1459)	19.53 (17.183)

	Tocilizumab 8 mg/kg
Change at Week 24 (n=1455)	-39.10 (21.984)

14. Secondary Outcome Measure:

Measure Title	Patient's Global Assessment of Pain by Visit
Measure Description	The participants assessed their pain using a 0 to 100 mm horizontal VAS. The left-hand extreme of the line=0 mm, and is described as “no pain” and the right-hand extreme=100 mm as “unbearable pain”. The participant marked the line and the distance from the left edge was recorded. A negative change from baseline indicated improvement.
Time Frame	Baseline, Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	1681
Patient's Global Assessment of Pain by Visit [units: mm] Mean (Standard Deviation)	
Baseline (n=1675)	57.51 (22.582)
Week 4 (n=1654)	43.10 (23.563)
Change at Week 4 (n=1648)	-14.41 (23.441)
Week 8 (n=1612)	34.93 (23.711)
Change at Week 8 (n=1606)	-22.51 (25.138)
Week 12 (n=1572)	31.02 (23.342)
Change at Week 12 (n=1566)	-26.21 (26.036)
Week 16 (n=1525)	28.56 (23.016)

	Tocilizumab 8 mg/kg
Change at Week 16 (n=1521)	-28.59 (26.079)
Week 20 (n=1489)	26.76 (22.456)
Change at Week 20 (n=1483)	-30.29 (26.417)
Week 24 (n=1473)	24.90 (21.398)
Change at Week 24 (n=1468)	-32.13 (25.925)

15. Secondary Outcome Measure:

Measure Title	C-Reactive Protein by Visit
Measure Description	The test for CRP (mg per deciliter [mg/dL]) is a laboratory measurement for evaluation of an acute phase reactant of inflammation through the use of an ultrasensitive assay. A decrease in the level of CRP indicates reduction in inflammation and therefore improvement.
Time Frame	Baseline, Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	1681
C-Reactive Protein by Visit [units: mg/dL] Mean (Standard Deviation)	
Baseline (n=1681)	1.94 (2.775)
Week 4 (n=1649)	0.52 (1.834)
Change at Week 4 (n=1649)	-1.40 (2.243)
Week 8 (n=1613)	0.36 (1.372)

	Tocilizumab 8 mg/kg
Change at Week 8 (n=1613)	-1.59 (2.474)
Week 12 (n=1571)	0.28 (1.247)
Change at Week 12 (n=1571)	-1.63 (2.532)
Week 16 (n=1525)	0.23 (0.798)
Change at Week 16 (n=1525)	-1.70 (2.655)
Week 20 (n=1481)	0.23 (1.078)
Change at Week 20 (n=1481)	-1.68 (2.573)
Week 24 (n=1448)	0.19 (0.802)
Change at Week 24 (n=1448)	-1.74 (2.608)

16. Secondary Outcome Measure:

Measure Title	Erythrocyte Sedimentation Rate by Visit
Measure Description	ESR (mm/hr) is a blood test used to monitor therapy in inflammatory diseases such as rheumatoid arthritis (RA) and reflects acute phase reactant levels. Active disease in RA is defined by an ESR greater than 30 mm/hr. Change from baseline is computed as the value at each week minus the baseline value. A negative value in change from baseline indicates an improvement.
Time Frame	Baseline, Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	1681
Erythrocyte Sedimentation Rate by Visit [units: mm/hr]	

	Tocilizumab 8 mg/kg
Mean (Standard Deviation)	
Baseline (n=1681)	39.20 (26.843)
Week 4 (n=1642)	13.13 (16.468)
Change at Week 4 (n=1642)	-26.07 (21.863)
Week 8 (n=1603)	10.26 (14.935)
Change at Week 8 (n=1603)	-28.93 (23.945)
Week 12 (n=1567)	8.97 (12.527)
Change at Week 12 (n=1567)	-30.02 (24.543)
Week 16 (n=1520)	8.39 (12.230)
Change at Week 16 (n=1520)	-30.43 (24.703)
Week 20 (n=1474)	7.81 (11.653)
Change at Week 20 (n=1474)	-31.01 (24.648)
Week 24 (n=1463)	7.90 (11.485)
Change at Week 24 (n=1463)	-31.01 (24.796)

17. Secondary Outcome Measure:

Measure Title	HAQ-DI Scores by Visit
Measure Description	HAQ-DI includes 20 questions concerning participant's activities of daily life, grouped in 8 scales of 2 to 3 questions for each activity. To respond to each question, a four-level response (score of 0 to 3 points), with higher scores showing larger functional limitations, was chosen. Scoring was as follows with respect to performance of participant's everyday activities: 0 (equals)=without difficulties; 1=with some difficulties; 2=with great difficulties; and 3=unable to perform these actions at all. Minimum score was 0, maximum score was 3.
Time Frame	Baseline, Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	1681
HAQ-DI Scores by Visit [units: units on a scale] Mean (Standard Deviation)	
Baseline (n=1673)	1.49 (0.637)
Week 4 (n=1648)	1.27 (0.665)
Change at Week 4 (n=1641)	-022 (0.448)
Week 8 (n=1607)	1.12 (0.677)
Change at Week 8 (n=1600)	-0.37 (0.511)
Week 12 (n=1570)	1.03 (0.684)
Change at Week 12 (n=1562)	-0.46 (0.553)
Week 16 (n=1524)	0.99 (0.690)
Change at Week 16 (n=1517)	-0.50 (0.566)
Week 20 (n=1483)	0.95 (0.687)
Change at Week 20 (n=1476)	-0.53 (0.573)
Week 24 (n=1459)	0.92 (0.697)
Change at Week 24 (n=1451)	-0.57 (0.585)

18. Secondary Outcome Measure:

Measure Title	Short Form-36 (SF-36) Physical Functioning Domain Scores by Visit
Measure Description	The SF-36 covers 8 health dimensions including 4 physical subscales (physical function, role-physical, bodily pain, and general health) and 4 mental subscales (vitality, social function, role-emotional, and mental health). The scores range from a minimum of 0 to a maximum of 100, with a higher score indicating better quality of life. Improvements of >3 points were considered clinically meaningful.

Time Frame	Baseline, Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	1681
Short Form-36 (SF-36) Physical Functioning Domain Scores by Visit [units: units on a scale] Mean (Standard Deviation)	
Baseline (n=1671)	31.39 (9.813)
Week 4 (n=1647)	34.17 (10.398)
Change at Week 4 (1639)	2.79 (8.064)
Week 8 (n=1608)	36.39 (10.829)
Change at Week 8 (n=1598)	4.95 (9.088)
Week 12 (n=1573)	37.69 (11.096)
Change at Week 12 (n=1564)	6.19 (9.751)
Week 16 (n=1529)	38.41 (11.139)
Change at Week 16 (n=1521)	6.89 (9.850)
Week 20 (n=1487)	39.21 (11.123)
Change at Week 20 (n=1479)	7.66 (10.306)
Week 24 (n=1465)	39.52 (11.302)
Change at Week 24 (n=1457)	7.92 (10.211)

19. Secondary Outcome Measure:

Measure Title	Percentage of Participants With HAQ-DI Clinical Remission and Clinically Meaningful Improvement By Visit
Measure Description	The HAQ-DI scale ranges from 0 to 3, where higher scores represent higher disease activity. A score of <0.5 represents clinical remission. A participant achieves a clinically meaningful improvement in HAQ-DI if they had a reduction from baseline of ≥0.22.
Time Frame	Baseline, Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	1681
Percentage of Participants With HAQ-DI Clinical Remission and Clinically Meaningful Improvement By Visit [units: percentage of participants]	
Baseline, Remission (n=1673)	5.9
Week 4, Remission (n=1648)	12.6
Week 4, Clinically meaningful improvement (n=1641)	47.7
Week 8, Remission (n=1607)	19.0
Week 8, Clinically meaningful improvement (n=1600)	60.4
Week 12, Remission (n=1570)	23.9
Week 12 Clinically meaningful improvement (n=1562)	65.7
Week 16, Remission (n=1524)	26.4
Week 16 Clinically meaningful improvement (n=1517)	68.7

	Tocilizumab 8 mg/kg
Week 20, Remission (n=1483)	28.1
Week 20 Clinically meaningful improvement (n=1476)	70.6
Week 24, Remission (n=1459)	31.5
Week 24, Clinically meaningful improvement(n=1451)	72.7

20. Secondary Outcome Measure:

Measure Title	Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-Fatigue) Score by Visit
Measure Description	FACIT-Fatigue 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. 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	Baseline, Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	1681
Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-Fatigue) Score by Visit [units: units on a scale] Mean (Standard Deviation)	
Baseline (n=1674)	25.91 (11.262)
Week 4 (n=1647)	30.95 (11.133)

	Tocilizumab 8 mg/kg
Change at Week 4 (n=1640)	5.01 (8.916)
Week 8 (n=1611)	33.51 (10.865)
Change at Week 8 (n=1605)	7.50 (10.036)
Week 12 (n=1573)	34.98 (11.069)
Change at Week 12 (n=1568)	8.86 (10.463)
Week 16 (n=1529)	35.78 (10.959)
Change at Week 16 (n=1524)	9.68 (10.890)
Week 20 (n=1488)	36.45 (10.848)
Change at Week 20 (n=1483)	10.31 (10.947)
Week 24 (n=1466)	36.92 (10.823)
Change at Week 24 (n=1461)	10.76 (10.934)

Reported Adverse Events

Time Frame	AE evaluation was done from the day of screening till the end of study at Week 24.
Additional Description	[Not specified]

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg IV once every 4 weeks for 20 weeks (total of 6 infusions).

Serious Adverse Events

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Total	131/1681 (7.79%)
Blood and lymphatic system disorders	
Thrombocytopenia [A] *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Cardiac disorders	
Acute myocardial infarction A *	1/1681 (0.06%)
Arrhythmia A *	1/1681 (0.06%)
Arteriospasm coronary A *	1/1681 (0.06%)
Atrial fibrillation A *	2/1681 (0.12%)
Cardiac arrest A *	1/1681 (0.06%)
Cardiac failure A *	1/1681 (0.06%)
Coronary artery disease A *	1/1681 (0.06%)
Eye disorders	
Corneal perforation A *	1/1681 (0.06%)
Ulcerative keratitis A *	1/1681 (0.06%)
Gastrointestinal disorders	
Abdominal pain A *	1/1681 (0.06%)
Abdominal wall haematoma A *	1/1681 (0.06%)
Crohn's disease A *	1/1681 (0.06%)
Diarrhoea A *	1/1681 (0.06%)
Diverticular perforation A *	1/1681 (0.06%)
Food poisoning A *	1/1681 (0.06%)
Intestinal perforation A *	1/1681 (0.06%)
Irritable bowel syndrome A *	1/1681 (0.06%)
Nausea A *	1/1681 (0.06%)
Pancreatitis A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Pancreatitis acute A *	1/1681 (0.06%)
Rectal haemorrhage A *	1/1681 (0.06%)
Umbilical hernia, obstructive A *	1/1681 (0.06%)
Vomiting A *	1/1681 (0.06%)
General disorders	
Chest pain A *	4/1681 (0.24%)
Ill-defined disorder A *	1/1681 (0.06%)
Infusion related reaction A *	1/1681 (0.06%)
Oedema peripheral A *	1/1681 (0.06%)
Pyrexia A *	1/1681 (0.06%)
Sudden death A *	1/1681 (0.06%)
Hepatobiliary disorders	
Cholecystitis acute A *	1/1681 (0.06%)
Cholelithiasis A *	1/1681 (0.06%)
Immune system disorders	
Hypersensitivity A *	2/1681 (0.12%)
Infections and infestations	
Alveolar osteitis A *	1/1681 (0.06%)
Appendicitis A *	1/1681 (0.06%)
Arthritis bacterial A *	1/1681 (0.06%)
Bordetella infection A *	1/1681 (0.06%)
Bursitis infective A *	2/1681 (0.12%)
Cellulitis A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Erysipelas A *	5/1681 (0.3%)
Folliculitis A *	1/1681 (0.06%)
Furuncle A *	1/1681 (0.06%)
Herpes zoster ophthalmic A *	1/1681 (0.06%)
Joint tuberculosis A *	1/1681 (0.06%)
Lower respiratory tract infection A *	1/1681 (0.06%)
Meningitis viral A *	1/1681 (0.06%)
Mycobacterium avium complex infection A *	1/1681 (0.06%)
Pneumonia A *	6/1681 (0.36%)
Postoperative abscess A *	1/1681 (0.06%)
Rectal abscess A *	1/1681 (0.06%)
Respiratory tract infection A *	1/1681 (0.06%)
Scrotal abscess A *	1/1681 (0.06%)
Sepsis A *	1/1681 (0.06%)
Skin infection A *	1/1681 (0.06%)
Streptococcal infection A *	1/1681 (0.06%)
Streptococcal sepsis A *	1/1681 (0.06%)
Tonsillitis A *	1/1681 (0.06%)
Wound infection A *	1/1681 (0.06%)
Injury, poisoning and procedural complications	
Fall A *	1/1681 (0.06%)
Femoral neck fracture A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Foot fracture A *	1/1681 (0.06%)
Humerus fracture A *	1/1681 (0.06%)
Incisional hernia A *	1/1681 (0.06%)
Lower limb fracture A *	1/1681 (0.06%)
Pelvic fracture A *	1/1681 (0.06%)
Spinal fracture A *	1/1681 (0.06%)
Tendon injury A *	2/1681 (0.12%)
Tendon rupture A *	2/1681 (0.12%)
Investigations	
Blood pressure increased A *	1/1681 (0.06%)
Musculoskeletal and connective tissue disorders	
Arthralgia A *	1/1681 (0.06%)
Arthritis A *	1/1681 (0.06%)
Bursitis A *	2/1681 (0.12%)
Intervertebral disc protrusion A *	1/1681 (0.06%)
Joint effusion A *	1/1681 (0.06%)
Osteoarthritis A *	1/1681 (0.06%)
Osteonecrosis A *	1/1681 (0.06%)
Soft tissue necrosis A *	1/1681 (0.06%)
Synovitis A *	1/1681 (0.06%)
Tendonitis A *	1/1681 (0.06%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Basal cell carcinoma A *	1/1681 (0.06%)
Breast cancer A *	2/1681 (0.12%)
Colon cancer A *	1/1681 (0.06%)
Laryngeal cancer A *	1/1681 (0.06%)
Lung neoplasm malignant A *	1/1681 (0.06%)
Malignant melanoma A *	1/1681 (0.06%)
Mycosis fungoides A *	1/1681 (0.06%)
Ovarian cancer A *	1/1681 (0.06%)
Nervous system disorders	
Cerebrovascular accident A *	1/1681 (0.06%)
Headache A *	2/1681 (0.12%)
Ischaemic stroke A *	1/1681 (0.06%)
Migraine A *	1/1681 (0.06%)
Sciatica A *	3/1681 (0.18%)
Subarachnoid haemorrhage A *	1/1681 (0.06%)
Syncope A *	2/1681 (0.12%)
Psychiatric disorders	
Anxiety A *	1/1681 (0.06%)
Depression A *	5/1681 (0.3%)
Suicide attempt A *	1/1681 (0.06%)
Reproductive system and breast disorders	
Testicular cyst A *	1/1681 (0.06%)
Respiratory, thoracic and mediastinal disorders	

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Asthma A *	2/1681 (0.12%)
Dyspnoea A *	1/1681 (0.06%)
Pneumonitis A *	1/1681 (0.06%)
Respiratory failure A *	1/1681 (0.06%)
Upper respiratory tract inflammation A *	1/1681 (0.06%)
Skin and subcutaneous tissue disorders	
Angioedema A *	1/1681 (0.06%)
Cutaneous vasculitis A *	1/1681 (0.06%)
Dermatitis allergic A *	1/1681 (0.06%)
Eczema A *	1/1681 (0.06%)
Psoriasis A *	1/1681 (0.06%)
Rash A *	1/1681 (0.06%)
Urticaria A *	1/1681 (0.06%)
Surgical and medical procedures	
Hip arthroplasty A *	1/1681 (0.06%)
Vascular disorders	
Aortic dissection A *	1/1681 (0.06%)
Deep vein thrombosis A *	2/1681 (0.12%)
Hypertension A *	1/1681 (0.06%)
Peripheral ischaemia A *	1/1681 (0.06%)
Rheumatoid vasculitis A *	1/1681 (0.06%)
Thrombosis A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Venous thrombosis A *	1/1681 (0.06%)
Venous thrombosis limb A *	1/1681 (0.06%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (13.0)

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

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Total	1301/1681 (77.39%)
Blood and lymphatic system disorders	
Anaemia A *	7/1681 (0.42%)
Anisocytosis A *	24/1681 (1.43%)
Elliptocytosis A *	2/1681 (0.12%)
Eosinophilia A *	8/1681 (0.48%)
Granulocytopenia A *	2/1681 (0.12%)
Hypochromasia A *	6/1681 (0.36%)
Idiopathic thrombocytopenic purpura A *	1/1681 (0.06%)
Iron deficiency anaemia A *	1/1681 (0.06%)
Leukocytosis A *	1/1681 (0.06%)
Leukopenia A *	26/1681 (1.55%)
Lymphadenopathy A *	13/1681 (0.77%)
Lymphocytosis A *	1/1681 (0.06%)
Lymphopenia A *	4/1681 (0.24%)
Macrocytosis A *	27/1681 (1.61%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Microcytic anaemia A *	2/1681 (0.12%)
Microcytosis A *	4/1681 (0.24%)
Neutropenia A *	55/1681 (3.27%)
Neutrophilia A *	2/1681 (0.12%)
Pancytopenia A *	1/1681 (0.06%)
Poikilocytosis A *	7/1681 (0.42%)
Polychromasia A *	4/1681 (0.24%)
Red blood cell abnormality A *	1/1681 (0.06%)
Thrombocytopenia A *	9/1681 (0.54%)
Cardiac disorders	
Acute myocardial infarction A *	1/1681 (0.06%)
Angina pectoris A *	5/1681 (0.3%)
Arrhythmia A *	2/1681 (0.12%)
Arteriospasm coronary A *	1/1681 (0.06%)
Atrial fibrillation A *	2/1681 (0.12%)
Bradycardia A *	3/1681 (0.18%)
Cardiac arrest A *	1/1681 (0.06%)
Cardiac failure A *	2/1681 (0.12%)
Coronary artery disease A *	1/1681 (0.06%)
Myocardial ischaemia A *	1/1681 (0.06%)
Palpitations A *	9/1681 (0.54%)
Sinus bradycardia A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Sinus tachycardia A *	4/1681 (0.24%)
Tachycardia A *	2/1681 (0.12%)
Tachycardia paroxysmal A *	1/1681 (0.06%)
Congenital, familial and genetic disorders	
Dermoid cyst A *	1/1681 (0.06%)
Ear and labyrinth disorders	
Deafness A *	1/1681 (0.06%)
Ear pain A *	4/1681 (0.24%)
External ear inflammation A *	1/1681 (0.06%)
Hearing impaired A *	2/1681 (0.12%)
Middle ear inflammation A *	2/1681 (0.12%)
Motion sickness A *	1/1681 (0.06%)
Tinnitus A *	2/1681 (0.12%)
Vertigo A *	14/1681 (0.83%)
Endocrine disorders	
Autoimmune thyroiditis A *	1/1681 (0.06%)
Goitre A *	1/1681 (0.06%)
Hypothyroidism A *	2/1681 (0.12%)
Eye disorders	
Blindness transient A *	1/1681 (0.06%)
Cataract A *	2/1681 (0.12%)
Conjunctival haemorrhage A *	3/1681 (0.18%)
Conjunctival hyperaemia A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Conjunctivitis A *	12/1681 (0.71%)
Conjunctivitis allergic A *	2/1681 (0.12%)
Corneal perforation A *	1/1681 (0.06%)
Diplopia A *	1/1681 (0.06%)
Dry eye A *	3/1681 (0.18%)
Eczema eyelids A *	1/1681 (0.06%)
Eye allergy A *	1/1681 (0.06%)
Eye disorder A *	1/1681 (0.06%)
Eye haemorrhage A *	1/1681 (0.06%)
Eye inflammation A *	1/1681 (0.06%)
Eye irritation A *	2/1681 (0.12%)
Eye pain A *	4/1681 (0.24%)
Eye pruritus A *	1/1681 (0.06%)
Eyelid oedema A *	1/1681 (0.06%)
Foreign body sensation in eyes A *	1/1681 (0.06%)
Glaucoma A *	2/1681 (0.12%)
Iritis A *	1/1681 (0.06%)
Keratitis A *	2/1681 (0.12%)
Keratoconjunctivitis sicca A *	1/1681 (0.06%)
Lacrimation increased A *	3/1681 (0.18%)
Macular degeneration A *	1/1681 (0.06%)
Maculopathy A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Neurotrophic keratopathy A *	1/1681 (0.06%)
Ocular hyperaemia A *	2/1681 (0.12%)
Ocular icterus A *	1/1681 (0.06%)
Photopsia A *	1/1681 (0.06%)
Retinal detachment A *	1/1681 (0.06%)
Scleral discolouration A *	1/1681 (0.06%)
Ulcerative keratitis A *	2/1681 (0.12%)
Vision blurred A *	6/1681 (0.36%)
Visual acuity reduced A *	1/1681 (0.06%)
Visual impairment A *	2/1681 (0.12%)
Vitreous floaters A *	1/1681 (0.06%)
Xerophthalmia A *	2/1681 (0.12%)
Gastrointestinal disorders	
Abdominal discomfort A *	7/1681 (0.42%)
Abdominal distension A *	5/1681 (0.3%)
Abdominal hernia A *	2/1681 (0.12%)
Abdominal pain A *	26/1681 (1.55%)
Abdominal pain lower A *	4/1681 (0.24%)
Abdominal pain upper A *	32/1681 (1.9%)
Abdominal tenderness A *	2/1681 (0.12%)
Abdominal wall haematoma A *	1/1681 (0.06%)
Abnormal faeces A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Aphthous stomatitis A *	13/1681 (0.77%)
Change of bowel habit A *	1/1681 (0.06%)
Cheilitis A *	3/1681 (0.18%)
Constipation A *	20/1681 (1.19%)
Crohn's disease A *	1/1681 (0.06%)
Dental caries A *	2/1681 (0.12%)
Diarrhoea A *	69/1681 (4.1%)
Diverticular perforation A *	1/1681 (0.06%)
Dry mouth A *	4/1681 (0.24%)
Dyspepsia A *	24/1681 (1.43%)
Dysphagia A *	1/1681 (0.06%)
Epigastric discomfort A *	2/1681 (0.12%)
Faecal volume increased A *	1/1681 (0.06%)
Flatulence A *	3/1681 (0.18%)
Food poisoning A *	1/1681 (0.06%)
Frequent bowel movements A *	1/1681 (0.06%)
Gastritis A *	1/1681 (0.06%)
Gastrointestinal disorder A *	4/1681 (0.24%)
Gastrointestinal haemorrhage A *	1/1681 (0.06%)
Gastrointestinal pain A *	1/1681 (0.06%)
Gastrointestinal ulcer A *	1/1681 (0.06%)
Gastrooesophageal reflux disease A *	9/1681 (0.54%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Gingival bleeding A *	5/1681 (0.3%)
Gingival pain A *	2/1681 (0.12%)
Gingival swelling A *	1/1681 (0.06%)
Gingival ulceration A *	2/1681 (0.12%)
Gingivitis A *	1/1681 (0.06%)
Glossitis A *	1/1681 (0.06%)
Glossodynia A *	2/1681 (0.12%)
Haematochezia A *	3/1681 (0.18%)
Haemorrhoidal haemorrhage A *	1/1681 (0.06%)
Haemorrhoids A *	2/1681 (0.12%)
Hiatus hernia A *	3/1681 (0.18%)
Intestinal perforation A *	1/1681 (0.06%)
Irritable bowel syndrome A *	1/1681 (0.06%)
Lip swelling A *	2/1681 (0.12%)
Lip ulceration A *	2/1681 (0.12%)
Mouth ulceration A *	36/1681 (2.14%)
Nausea A *	79/1681 (4.7%)
Oesophageal pain A *	1/1681 (0.06%)
Oral pain A *	3/1681 (0.18%)
Palatal oedema A *	1/1681 (0.06%)
Pancreatitis A *	1/1681 (0.06%)
Pancreatitis acute A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Paraesthesia oral A *	2/1681 (0.12%)
Periodontal disease A *	1/1681 (0.06%)
Proctitis A *	1/1681 (0.06%)
Rectal haemorrhage A *	6/1681 (0.36%)
Rectal ulcer A *	1/1681 (0.06%)
Retching A *	1/1681 (0.06%)
Salivary duct obstruction A *	1/1681 (0.06%)
Salivary gland calculus A *	1/1681 (0.06%)
Sensitivity of teeth A *	1/1681 (0.06%)
Stomatitis A *	5/1681 (0.3%)
Tongue ulceration A *	1/1681 (0.06%)
Toothache A *	4/1681 (0.24%)
Umbilica hernia, obstructive A *	1/1681 (0.06%)
Vomiting A *	24/1681 (1.43%)
General disorders	
Adverse drug reaction A *	2/1681 (0.12%)
Asthenia A *	17/1681 (1.01%)
Catheter site pruritus A *	1/1681 (0.06%)
Chest discomfort A *	7/1681 (0.42%)
Chest pain A *	17/1681 (1.01%)
Chills A *	5/1681 (0.3%)
Cyst A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Cyst rupture A *	1/1681 (0.06%)
Device failure A *	1/1681 (0.06%)
Discomfort A *	4/1681 (0.24%)
Fatigue A *	32/1681 (1.9%)
Feeling cold A *	5/1681 (0.3%)
Feeling hot A *	2/1681 (0.12%)
Feeling jittery A *	1/1681 (0.06%)
Feeling of body temperature change A *	1/1681 (0.06%)
Gait disturbance A *	1/1681 (0.06%)
Generalised oedema A *	1/1681 (0.06%)
Ill-defined disorder A *	1/1681 (0.06%)
Impaired healing A *	3/1681 (0.18%)
Inflammation A *	2/1681 (0.12%)
Influenza like illness A *	7/1681 (0.42%)
Infusion related reaction A *	7/1681 (0.42%)
Infusion site swelling A *	1/1681 (0.06%)
Local swelling A *	2/1681 (0.12%)
Malaise A *	12/1681 (0.71%)
Nodule A *	1/1681 (0.06%)
Non-cardiac chest pain A *	1/1681 (0.06%)
Oedema A *	8/1681 (0.48%)
Oedema peripheral A *	30/1681 (1.78%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Pain A *	14/1681 (0.83%)
Pyrexia A *	14/1681 (0.83%)
Secretion discharge A *	1/1681 (0.06%)
Sensation of pressure A *	1/1681 (0.06%)
Sudden death A *	1/1681 (0.06%)
Swelling A *	1/1681 (0.06%)
Tenderness A *	1/1681 (0.06%)
Thirst decreased A *	1/1681 (0.06%)
Ulcer A *	1/1681 (0.06%)
Unevaluable event A *	2/1681 (0.12%)
Vaccination site pain A *	1/1681 (0.06%)
Vaccination site rash A *	1/1681 (0.06%)
Xerosis A *	2/1681 (0.12%)
Hepatobiliary disorders	
Biliary colic A *	1/1681 (0.06%)
Cholecystitis acute A *	1/1681 (0.06%)
Cholecystitis chronic A *	1/1681 (0.06%)
Cholelithiasis A *	3/1681 (0.18%)
Cytolytic hepatitis A *	3/1681 (0.18%)
Hepatic function abnormal A *	3/1681 (0.18%)
Hepatic steatosis A *	1/1681 (0.06%)
Hepatitis toxic A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Hepatomegaly A *	1/1681 (0.06%)
Hepatotoxicity A *	1/1681 (0.06%)
Hyperbilirubinaemia A *	2/1681 (0.12%)
Hypertransaminasaemia A *	8/1681 (0.48%)
Jaundice A *	1/1681 (0.06%)
Liver disorder A *	2/1681 (0.12%)
Immune system disorders	
Allergy to chemicals A *	1/1681 (0.06%)
Behcet's syndrome A *	1/1681 (0.06%)
Drug hypersensitivity A *	3/1681 (0.18%)
Food allergy A *	1/1681 (0.06%)
Hypersensitivity A *	8/1681 (0.48%)
Seasonal allergy A *	7/1681 (0.42%)
Infections and infestations	
Abscess A *	1/1681 (0.06%)
Abscess limb A *	1/1681 (0.06%)
Abscess neck A *	1/1681 (0.06%)
Abscess oral A *	1/1681 (0.06%)
Acute tonsillitis A *	2/1681 (0.12%)
Alveolar osteitis A *	1/1681 (0.06%)
Appendicitis A *	1/1681 (0.06%)
Arthritis bacterial A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Arthritis infective A *	1/1681 (0.06%)
Asymptomatic bacteriuria A *	1/1681 (0.06%)
Blister infected A *	1/1681 (0.06%)
Bordetella infection A *	1/1681 (0.06%)
Bronchiectasis A *	1/1681 (0.06%)
Bronchitis A *	38/1681 (2.26%)
Bursitis infective A *	2/1681 (0.12%)
Candidiasis A *	4/1681 (0.24%)
Cellulitis A *	4/1681 (0.24%)
Cellulitis orbital A *	1/1681 (0.06%)
Cervicitis A *	1/1681 (0.06%)
Chronic sinusitis A *	3/1681 (0.18%)
Corneal infection A *	2/1681 (0.12%)
Cystitis A *	6/1681 (0.36%)
Dermatitis infected A *	1/1681 (0.06%)
Diverticulitis A *	2/1681 (0.12%)
Ear infection A *	10/1681 (0.59%)
Erysipelas A *	9/1681 (0.54%)
Erythema migrans A *	1/1681 (0.06%)
Eye infection A *	5/1681 (0.3%)
Folliculitis A *	11/1681 (0.65%)
Fungal infection A *	3/1681 (0.18%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Fungal skin infection A *	2/1681 (0.12%)
Furuncle A *	6/1681 (0.36%)
Gastric infection A *	1/1681 (0.06%)
Gastroenteritis A *	19/1681 (1.13%)
Gastroenteritis norovirus A *	1/1681 (0.06%)
Gastrointestinal infection A *	1/1681 (0.06%)
Genital infection female A *	1/1681 (0.06%)
Genitourinary tract infection A *	1/1681 (0.06%)
Helicobacter infection A *	1/1681 (0.06%)
Herpes simplex A *	8/1681 (0.48%)
Herpes virus infection A *	2/1681 (0.12%)
Herpes zoster A *	11/1681 (0.65%)
Herpes zoster ophthalmic A *	1/1681 (0.06%)
Hordeolum A *	3/1681 (0.18%)
Infected bites A *	2/1681 (0.12%)
Infected cyst A *	1/1681 (0.06%)
Infection A *	1/1681 (0.06%)
Influenza A *	18/1681 (1.07%)
Joint tuberculosis A *	1/1681 (0.06%)
Keratitis herpetic A *	1/1681 (0.06%)
Kidney infection A *	1/1681 (0.06%)
Labyrinthitis A *	2/1681 (0.12%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Laryngitis A *	6/1681 (0.36%)
Laryngitis viral A *	1/1681 (0.06%)
Localised infection A *	6/1681 (0.36%)
Lower respiratory tract infection A *	41/1681 (2.44%)
Lower respiratory tract infection viral A *	1/1681 (0.06%)
Lung infection A *	1/1681 (0.06%)
Lymphangitis A *	2/1681 (0.12%)
Meningitis viral A *	1/1681 (0.06%)
Mycobacterium avium complex infection A *	1/1681 (0.06%)
Nail bed infection A *	1/1681 (0.06%)
Nail bed infection fungal A *	1/1681 (0.06%)
Nail infection A *	4/1681 (0.24%)
Nasopharyngitis A *	116/1681 (6.9%)
Onychomycosis A *	7/1681 (0.42%)
Oral candidiasis A *	4/1681 (0.24%)
Oral fungal infection A *	2/1681 (0.12%)
Oral herpes A *	36/1681 (2.14%)
Osteomyelitis A *	1/1681 (0.06%)
Otitis externa A *	2/1681 (0.12%)
Otitis media A *	3/1681 (0.18%)
Paronychia A *	6/1681 (0.36%)
Parotitis A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Periodontal infection A *	1/1681 (0.06%)
Pharyngitis A *	14/1681 (0.83%)
Pharyngotonsillitis A *	1/1681 (0.06%)
Pneumococcal infection A *	1/1681 (0.06%)
Pneumonia A *	12/1681 (0.71%)
Post procedural infection A *	1/1681 (0.06%)
Postoperative abscess A *	1/1681 (0.06%)
Postoperative wound infection A *	3/1681 (0.18%)
Rash pustular A *	5/1681 (0.3%)
Rectal abscess A *	1/1681 (0.06%)
Respiratory tract infection A *	16/1681 (0.95%)
Respiratory tract infection viral A *	1/1681 (0.06%)
Rhinitis A *	19/1681 (1.13%)
Rubella A *	1/1681 (0.06%)
Scrotal abscess A *	1/1681 (0.06%)
Sepsis A *	2/1681 (0.12%)
Sinusitis A *	25/1681 (1.49%)
Skin infection A *	4/1681 (0.24%)
Staphylococcal infection A *	2/1681 (0.12%)
Streptococcal infection A *	1/1681 (0.06%)
Streptococcal sepsis A *	1/1681 (0.06%)
Subcutaneous abscess A *	3/1681 (0.18%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Tinea infection A *	1/1681 (0.06%)
Tinea pedis A *	5/1681 (0.3%)
Tinea versicolour A *	1/1681 (0.06%)
Tonsillitis A *	8/1681 (0.48%)
Tooth abscess A *	12/1681 (0.71%)
Tooth infection A *	7/1681 (0.42%)
Tracheitis A *	2/1681 (0.12%)
Tracheobronchitis A *	2/1681 (0.12%)
Upper respiratory tract infection A *	71/1681 (4.22%)
Urinary tract infection A *	46/1681 (2.74%)
Vaginal infection A *	6/1681 (0.36%)
Viral infection A *	5/1681 (0.3%)
Viral pharyngitis A *	2/1681 (0.12%)
Viral rash A *	1/1681 (0.06%)
Viral respiratory tract infection A *	13/1681 (0.77%)
Vulvovaginal candidiasis A *	5/1681 (0.3%)
Vulvovaginal mycotic infection A *	3/1681 (0.18%)
Wound infection A *	6/1681 (0.36%)
Injury, poisoning and procedural complications	
Anaemia postoperative A *	1/1681 (0.06%)
Animal bite A *	1/1681 (0.06%)
Arthropod bite A *	10/1681 (0.59%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Arthropod sting A *	1/1681 (0.06%)
Avulsion fracture A *	1/1681 (0.06%)
Chest injury A *	1/1681 (0.06%)
Contusion A *	19/1681 (1.13%)
Corneal abrasion A *	1/1681 (0.06%)
Dermatitis artefacta A *	1/1681 (0.06%)
Excoriation A *	2/1681 (0.12%)
Fall A *	18/1681 (1.07%)
Femoral neck fracture A *	1/1681 (0.06%)
Femur fracture A *	1/1681 (0.06%)
Foot fracture A *	5/1681 (0.3%)
Head injury A *	1/1681 (0.06%)
Humerus fracture A *	1/1681 (0.06%)
Incisional hernia A *	1/1681 (0.06%)
Incorrect dose administered A *	1/1681 (0.06%)
Joint dislocation A *	4/1681 (0.24%)
Joint sprain A *	4/1681 (0.24%)
Laceration A *	1/1681 (0.06%)
Limb injury A *	3/1681 (0.18%)
Lower limb fracture A *	2/1681 (0.12%)
Muscle injury A *	1/1681 (0.06%)
Muscle rupture A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Muscle strain A *	2/1681 (0.12%)
Nail injury A *	1/1681 (0.06%)
Patella fracture A *	1/1681 (0.06%)
Pelvic fracture A *	1/1681 (0.06%)
Post-traumatic pain A *	2/1681 (0.12%)
Procedural complication A *	1/1681 (0.06%)
Procedural headache A *	1/1681 (0.06%)
Procedural nausea A *	1/1681 (0.06%)
Pubis fracture A *	1/1681 (0.06%)
Radius fracture A *	1/1681 (0.06%)
Rib fracture A *	2/1681 (0.12%)
Road traffic accident A *	1/1681 (0.06%)
Skin injury A *	2/1681 (0.12%)
Skin laceration A *	6/1681 (0.36%)
Spinal fracture A *	1/1681 (0.06%)
Stress fracture A *	1/1681 (0.06%)
Subcutaneous haematoma A *	1/1681 (0.06%)
Sunburn A *	1/1681 (0.06%)
Synovial rupture A *	1/1681 (0.06%)
Tendon injury A *	2/1681 (0.12%)
Tendon rupture A *	5/1681 (0.3%)
Thermal burn A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Tooth avulsion A *	1/1681 (0.06%)
Tooth fracture A *	1/1681 (0.06%)
Traumatic ulcer A *	1/1681 (0.06%)
Vaccination complication A *	1/1681 (0.06%)
Whiplash injury A *	1/1681 (0.06%)
Wound A *	17/1681 (1.01%)
Investigations	
Alanine aminotransferase A *	3/1681 (0.18%)
Alanine aminotransferase abnormal A *	2/1681 (0.12%)
Alanine aminotransferase increased A *	58/1681 (3.45%)
Aspartate aminotransferase A *	1/1681 (0.06%)
Aspartate aminotransferase increased A *	24/1681 (1.43%)
Aspiration joint A *	3/1681 (0.18%)
Bacterial test positive A *	1/1681 (0.06%)
Blast cells present A *	1/1681 (0.06%)
Blood alkaline phosphatase decreased A *	2/1681 (0.12%)
Blood alkaline phosphatase increased A *	2/1681 (0.12%)
Blood bilirubin increased A *	6/1681 (0.36%)
Blood calcium decreased A *	1/1681 (0.06%)
Blood calcium increased A *	2/1681 (0.12%)
Blood cholesterol A *	2/1681 (0.12%)
Blood cholesterol abnormal A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Blood cholesterol increased A *	105/1681 (6.25%)
Blood creatine increased A *	1/1681 (0.06%)
Blood creatinine increased A *	3/1681 (0.18%)
Blood glucose A *	1/1681 (0.06%)
Blood glucose decreased A *	1/1681 (0.06%)
Blood glucose increased A *	7/1681 (0.42%)
Blood lactate dehydrogenase increased A *	1/1681 (0.06%)
Blood phosphorus decreased A *	1/1681 (0.06%)
Blood potassium decreased A *	1/1681 (0.06%)
Blood pressure decreased A *	2/1681 (0.12%)
Blood pressure increased A *	7/1681 (0.42%)
Blood sodium increased A *	1/1681 (0.06%)
Blood temperature increased A *	3/1681 (0.18%)
Blood triglycerides A *	1/1681 (0.06%)
Blood triglycerides increased A *	10/1681 (0.59%)
Blood urea increased A *	4/1681 (0.24%)
Blood uric acid A *	1/1681 (0.06%)
Blood uric acid increased A *	2/1681 (0.12%)
C-reactive protein increased A *	17/1681 (1.01%)
Cardiac murmur A *	4/1681 (0.24%)
Carotid bruit A *	1/1681 (0.06%)
Cryoglobulins present A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Endoscopy upper gastrointestinal tract A *	1/1681 (0.06%)
Eosinophil count increased A *	6/1681 (0.36%)
Haematocrit increased A *	1/1681 (0.06%)
Haemoglobin A *	1/1681 (0.06%)
Haemoglobin decreased A *	6/1681 (0.36%)
Haemoglobin increased A *	1/1681 (0.06%)
Heart rate decreased A *	1/1681 (0.06%)
Heart sounds abnormal A *	1/1681 (0.06%)
Helicobacter test positive A *	2/1681 (0.12%)
Hepatic enzyme abnormal A *	1/1681 (0.06%)
Hepatic enzyme increased A *	9/1681 (0.54%)
High density lipoprotein decreased A *	3/1681 (0.18%)
High density lipoprotein increased A *	5/1681 (0.3%)
Intraocular pressure increased A *	1/1681 (0.06%)
Laboratory test abnormal A *	1/1681 (0.06%)
Lipid increased A *	9/1681 (0.54%)
Liver function test abnormal A *	1/1681 (0.06%)
Low density lipoprotein A *	2/1681 (0.12%)
Low density lipoprotein increased A *	51/1681 (3.03%)
Lymph node palpable A *	1/1681 (0.06%)
Lymphocyte count decreased A *	2/1681 (0.12%)
Lymphocyte count increased A *	3/1681 (0.18%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Lymphocyte morphology abnormal A *	1/1681 (0.06%)
Mammogram A *	1/1681 (0.06%)
Microbiology test abnormal A *	1/1681 (0.06%)
Monocyte count decreased A *	2/1681 (0.12%)
Monocyte count increased A *	2/1681 (0.12%)
Myelocyte count increased A *	2/1681 (0.12%)
Myelocyte present A *	1/1681 (0.06%)
Neutrophil count A *	1/1681 (0.06%)
Neutrophil count decreased A *	39/1681 (2.32%)
Neutrophil count increased A *	4/1681 (0.24%)
Neutrophil toxic granulation present A *	1/1681 (0.06%)
Nitrite urine A *	1/1681 (0.06%)
Nuclear magnetic resonance imaging A *	1/1681 (0.06%)
Platelet count decreased A *	8/1681 (0.48%)
Platelet morphology abnormal A *	8/1681 (0.48%)
Red blood cell burr cells present A *	12/1681 (0.71%)
Red blood cell morphology abnormal A *	3/1681 (0.18%)
Red blood cell sedimentation rate increased A *	4/1681 (0.24%)
Smear site unspecified abnormal A *	1/1681 (0.06%)
Transaminases increased A *	27/1681 (1.61%)
Ultrasound scan abnormal A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Weight decreased A *	3/1681 (0.18%)
Weight increased A *	23/1681 (1.37%)
White blood cell count A *	1/1681 (0.06%)
White blood cell count decreased A *	21/1681 (1.25%)
White blood cell count increased A *	2/1681 (0.12%)
White blood cells urine positive A *	1/1681 (0.06%)
Metabolism and nutrition disorders	
Cell death A *	1/1681 (0.06%)
Decreased appetite A *	5/1681 (0.3%)
Dehydration A *	1/1681 (0.06%)
Diabetes mellitus A *	1/1681 (0.06%)
Diabetes mellitus inadequate control A *	1/1681 (0.06%)
Dyslipidaemia A *	46/1681 (2.74%)
Fluid retention A *	1/1681 (0.06%)
Gout A *	1/1681 (0.06%)
Hypercalcaemia A *	1/1681 (0.06%)
Hypercholesterolaemia A *	101/1681 (6.01%)
Hyperglycaemia A *	2/1681 (0.12%)
Hyperlipidaemia A *	29/1681 (1.73%)
Hypernatraemia A *	1/1681 (0.06%)
Hypertriglyceridaemia A *	3/1681 (0.18%)
Hyperuricaemia A *	2/1681 (0.12%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Hypoglycaemia A *	1/1681 (0.06%)
Hypokalaemia A *	3/1681 (0.18%)
Hyponatraemia A *	1/1681 (0.06%)
Increased appetite A *	2/1681 (0.12%)
Iron deficiency A *	1/1681 (0.06%)
Type 2 diabetes mellitus A *	1/1681 (0.06%)
Vitamin D deficiency A *	1/1681 (0.06%)
Musculoskeletal and connective tissue disorders	
Arthralgia A *	44/1681 (2.62%)
Arthritis A *	7/1681 (0.42%)
Arthropathy A *	1/1681 (0.06%)
Back pain A *	51/1681 (3.03%)
Bone pain A *	7/1681 (0.42%)
Bunion A *	3/1681 (0.18%)
Bursitis A *	8/1681 (0.48%)
Dupuytren's contracture A *	1/1681 (0.06%)
Elbow deformity A *	1/1681 (0.06%)
Fibromyalgia A *	3/1681 (0.18%)
Flank pain A *	1/1681 (0.06%)
Foot deformity A *	4/1681 (0.24%)
Groin pain A *	3/1681 (0.18%)
Hand deformity A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Intervertebral disc degeneration A *	1/1681 (0.06%)
Intervertebral disc disorder A *	1/1681 (0.06%)
Intervertebral disc protrusion A *	3/1681 (0.18%)
Joint effusion A *	5/1681 (0.3%)
Joint lock A *	1/1681 (0.06%)
Joint stiffness A *	1/1681 (0.06%)
Joint swelling A *	14/1681 (0.83%)
Knee deformity A *	2/1681 (0.12%)
Ligamentitis A *	1/1681 (0.06%)
Monarthritis A *	2/1681 (0.12%)
Muscle contracture A *	3/1681 (0.18%)
Muscle spasms A *	14/1681 (0.83%)
Muscle twitching A *	1/1681 (0.06%)
Muscle weakness A *	1/1681 (0.06%)
Musculoskeletal chest pain A *	4/1681 (0.24%)
Musculoskeletal disorder A *	1/1681 (0.06%)
Musculoskeletal pain A *	15/1681 (0.89%)
Musculoskeletal stiffness A *	4/1681 (0.24%)
Myalgia A *	13/1681 (0.77%)
Neck pain A *	14/1681 (0.83%)
Nodule on extremity A *	2/1681 (0.12%)
Osteitis A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Osteoarthritis A *	10/1681 (0.59%)
Osteonecrosis A *	2/1681 (0.12%)
Osteopenia A *	1/1681 (0.06%)
Osteoporosis A *	7/1681 (0.42%)
Pain in extremity A *	20/1681 (1.19%)
Pain in jaw A *	6/1681 (0.36%)
Plantar fasciitis A *	2/1681 (0.12%)
Rheumatoid arthritis A *	56/1681 (3.33%)
Rheumatoid nodule A *	4/1681 (0.24%)
Rotator cuff syndrome A *	1/1681 (0.06%)
Sjogren's syndrome A *	1/1681 (0.06%)
Soft tissue necrosis A *	1/1681 (0.06%)
Spinal osteoarthritis A *	2/1681 (0.12%)
Spondylolisthesis A *	1/1681 (0.06%)
Synovial cyst A *	5/1681 (0.3%)
Synovitis A *	8/1681 (0.48%)
Tendon disorder A *	1/1681 (0.06%)
Tendonitis A *	10/1681 (0.59%)
Tenosynovitis A *	1/1681 (0.06%)
Tenosynovitis stenosans A *	3/1681 (0.18%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Basal cell carcinoma A *	3/1681 (0.18%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Breast cancer A *	2/1681 (0.12%)
Colon cancer A *	1/1681 (0.06%)
Laryngeal cancer A *	1/1681 (0.06%)
Lipoma A *	1/1681 (0.06%)
Lipoma of breast A *	1/1681 (0.06%)
Lung neoplasm malignant A *	1/1681 (0.06%)
Malignant melanoma A *	1/1681 (0.06%)
Melanocytic naevus A *	1/1681 (0.06%)
Mycosis fungoides A *	1/1681 (0.06%)
Ovarian cancer A *	1/1681 (0.06%)
Parathyroid tumour A *	1/1681 (0.06%)
Renal neoplasm A *	1/1681 (0.06%)
Skin cancer A *	1/1681 (0.06%)
Skin papilloma A *	2/1681 (0.12%)
Uterine leiomyoma A *	2/1681 (0.12%)
Nervous system disorders	
Ageusia A *	1/1681 (0.06%)
Anosmia A *	1/1681 (0.06%)
Aphonia A *	1/1681 (0.06%)
Balance disorder A *	1/1681 (0.06%)
Burning sensation A *	1/1681 (0.06%)
Carotid arteriosclerosis A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Carpal tunnel syndrome A *	5/1681 (0.3%)
Cerebrovascular accident A *	1/1681 (0.06%)
Cervicobrachial syndrome A *	1/1681 (0.06%)
Crying A *	1/1681 (0.06%)
Diabetic neuropathy A *	1/1681 (0.06%)
Dizziness A *	38/1681 (2.26%)
Dizziness postural A *	1/1681 (0.06%)
Dysaesthesia A *	2/1681 (0.12%)
Dysarthria A *	1/1681 (0.06%)
Dysgeusia A *	5/1681 (0.3%)
Essential tremor A *	1/1681 (0.06%)
Formication A *	1/1681 (0.06%)
Headache A *	94/1681 (5.59%)
Hyperaesthesia A *	3/1681 (0.18%)
Hypersomnia A *	1/1681 (0.06%)
Hypoaesthesia A *	7/1681 (0.42%)
Hyporeflexia A *	1/1681 (0.06%)
Intercostal neuralgia A *	1/1681 (0.06%)
Ischaemic stroke A *	1/1681 (0.06%)
Lacunar infarction A *	1/1681 (0.06%)
Lethargy A *	3/1681 (0.18%)
Memory impairment A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Migraine A *	10/1681 (0.59%)
Migraine with aura A *	1/1681 (0.06%)
Muscle contractions involuntary A *	1/1681 (0.06%)
Nerve root lesion A *	1/1681 (0.06%)
Neuralgia A *	1/1681 (0.06%)
Paraesthesia A *	18/1681 (1.07%)
Presyncope A *	3/1681 (0.18%)
Restless legs syndrome A *	2/1681 (0.12%)
Sciatica A *	10/1681 (0.59%)
Sinus headache A *	1/1681 (0.06%)
Somnolence A *	1/1681 (0.06%)
Subarachnoid haemorrhage A *	1/1681 (0.06%)
Syncope A *	4/1681 (0.24%)
Tremor A *	1/1681 (0.06%)
Trigeminal neuralgia A *	1/1681 (0.06%)
Visual field defect A *	1/1681 (0.06%)
Psychiatric disorders	
Aggression A *	1/1681 (0.06%)
Agitation A *	1/1681 (0.06%)
Anticipatory anxiety A *	1/1681 (0.06%)
Anxiety A *	11/1681 (0.65%)
Depressed mood A *	3/1681 (0.18%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Depression A *	14/1681 (0.83%)
Flat affect A *	1/1681 (0.06%)
Insomnia A *	10/1681 (0.59%)
Libido decreased A *	1/1681 (0.06%)
Mood swings A *	1/1681 (0.06%)
Nervousness A *	1/1681 (0.06%)
Nightmare A *	1/1681 (0.06%)
Panic disorder A *	1/1681 (0.06%)
Sleep disorder A *	5/1681 (0.3%)
Stress A *	2/1681 (0.12%)
Suicide attempt A *	1/1681 (0.06%)
Renal and urinary disorders	
Bladder cyst A *	1/1681 (0.06%)
Cystitis noninfective A *	1/1681 (0.06%)
Dysuria A *	3/1681 (0.18%)
Haematuria A *	2/1681 (0.12%)
Hypertonic bladder A *	1/1681 (0.06%)
Nephrolithiasis A *	1/1681 (0.06%)
Pollakiuria A *	2/1681 (0.12%)
Renal colic A *	1/1681 (0.06%)
Renal disorder A *	1/1681 (0.06%)
Stress urinary incontinence A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Urinary incontinence A *	3/1681 (0.18%)
Reproductive system and breast disorders	
Bartholinitis A *	1/1681 (0.06%)
Breast pain A *	1/1681 (0.06%)
Cervical polyp A *	1/1681 (0.06%)
Cystocele A *	1/1681 (0.06%)
Erectile dysfunction A *	2/1681 (0.12%)
Erosive balanitis A *	1/1681 (0.06%)
Galactorrhoea A *	1/1681 (0.06%)
Genital discharge A *	1/1681 (0.06%)
Menorrhagia A *	2/1681 (0.12%)
Metrorrhagia A *	3/1681 (0.18%)
Polymenorrhoea A *	2/1681 (0.12%)
Pruritus genital A *	1/1681 (0.06%)
Testicular cyst A *	1/1681 (0.06%)
Vaginal haemorrhage A *	3/1681 (0.18%)
Vaginal inflammation A *	1/1681 (0.06%)
Vulvovaginal pruritus A *	1/1681 (0.06%)
Respiratory, thoracic and mediastinal disorders	
Asthma A *	10/1681 (0.59%)
Chronic obstructive pulmonary disease A *	2/1681 (0.12%)
Cough A *	54/1681 (3.21%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Dry throat A *	1/1681 (0.06%)
Dysphonia A *	1/1681 (0.06%)
Dyspnoea A *	8/1681 (0.48%)
Dyspnoea exertional A *	1/1681 (0.06%)
Epistaxis A *	7/1681 (0.42%)
Haemoptysis A *	3/1681 (0.18%)
Hypoventilation A *	1/1681 (0.06%)
Increased viscosity of bronchial secretion A *	1/1681 (0.06%)
Lung disorder A *	1/1681 (0.06%)
Nasal congestion A *	4/1681 (0.24%)
Nasal disorder A *	1/1681 (0.06%)
Nocturnal dyspnoea A *	1/1681 (0.06%)
Oropharyngeal blistering A *	4/1681 (0.24%)
Oropharyngeal pain A *	48/1681 (2.86%)
Pharyngeal erythema A *	2/1681 (0.12%)
Pharyngeal inflammation A *	2/1681 (0.12%)
Pharyngeal oedema A *	1/1681 (0.06%)
Pharyngeal ulceration A *	2/1681 (0.12%)
Pneumonitis A *	1/1681 (0.06%)
Postnasal drip A *	1/1681 (0.06%)
Productive cough A *	5/1681 (0.3%)
Rales A *	2/1681 (0.12%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Respiratory disorder A *	1/1681 (0.06%)
Respiratory failure A *	1/1681 (0.06%)
Respiratory tract congestion A *	1/1681 (0.06%)
Respiratory tract irritation A *	1/1681 (0.06%)
Rhinalgia A *	1/1681 (0.06%)
Rhinitis allergic A *	3/1681 (0.18%)
Rhinorrhoea A *	6/1681 (0.36%)
Sinus congestion A *	1/1681 (0.06%)
Throat irritation A *	1/1681 (0.06%)
Throat tightness A *	1/1681 (0.06%)
Upper airway obstruction A *	1/1681 (0.06%)
Upper respiratory tract inflammation A *	1/1681 (0.06%)
Wheezing A *	5/1681 (0.3%)
Skin and subcutaneous tissue disorders	
Acne A *	8/1681 (0.48%)
Alopecia A *	23/1681 (1.37%)
Angioedema A *	1/1681 (0.06%)
Blister A *	8/1681 (0.48%)
Butterfly rash A *	1/1681 (0.06%)
Cutaneous lupus erythematosus A *	1/1681 (0.06%)
Cutaneous vasculitis A *	1/1681 (0.06%)
Decubitus ulcer A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Dermatitis A *	6/1681 (0.36%)
Dermatitis acneiform A *	1/1681 (0.06%)
Dermatitis allergic A *	3/1681 (0.18%)
Dermatitis atopic A *	2/1681 (0.12%)
Dermatitis contact A *	2/1681 (0.12%)
Dermatosis A *	1/1681 (0.06%)
Drug eruption A *	3/1681 (0.18%)
Dry skin A *	5/1681 (0.3%)
Dyshidrosis A *	2/1681 (0.12%)
Ecchymosis A *	5/1681 (0.3%)
Eczema A *	26/1681 (1.55%)
Ephelides A *	1/1681 (0.06%)
Erythema A *	11/1681 (0.65%)
Erythema nodosum A *	1/1681 (0.06%)
Exfoliative rash A *	1/1681 (0.06%)
Heat rash A *	2/1681 (0.12%)
Hyperhidrosis A *	8/1681 (0.48%)
Hypoaesthesia facial A *	1/1681 (0.06%)
Increased tendency to bruise A *	1/1681 (0.06%)
Ingrowing nail A *	2/1681 (0.12%)
Intertrigo A *	1/1681 (0.06%)
Lividity A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Night sweats A *	2/1681 (0.12%)
Onychoclasis A *	2/1681 (0.12%)
Onycholysis A *	1/1681 (0.06%)
Petechiae A *	1/1681 (0.06%)
Photodermatosis A *	1/1681 (0.06%)
Photosensitivity reaction A *	3/1681 (0.18%)
Prurigo A *	2/1681 (0.12%)
Pruritus A *	40/1681 (2.38%)
Pruritus generalised A *	3/1681 (0.18%)
Psoriasis A *	7/1681 (0.42%)
Purpura A *	3/1681 (0.18%)
Rash A *	66/1681 (3.93%)
Rash erythematous A *	6/1681 (0.36%)
Rash macular A *	10/1681 (0.59%)
Rash maculo-papular A *	7/1681 (0.42%)
Rash papular A *	8/1681 (0.48%)
Rash pruritic A *	9/1681 (0.54%)
Scab A *	3/1681 (0.18%)
Seborrhoeic dermatitis A *	1/1681 (0.06%)
Skin burning sensation A *	1/1681 (0.06%)
Skin chapped A *	1/1681 (0.06%)
Skin discolouration A *	2/1681 (0.12%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Skin disorder A *	1/1681 (0.06%)
Skin erosion A *	1/1681 (0.06%)
Skin exfoliation A *	3/1681 (0.18%)
Skin fissures A *	4/1681 (0.24%)
Skin hyperpigmentation A *	1/1681 (0.06%)
Skin irritation A *	2/1681 (0.12%)
Skin lesion A *	11/1681 (0.65%)
Skin reaction A *	3/1681 (0.18%)
Skin ulcer A *	8/1681 (0.48%)
Swelling face A *	3/1681 (0.18%)
Systemic lupus erythematosus rash A *	1/1681 (0.06%)
Toxic skin eruption A *	1/1681 (0.06%)
Umbilical erythema A *	1/1681 (0.06%)
Urticaria A *	19/1681 (1.13%)
Social circumstances	
Menopause A *	2/1681 (0.12%)
Tattoo A *	1/1681 (0.06%)
Surgical and medical procedures	
Bariatric gastric balloon insertion A *	1/1681 (0.06%)
Cataract operation A *	4/1681 (0.24%)
Hip arthroplasty A *	2/1681 (0.12%)
Joint arthroplasty A *	1/1681 (0.06%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Joint injection A *	2/1681 (0.12%)
Laryngeal operation A *	1/1681 (0.06%)
Limb operation A *	1/1681 (0.06%)
Lymphadenectomy A *	1/1681 (0.06%)
Mole excision A *	1/1681 (0.06%)
Nail operation A *	1/1681 (0.06%)
Rectal polypectomy A *	1/1681 (0.06%)
Skin neoplasm excision A *	1/1681 (0.06%)
Spinal laminectomy A *	1/1681 (0.06%)
Synovectomy A *	1/1681 (0.06%)
Tooth extraction A *	7/1681 (0.42%)
Uterine dilation and curettage A *	1/1681 (0.06%)
Wisdom teeth removal A *	1/1681 (0.06%)
Wrist surgery A *	1/1681 (0.06%)
Vascular disorders	
Aortic dissection A *	1/1681 (0.06%)
Deep vein thrombosis A *	3/1681 (0.18%)
Flushing A *	9/1681 (0.54%)
Haematoma A *	11/1681 (0.65%)
Haemorrhage A *	1/1681 (0.06%)
Hot flush A *	8/1681 (0.48%)
Hypertension A *	41/1681 (2.44%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Hypertensive crisis A *	1/1681 (0.06%)
Hypotension A *	12/1681 (0.71%)
Lymphoedema A *	1/1681 (0.06%)
Pallor A *	2/1681 (0.12%)
Peripheral coldness A *	1/1681 (0.06%)
Peripheral ischaemia A *	1/1681 (0.06%)
Phlebitis A *	4/1681 (0.24%)
Poor venous access A *	1/1681 (0.06%)
Raynaud's phenomenon A *	2/1681 (0.12%)
Rheumatoid vasculitis A *	1/1681 (0.06%)
Spider vein A *	1/1681 (0.06%)
Thrombophlebitis superficial A *	2/1681 (0.12%)
Thrombosis A *	1/1681 (0.06%)
Varicose vein A *	3/1681 (0.18%)
Vasculitis A *	2/1681 (0.12%)
Venous insufficiency A *	1/1681 (0.06%)
Venous thrombosis A *	1/1681 (0.06%)
Venous thrombosis limb A *	2/1681 (0.12%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (13.0)

Limitations and Caveats

Nonserious AEs presented in this record include all AEs 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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