ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 08/04/2014

An Extension to Study MA21573, Evaluating Tocilizumab in Patients With Active Rheumatoid Arthritis and an Inadequate Response to Current Non-Biological DMARDs and/or Anti-tumor Necrosis Factor (TNF) Therapy

This study has been completed.

Sponsor:	Hoffmann-La Roche
Collaborators:	
Information provided by (Responsible Party):	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT00883753

Purpose

This study was an extension to study MA21573 [NCT00750880], which was an open label single arm study to investigate the safety, tolerability and efficacy of tocilizumab monotherapy, or combination therapy with non-biological disease-modifying antirheumatic drugs (DMARDS), in patients with moderate to severe active rheumatoid arthritis. Patients who completed the 24 week core study, and had at least a moderate European League Against Rheumatism (EULAR) response, were eligible to enter this long-term extension study, and received tocilizumab 8 mg/kg intravenous (iv) every 4 weeks. The anticipated time on study treatment was 1-2 years, and the target sample size was > 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: An Extension Phase of the Multi-National Open-Label Study (MA21573) 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 and/or Anti-TNF Therapy.

Further study details as provided by Hoffmann-La Roche:

Primary Outcome Measure:

- Percentage of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs) [Time Frame: 108 Weeks] [Designated as safety issue: No]
  An AE was considered any unfavorable and unintended sign, symptom, or disease associated with the use of the study drug, whether or not considered related to the study drug. Preexisting conditions that worsened during the study and laboratory or clinical tests that resulted in a change in treatment or discontinuation from study drug were reported as adverse events. A SAE was any experience that: resulted in death, was life-threatening, required in-patient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect or was medically significant. The percentage of participants with AEs and SAEs that occurred in the Extension Study grouped according to the number of disease-modifying anti-rheumatic drugs (DMARD) a participant was taking at Core Baseline is presented.

Secondary Outcome Measures:

- Percentage of Participants With Adverse Events Leading to Withdraw [Time Frame: 108 Weeks] [Designated as safety issue: No]
  An Adverse Event was considered any unfavorable and unintended sign, symptom, or disease associated with the use of the study drug, whether or not considered related to the study drug. Preexisting conditions that worsened during the study and laboratory or clinical tests that resulted in a change in treatment or discontinuation from study drug were reported as adverse events.
- Time to Withdrawal Due to an Adverse Event (AE) [Time Frame: 108 Weeks] [Designated as safety issue: No]
  Time to withdrawal was defined as the number of days from Core Study Day 1 to the first date of onset of the AE leading to discontinuation of tocilizumab.
- Percentage of Participants With Discontinuation of Treatment Due to Any Cause [Time Frame: 108 Weeks] [Designated as safety issue: No]
  Percentage of participants who discontinued treatment with tocilizumab for any reason.
- Time to Discontinuation of Tocilizumab Treatment for Any Cause [Time Frame: 108 Weeks] [Designated as safety issue: No]
  Time in days from start of the Core Study Day 1 to discontinuation of tocilizumab for any reason.
- Percentage of Participants With Marked Lipid Abnormalities [Time Frame: 108 Weeks] [Designated as safety issue: No]
  Fasting blood samples were collected for Lipids: Cholesterol, Triglyceride, High-density lipoprotein (HDL) Cholesterol, Low-density lipoprotein (LDL) Cholesterol every 12 weeks and at follow-up in the Extension study and were sent to a central laboratory for analysis. Lipid abnormalities were defined as a High Cholesterol, High Triglyceride, Low HDL Cholesterol and a High LDL Cholesterol that occurred at any time in the extension study.
- Percentage of Participants With Adverse Events (AEs) of Special Interest [Time Frame: 108 Weeks] [Designated as safety issue: No]
  An Adverse Event was considered any unfavorable and unintended sign, symptom, or disease associated with the use of the study drug, whether or not considered related to the study drug. Preexisting conditions that worsened during the study and laboratory or clinical tests that resulted in a change in treatment or discontinuation from study drug were reported as adverse events. Adverse Events of special interest for this study were: Infections (preferred term in the infection adverse event group term), Serious Infections (an infection that qualified as Serious Adverse Event), Infusion Reactions (occurred during infusion or within 24 hours of infusion), Major Cardiac AE (Myocardial Infarction/ Acute Coronary Syndrome), Stroke or Death.
- Percentage of Participants With ALT Elevations > 3*ULN [Time Frame: 108 Weeks] [Designated as safety issue: No]
  Blood samples were collected for the Liver Function Test: Alanine aminotransferase (ALT) every 12 weeks and at the follow-up visit in the Extension study and were sent to a central laboratory for analysis. Percentage of participants with any values greater than 3 times the Upper Limit of Normal (3*ULN) is reported. ULN= 55 Units/Liter.
- Percentage of Participants With AST Elevations > 3*ULN [Time Frame: 108 Weeks] [Designated as safety issue: No]
  Blood was collected for the Liver Function Test: Aspartate aminotransferase (AST) every 12 weeks and at the follow-up visit in the Extension study and were sent to a central laboratory for analysis. Percentage of participants with any values greater than 3 times the Upper Limit of Normal (3*ULN) is reported. ULN= 40 Units/Liter.
- Number of Participants Categorized by Highest Value for ALT (SGPT) During the Study [Time Frame: 108 Weeks] [Designated as safety issue: No]
  Blood samples were collected for liver function test: Alanine aminotransferase (serum glutamic-pyruvic transaminase) [ALT(SGPT)] every 12 weeks and at the follow-up visit in the Extension study and were sent to a central laboratory for analysis. The Upper Limit of Normal (ULN) for ALT=55 Units/ Liter. The number of participants categorized by the highest value for ALT/GPT during the study is reported: Normal (ALT result within the central lab reference range), Greater than the ULN to 1.5 times the ULN (>ULN to 1.5*ULN), 1.5 times the ULN to 3 times the ULN (1.5*ULN to 3*ULN) and 3 times the ULN to 5 times the ULN (3*ULN to 5*ULN).
- Number of Participants Categorized by Worst Value for AST (SGOT) During the Study [Time Frame: 108 Weeks] [Designated as safety issue: No]

Blood samples were collected for liver function test: Aspartate aminotransferase (serum glutamic-oxaloacetic transaminase) [AST (SGOT)] every 12 weeks and at the follow-up visit in the Extension study and were sent to a central laboratory for analysis. The Upper Limit of Normal (ULN) for AST=40 Units/Liter. The number of participants categorized by worst value for AST(SGOT) during the study is reported: Normal (AST result is within the central lab reference range), Greater than the ULN to 1.5 times the ULN (>ULN to 1.5*ULN), 1.5 times the ULN to 3 times the ULN (1.5*ULN to 3*ULN) and 3 times the ULN to 5 times the ULN (3*ULN to 5*ULN).

- Number of Participants Categorized by Worst Value for LDL Cholesterol During the Study [Time Frame: 108 Weeks] [Designated as safety issue: No]
  Blood samples were collected for LDL Cholesterol every 12 weeks and at the follow-up visit in the Extension study and were sent to a central laboratory for analysis. The number of participants categorized by the worst value for LDL Cholesterol during the study is reported: Low is below central lab reference range, Normal is within the central lab reference range and High is above central lab reference range.
- Number of Participants Categorized by Worst Value for Total Cholesterol During the Study [Time Frame: 108 Weeks] [Designated as safety issue: No]
  Blood samples were collected for Total Cholesterol every 12 weeks and at the follow-up visit in the Extension study and were sent to a central laboratory for analysis. The number of participants categorized by worst value for Total Cholesterol during the study is reported: Low is below central lab reference range, Normal is within the central lab reference range and High is above central lab reference range.
- Number of Participants Categorized by Worst Value for Neutrophil Count During the Study [Time Frame: 108 Weeks] [Designated as safety issue: No]
  Blood samples were collected for a Neutrophil Count every 12 weeks and at the follow-up visit in the Extension study and were sent to a central laboratory for analysis. The number of participants categorized by the worst value for Neutrophil Count during the study is reported: Low is below central lab reference range, Normal is within the central lab reference range and High is above central lab reference range.
- Percentage of Participants With Clinically Meaningful Improvement in Disease Activity Score-28 (DAS28) [Time Frame: Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108] [Designated as safety issue: No]
  The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 0 to approximately 10. Scores below 2.6 indicate best disease control and scores above 5.1 indicate worse disease control. Clinical meaningful improvement was defined as a ≥ 1.2 unit reduction in DAS28.
- Percentage of Participants With DAS28 Low Disease Activity [Time Frame: Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108] [Designated as safety issue: No]
  The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 0 to approximately 10. Scores below 2.6 indicate best disease control and scores above 5.1 indicate worse disease control. Low Disease Activity was defined as a score of < 3.2.
- Percentage of Participants With DAS28 Remission [Time Frame: Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108] [Designated as safety issue: No]
  The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 0 to approximately 10. Scores below 2.6 indicate best disease control and scores above 5.1 indicate worse disease control. DAS28 Remission was defined as a DAS28 score < 2.6.
- Change From Baseline in DAS28 [Time Frame: Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108] [Designated as safety issue: No]
  The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 0 to approximately 10. Scores below 2.6 indicate best disease control and scores above 5.1 indicate worse disease control. A negative change from Baseline indicated improvement.
- Change From Baseline in Tender Joint Count [Time Frame: Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108] [Designated as safety issue: No]
  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. A negative change from Baseline indicated improvement.
- Change From Baseline in Swollen Joint Count [Time Frame: Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108] [Designated as safety issue: No]

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. A negative change from Baseline indicated improvement.

- Change From Baseline in Patient Assessment of Pain Visual Analog Scale (VAS) [Time Frame: Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108] [Designated as safety issue: No]
  The patient assessed their pain using a 0 to 100 millimeter (mm) horizontal visual analogue scale (VAS). The left-hand extreme of the line equals 0 mm, and is described as "no pain" and the right-hand extreme equals 100 mm as "unbearable pain". A negative change from Baseline indicated improvement.
- Change From Baseline in Patient Global Assessment of Disease Activity VAS [Time Frame: Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108] [Designated as safety issue: No]
  The patients global assessment of disease activity was assessed on a 0 to 100 millimeter (mm) horizontal visual analogue scale (VAS) by the patient. The left-hand extreme of the line equals 0 mm, and is described as "no disease activity" (symptom-free and no arthritis symptoms) and the right-hand extreme equals 100 mm, as "maximum disease activity" (maximum arthritis disease activity). A negative change from Baseline indicated improvement.
- Change From Baseline in Physician Global Assessment of Disease Activity VAS [Time Frame: Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108] [Designated as safety issue: No]
  The physician global assessment of disease activity was assessed using a 0 to 100 mm horizontal visual analogue scale (VAS) by the physician. The left-hand extreme of the line equals 0 mm, and is described as "no disease activity" (symptom-free and no arthritis symptoms) and the right-hand extreme equals 100 mm, as "maximum disease activity" (maximum arthritis disease activity). A negative change from Baseline indicated improvement.
- Change From Baseline in Erythrocyte Sedimentation Rate (ESR) [Time Frame: Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108] [Designated as safety issue: No]
  Blood was collected for Erythrocyte Sedimentation Rate (ESR) (a test that assesses tissue inflammation) and was analyzed at a local laboratory. ESR was measured in millimeters/hour (mm/hr). A reduction in the level is considered an improvement.
- Change From Baseline in C-Reactive Protein (CRP) [Time Frame: Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108] [Designated as safety issue: No]
  Blood was collected for C-Reactive Protein (CRP) (a test for analysis of inflammatory and infectious disorders) and was analyzed at a central laboratory. The serum concentration of CRP was measured in milligrams/deciliter (mg/dL). A reduction in the level is considered an improvement.
- Percentage of Participants With American College of Rheumatology 20 (ACR20) Response [Time Frame: Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108] [Designated as safety issue: No]
  ACR20 response was defined as a ≥ 20 % improvement (reduction) compared with baseline for both total joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: Patient's Assessment of Pain over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain; Patient's Global Assessment of Disease Activity and Physician's Global Assessment of Disease Activity over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity; Health Assessment Questionnaire: 20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do; and acute-phase reactant [either C-reactive protein or Erythrocyte Sedimentation Rate].
- Percentage of Participants With American College of Rheumatology 50 (ACR50) Response [Time Frame: Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108] [Designated as safety issue: No]
  ACR50 response is defined as a ≥ 50 % improvement (reduction) compared with baseline for both total joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: Patient's Assessment of Pain over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain; Patient's Global Assessment of Disease Activity and Physician's Global Assessment of Disease Activity over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity; Health Assessment Questionnaire: 20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do; and acute-phase reactant [either C-reactive protein or Erythrocyte Sedimentation Rate].
- Percentage of Participants With American College of Rheumatology 70 (ACR70) Response [Time Frame: Core Baseline, Extension Weeks 12, 24, 36 ,48, 60, 72, 84, 96, 108] [Designated as safety issue: No]

ACR70 response is defined as a ≥ 70 % improvement (reduction) compared with baseline for both total joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: Patient's Assessment of Pain over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain; Patient's Global Assessment of Disease Activity and Physician's Global Assessment of Disease Activity over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity; Health Assessment Questionnaire: 20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do; and acute-phase reactant [either C-reactive protein or Erythrocyte Sedimentation Rate].

- Percentage of Participants With American College of Rheumatology 90 (ACR90) Response [Time Frame: Core Baseline, Extension Weeks 12, 24, 36 ,48, 60, 72, 84, 96, 108] [Designated as safety issue: No]

  ACR90 response is defined as a ≥ 90 % improvement (reduction) compared with baseline for both total joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: Patient's Assessment of Pain over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain; Patient's Global Assessment of Disease Activity and Physician's Global Assessment of Disease Activity over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity; Health Assessment Questionnaire: 20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do; and acute-phase reactant [either C-reactive protein or Erythrocyte Sedimentation Rate].
- Change From Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) Response [Time Frame: Core Baseline, Extension Weeks 12, 24, 36 ,48, 60, 72, 84, 96, 108] [Designated as safety issue: No]

  The Stanford Health Assessment Questionnaire Disability Index (HAQ-DI) is a patient completed questionnaire specific for rheumatoid arthritis, consisting of 20 questions in 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. There are 4 possible responses for each question: 0=without any difficulty, 1=with some difficulty, 2=with much difficulty and 3=unable to do. The score for each of the domains is the highest (worst) score in each domain. A patient must have a domain score for at least 6 of 8 domains to calculate a valid HAQ-DI score which is the sum of domain scores, divided by the number of domains that have a score for a total possible score minimum/maximum 0 (best) to 3 (worst). A negative change from Baseline indicated improvement.
- Percentage of Participants Achieving Clinical Meaningful Health Assessment Questionnaire Disability Index (HAQ-DI) Response [Time Frame: Core Baseline, Extension Weeks 12, 24, 36 ,48, 60, 72, 84, 96, 108] [Designated as safety issue: No]

  The Stanford Health Assessment Questionnaire Disability Index (HAQ-DI) is a patient completed questionnaire specific for rheumatoid arthritis, consisting of 20 questions in 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. There are 4 possible responses for each question: 0=without any difficulty, 1=with some difficulty, 2=with much difficulty and 3=unable to do. The score for each of the domains is the highest (worst) score in each domain. A patient must have a domain score for at least 6 of 8 domains to calculate a valid HAQ-DI score which is the sum of domain scores, divided by the number of domains that have a score for a total possible score minimum/maximum 0 (best) to 3 (worst). Clinically meaningful improvement is defined as a reduction from Baseline in the HAQ-DI score ≥ 0.2.
- Percentage of Participants Achieving Health Assessment Questionnaire Disability Index (HAQ-DI) Clinical Remission [Time Frame: Extension Weeks 12, 24, 36 ,48, 60, 72, 84, 96, 108] [Designated as safety issue: No]

  The Stanford Health Assessment Questionnaire Disability Index (HAQ-DI) is a patient completed questionnaire specific for rheumatoid arthritis, consisting of 20 questions in 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. There are 4 possible responses for each question: 0=without any difficulty, 1=with some difficulty, 2=with much difficulty and 3=unable to do. The score for each of the domains is the highest (worst) score in each domain. A patient must have a domain score for at least 6 of 8 domains to calculate a valid HAQ-DI score which is the sum of domain scores, divided by the number of domains that have a score for a total possible score minimum/maximum 0 (best) to 3 (worst). Clinical Remission is defined as a HAQ-DI score < 0.5.
- Change From Baseline in Quality of Life Short Form (SF-36): Physical Component Score [Time Frame: Core Baseline, Extension Weeks 12, 24, 36 ,48, 60, 72, 84, 96, 108] [Designated as safety issue: No]

  The SF-36 is a questionnaire used to assess physical functioning and is made up of eight domains: Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional and Mental Health. Transforming and standardizing these domains leads to the calculation

of the Physical (PCS) and Mental (MCS) Component Summary measures. Scores ranging from 0 to 100, with 0=worst score (or quality of life) and 100=best score. A positive change from Baseline indicated improvement.

- Change From Baseline in Quality of Life Short Form (SF-36):Mental Component Score [Time Frame: Core Baseline, Extension Weeks 12, 24, 36 ,48, 60, 72, 84, 96, 108] [Designated as safety issue: No]
  The SF-36 is a questionnaire used to assess physical functioning and is made up of eight domains: Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional and Mental Health. Transforming and standardizing these domains leads to the calculation of the Physical (PCS) and Mental (MCS) Component Summary measures. Scores ranging from 0 to 100, with 0=worst score (or quality of life) and 100=best score. A positive change from Baseline indicated improvement.
- Change From Baseline in FACIT-Fatigue Score [Time Frame: Core Baseline, Extension Weeks 12, 24, 36 ,48, 60, 72, 84, 96, 108] [Designated as safety issue: No]
  FACIT-F is a 13-item questionnaire. Patients scored each item on a 5-point scale: 0 (Not at all) to 4 (Very much). The larger the patient's response to the questions (with the exception of 2 negatively stated), the greater the patient'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 patient'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 patient's health status. A positive change from Baseline indicated improvement.

Enrollment: 934
Study Start Date: March 2009
Primary Completion Date: April 2012
Study Completion Date: April 2012

Arms	Assigned Interventions
Experimental: tocilizumab Participants received tocilizumab 8 mg/kg intravenous (IV), maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.	Drug: tocilizumab [RoActemra/Actemra] 8 mg/kg IV (maximum dose not exceeding 800 mg in a single infusion) every 4 weeks.

Eligibility

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

Criteria

Inclusion Criteria:

- patients who completed the 24-week MA21573 core study, had at least a moderate response based on EULAR definition criteria and no adverse events (AEs), serious adverse events (SAEs) or conditions that led to unacceptable risk of continued treatment.

Exclusion Criteria:

-as for MA21573.

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
- Australia, Queensland
  - Cairns, Queensland, Australia, 4870
- Australia, South Australia
  - Adelaide, South Australia, Australia, 5041
- Australia, Victoria
  - Fitzroy, Victoria, Australia, 3065
  - Geelong, Victoria, Australia, 3220
  - Melbourne, Victoria, Australia, 3168
- Canada, Alberta
  - Edmonton, Alberta, Canada, T5M 0H4
  - Lethbridge, Alberta, Canada, T1J 0N9
- Canada, British Columbia
  - Kelowna, British Columbia, Canada, V1Y 3G8
  - Nanaimo, British Columbia, Canada, V9S 4S1
  - Vancouver, British Columbia, Canada, V5Z 1L7
  - Vancouver, British Columbia, Canada, V5Z 3Y1
- Canada, New Brunswick
  - Quispamsis, New Brunswick, Canada, E2E 4J8
- Canada, Newfoundland and Labrador
  - St John's, Newfoundland and Labrador, Canada, A1C 5B8
- Canada, Ontario
  - Hamilton, Ontario, Canada, L8N 1Y2
  - Ottawa, Ontario, Canada, K1H 8L6
  - Toronto, Ontario, Canada, M4K 1N2
  - Toronto, Ontario, Canada, M5G 1X5
  - 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
  - Sherbrooke, Quebec, Canada, J1H 5N4

St-eustache, Quebec, Canada, J7P 4J2
Trois-rivieres, Quebec, Canada, G8Z 1Y2
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Bruntal, Czech Republic, 792 01
Ostrava, Czech Republic, 722 00
Praha, Czech Republic, 128 50
Sokolov, Czech Republic, 356 01
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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
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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Eger, Hungary, 3300
Szeged, Hungary, 6724
Veszprem, Hungary, 8200
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Milano, Italy, 20132
Milano, Italy, 20122
Modena, Italy, 41100
Monserrato, Italy, 09042
Novara, Italy, 28100
Palermo, Italy, 90127
Potenza, Italy, 85100
Roma, Italy, 00144
Roma, Italy, 00152
Siena, Italy, 53100
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Amsterdam, Netherlands, 1056 AB
Apeldoorn, Netherlands, 7300 DS
Arnhem, Netherlands, 6815 AD
Bergen Op Zoom, Netherlands, 4624 VT
Den Haag, Netherlands, 2597 AX
Den Haag, Netherlands, 2545 CH
Den Helder, Netherlands, 1782GZ
Enschede, Netherlands, 7511 JX
Gouda, Netherlands, 2803 HH
Heerlen, Netherlands, 6419 PC
Hilversum, Netherlands, 1213 HX
Leeuwarden, Netherlands, 8934 AD
Nieuwegein, Netherlands, 3430 EM
Nijmegen, Netherlands, 6522 JV
Roosendaal, Netherlands, 4708 AE
Rotterdam, Netherlands, 3079 DZ
Rotterdam, Netherlands, 3015 CE
Schiedam, Netherlands, 3116 BA
Spijkenisse, Netherlands, 3201 GZ
Vlissingen, Netherlands, 4382 EE

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Poznan, Poland, 61-545
Wroclaw, Poland, 50-556

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Coimbra, Portugal, 3000-075
Lisboa, Portugal, 1349-019
Lisboa, Portugal, 1649-035

Porto, Portugal, 4200-319

Romania

Bucharest, Romania, 011172
Bucharest, Romania, 020475
Cluj-napoca, Romania, 400006

Saudi Arabia

Jeddah, Saudi Arabia, 21423
Jeddah, Saudi Arabia, 21499
Jeddah, Saudi Arabia, 21461

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Alicante, Alicante, Spain, 03010
Elche, Alicante, Spain, 03203
Elda, Alicante, Spain, 03600
Almeria, Almeria, Spain, 04009
Barcelona, Barcelona, Spain, 08035
Barcelona, Barcelona, Spain, 08036
Barcelona, Barcelona, Spain, 08907
Barcelona, Barcelona, Spain, 08025
Sabadell, Barcelona, Spain, 08208
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Caceres, Caceres, Spain, 10310
Cordoba, Cordoba, Spain, 14004
Granada, Granada, Spain, 18014
Huesca, Huesca, Spain, 22004
La Coruna, La Coruña, Spain, 15006
Las Palmas De Gran Canaria, Las Palmas, Spain, 35020
Lugo, Lugo, Spain, 27004
Madrid, Madrid, Spain, 28006
Madrid, Madrid, Spain, 28905
Malaga, Malaga, Spain, 29010
Salamanca, Salamanca, Spain, 37007
Sevilla, Sevilla, Spain, 41013
La Laguna, Tenerife, Spain, 38320
Valencia, Valencia, Spain, 46017
Valencia, Valencia, Spain, 46010

United Kingdom

Barnsley, United Kingdom, S75 2EP
Basingstoke, United Kingdom, RG24 9NA
Bournemouth, United Kingdom, BH23 2JX
Brighton, United Kingdom, BN2 5BE
Burton on Trent, United Kingdom, DE13 0RB
Bury St Edmonds, United Kingdom, IP33 2QZ
Cambridge, United Kingdom, CB2 2QQ
Cardiff, United Kingdom, CF14 4XW
Chelmsford, United Kingdom, CM1 7ET

Dudley, United Kingdom, DY1 2HQ
Eastbourne, United Kingdom, BN21 2UD
Gillingham, United Kingdom, ME7 5NY
Harrogate, United Kingdom, HG2 7SX
Ipswich, United Kingdom, IP4 5PD
Liverpool, United Kingdom, L9 7AL
Llantrisant, United Kingdom, CF72 8XR
London, United Kingdom, E11 1NR
Londonderry, United Kingdom, BT47 6SB
Maidstone, United Kingdom, ME16 9QQ
Middlesborough, United Kingdom, TS4 3BW
Newcastle Upon Tyne, United Kingdom, NE7 7DN
Nottingham, United Kingdom, NG5 1PB
Reading, United Kingdom, RG1 5AN
Salford, United Kingdom, M6 8HD
Sheffield, United Kingdom, S10 2JF
Southport, United Kingdom, PR8 6PN
Swindon, United Kingdom, SN3 6BB
Torquay, United Kingdom, TQ2 7AA
Westcliffe-on-sea, United Kingdom, SS0 0RY
Wirral, United Kingdom, CH49 5PE
Worthing, United Kingdom, BN11 2DH

Investigators

Study Director:	Clinical Trials	Hoffmann-La Roche

More Information

Responsible Party:	Hoffmann-La Roche
Study ID Numbers:	MA22460 2008-006924-68
Health Authority:	Canada: Health Canada

Study Results

Participant Flow

Pre-Assignment Details	Patients participated in the 24 Week Core Study: MA21573 [NCT00750880] then continued to receive tocilizumab in this extension study for total treatment time of up to 104 weeks + a 4 week follow-up.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg intravenous (IV), maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Overall Study

	Tocilizumab
Started	934
Completed	827
Not Completed	107
Adverse Event	37
Death	2
Insufficient therapeutic response	16
Lost to Follow-up	4
Violation of selection criteria at entry	7
Protocol Violation	2
Refused treatment	4
Withdrew consent	10
Investigator's decision	17
Administrative/Other	8

Baseline Characteristics

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg intravenous (IV), maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Baseline Measures

	Tocilizumab
Number of Participants	934

	Tocilizumab
Age, Continuous [units: years] Mean (Standard Deviation)	54.3 (12.02)
Gender, Male/Female [units: participants]	
Female	753
Male	181

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)
Measure Description	An AE was considered any unfavorable and unintended sign, symptom, or disease associated with the use of the study drug, whether or not considered related to the study drug. Preexisting conditions that worsened during the study and laboratory or clinical tests that resulted in a change in treatment or discontinuation from study drug were reported as adverse events. A SAE was any experience that: resulted in death, was life-threatening, required in-patient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect or was medically significant. The percentage of participants with AEs and SAEs that occurred in the Extension Study grouped according to the number of disease-modifying anti-rheumatic drugs (DMARD) a participant was taking at Core Baseline is presented.
Time Frame	108 Weeks
Safety Issue?	No

Analysis Population Description

LTE Safety population included all participants who received study drug and had at least one assessment of safety in the long term extension (LTE).

Reporting Groups

	Description
Tocilizumab Monotherapy	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first, in a subset of patients who were not taking DMARDS at Core Baseline.
Tocilizumab + 1 DMARD	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first, in a subset of patients who were taking one DMARD at Core study Baseline.

	Description
Tocilizumab + > 1 DMARD	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first, in a subset of patients who were taking more than one DMARD at Core study Baseline.

Measured Values

	Tocilizumab Monotherapy	Tocilizumab + 1 DMARD	Tocilizumab + > 1 DMARD
Number of Participants Analyzed	117	612	205
Percentage of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs) [units: percentage of participants] Number (95% Confidence Interval)			
AEs	65.0 (55.6 to 73.5)	68.6 (64.8 to 72.3)	73.2 (66.6 to 79.1)
SAEs	8.5 (4.2 to 15.2)	5.7 (4.0 to 7.9)	7.3 (4.2 to 11.8)

2. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Adverse Events Leading to Withdraw
Measure Description	An Adverse Event was considered any unfavorable and unintended sign, symptom, or disease associated with the use of the study drug, whether or not considered related to the study drug. Preexisting conditions that worsened during the study and laboratory or clinical tests that resulted in a change in treatment or discontinuation from study drug were reported as adverse events.
Time Frame	108 Weeks
Safety Issue?	No

Analysis Population Description

LTE Safety population included all participants who received study drug and had at least one assessment of safety in the long term extension (LTE).

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Percentage of Participants With Adverse Events Leading to Withdraw [units: percentage of participants]	4.0

3. Secondary Outcome Measure:

Measure Title	Time to Withdrawal Due to an Adverse Event (AE)
Measure Description	Time to withdrawal was defined as the number of days from Core Study Day 1 to the first date of onset of the AE leading to discontinuation of tocilizumab.
Time Frame	108 Weeks
Safety Issue?	No

Analysis Population Description

LTE Safety population included all participants who received study drug and had at least one assessment of safety in the long term extension(LTE). Participants who did not experience an AE-related treatment discontinuation of tocilizumab were censored.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Time to Withdrawal Due to an Adverse Event (AE) [units: days] Median (95% Confidence Interval)	374.5 (286.0 to 441.0)

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Discontinuation of Treatment Due to Any Cause

Measure Description	Percentage of participants who discontinued treatment with tocilizumab for any reason.
Time Frame	108 Weeks
Safety Issue?	No

Analysis Population Description

LTE Safety population included all participants who received study drug and had at least one assessment of safety in the long term extension (LTE).

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Percentage of Participants With Discontinuation of Treatment Due to Any Cause [units: percentage of participants]	11.5

5. Secondary Outcome Measure:

Measure Title	Time to Discontinuation of Tocilizumab Treatment for Any Cause
Measure Description	Time in days from start of the Core Study Day 1 to discontinuation of tocilizumab for any reason.
Time Frame	108 Weeks
Safety Issue?	No

Analysis Population Description

LTE Safety population included all participants who received study drug and had at least one assessment of safety in the long term extension (LTE). Participants who did not experience discontinuation of tocilizumab treatment were censored.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Time to Discontinuation of Tocilizumab Treatment for Any Cause [units: days] Median (95% Confidence Interval)	339.0 (294.0 to 370.0)

6. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Marked Lipid Abnormalities
Measure Description	Fasting blood samples were collected for Lipids: Cholesterol, Triglyceride, High-density lipoprotein (HDL) Cholesterol, Low-density lipoprotein (LDL) Cholesterol every 12 weeks and at follow-up in the Extension study and were sent to a central laboratory for analysis. Lipid abnormalities were defined as a High Cholesterol, High Triglyceride, Low HDL Cholesterol and a High LDL Cholesterol that occurred at any time in the extension study.
Time Frame	108 Weeks
Safety Issue?	No

Analysis Population Description

LTE Safety population included all participants who received study drug and had at least one assessment of safety in the long term extension (LTE).

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Percentage of Participants With Marked Lipid Abnormalities [units: percentage of participants]	
Cholesterol (high)	4.2
HDL Cholesterol (low)	0.0

	Tocilizumab
LDL Cholesterol (high)	6.5
Triglyceride (high)	14.9

7. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Adverse Events (AEs) of Special Interest
Measure Description	An Adverse Event was considered any unfavorable and unintended sign, symptom, or disease associated with the use of the study drug, whether or not considered related to the study drug. Preexisting conditions that worsened during the study and laboratory or clinical tests that resulted in a change in treatment or discontinuation from study drug were reported as adverse events. Adverse Events of special interest for this study were: Infections (preferred term in the infection adverse event group term), Serious Infections (an infection that qualified as Serious Adverse Event), Infusion Reactions (occurred during infusion or within 24 hours of infusion), Major Cardiac AE (Myocardial Infarction/ Acute Coronary Syndrome), Stroke or Death.
Time Frame	108 Weeks
Safety Issue?	No

Analysis Population Description

LTE Safety population included all participants who received study drug and had at least one assessment of safety in the long term extension (LTE).

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Percentage of Participants With Adverse Events (AEs) of Special Interest [units: percentage of participants]	
Infections	40.4
Serious Infections	2.4
Infusion Reaction	2.9

	Tocilizumab
Major Cardiac AE	0.3
Stroke	0.9
Death	0.3

8. Secondary Outcome Measure:

Measure Title	Percentage of Participants With ALT Elevations > 3*ULN
Measure Description	Blood samples were collected for the Liver Function Test: Alanine aminotransferase (ALT) every 12 weeks and at the follow-up visit in the Extension study and were sent to a central laboratory for analysis. Percentage of participants with any values greater than 3 times the Upper Limit of Normal (3*ULN) is reported. ULN= 55 Units/Liter.
Time Frame	108 Weeks
Safety Issue?	No

Analysis Population Description

LTE Safety population included all participants who received study drug and had at least one assessment of safety in the long term extension (LTE).

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Percentage of Participants With ALT Elevations > 3*ULN [units: percentage of participants]	1.9

9. Secondary Outcome Measure:

Measure Title	Percentage of Participants With AST Elevations > 3*ULN

Measure Description	Blood was collected for the Liver Function Test: Aspartate aminotransferase (AST) every 12 weeks and at the follow-up visit in the Extension study and were sent to a central laboratory for analysis. Percentage of participants with any values greater than 3 times the Upper Limit of Normal (3*ULN) is reported. ULN= 40 Units/Liter.
Time Frame	108 Weeks
Safety Issue?	No

Analysis Population Description

LTE Safety population included all participants who received study drug and had at least one assessment of safety in the long term extension (LTE).

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Percentage of Participants With AST Elevations > 3*ULN [units: percentage of participants]	0.4

10. Secondary Outcome Measure:

Measure Title	Number of Participants Categorized by Highest Value for ALT (SGPT) During the Study
Measure Description	Blood samples were collected for liver function test: Alanine aminotransferase (serum glutamic-pyruvic transaminase) [ALT(SGPT)] every 12 weeks and at the follow-up visit in the Extension study and were sent to a central laboratory for analysis. The Upper Limit of Normal (ULN) for ALT=55 Units/Liter. The number of participants categorized by the highest value for ALT/GPT during the study is reported: Normal (ALT result within the central lab reference range), Greater than the ULN to 1.5 times the ULN (>ULN to 1.5*ULN), 1.5 times the ULN to 3 times the ULN (1.5*ULN to 3*ULN) and 3 times the ULN to 5 times the ULN (3*ULN to 5*ULN).
Time Frame	108 Weeks
Safety Issue?	No

Analysis Population Description

Participants from the LTE Safety population included all participants who received study drug and had at least one assessment of safety in the long term extension (LTE) with data available for analysis.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Number of Participants Categorized by Highest Value for ALT (SGPT) During the Study [units: participants]	
Normal	874
>ULN - 1.5*ULN	50
1.5*ULN to 3*ULN	8
3*ULN to 5*ULN	2

11. Secondary Outcome Measure:

Measure Title	Number of Participants Categorized by Worst Value for AST (SGOT) During the Study
Measure Description	Blood samples were collected for liver function test: Aspartate aminotransferase (serum glutamic-oxaloacetic transaminase) [AST (SGOT)] every 12 weeks and at the follow-up visit in the Extension study and were sent to a central laboratory for analysis. The Upper Limit of Normal (ULN) for AST=40 Units/Liter. The number of participants categorized by worst value for AST(SGOT) during the study is reported: Normal (AST result is within the central lab reference range), Greater than the ULN to 1.5 times the ULN (>ULN to 1.5*ULN), 1.5 times the ULN to 3 times the ULN (1.5*ULN to 3*ULN) and 3 times the ULN to 5 times the ULN (3*ULN to 5*ULN).
Time Frame	108 Weeks
Safety Issue?	No

Analysis Population Description

Participants from the LTE Safety population included all participants who received study drug and had at least one assessment of safety in the long term extension (LTE) with data available for analysis.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Number of Participants Categorized by Worst Value for AST (SGOT) During the Study [units: participants]	
Normal	903
>ULN to 1.5*ULN	26
1.5*ULN to 3*ULN	4
3*ULN to 5*ULN	1

12. Secondary Outcome Measure:

Measure Title	Number of Participants Categorized by Worst Value for LDL Cholesterol During the Study
Measure Description	Blood samples were collected for LDL Cholesterol every 12 weeks and at the follow-up visit in the Extension study and were sent to a central laboratory for analysis. The number of participants categorized by the worst value for LDL Cholesterol during the study is reported: Low is below central lab reference range, Normal is within the central lab reference range and High is above central lab reference range.
Time Frame	108 Weeks
Safety Issue?	No

Analysis Population Description

Participants from the LTE Safety population (all participants who received study drug and had at least one assessment of safety in the long term extension) with data available for analysis.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	933
Number of Participants Categorized by Worst Value for LDL Cholesterol During the Study [units: participants]	
Low	0
Normal	368
High	565

13. Secondary Outcome Measure:

Measure Title	Number of Participants Categorized by Worst Value for Total Cholesterol During the Study
Measure Description	Blood samples were collected for Total Cholesterol every 12 weeks and at the follow-up visit in the Extension study and were sent to a central laboratory for analysis. The number of participants categorized by worst value for Total Cholesterol during the study is reported: Low is below central lab reference range, Normal is within the central lab reference range and High is above central lab reference range.
Time Frame	108 Weeks
Safety Issue?	No

Analysis Population Description

Participants from the LTE Safety population (all participants who received study drug and had at least one assessment of safety in the long term extension) with data available for analysis.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	933
Number of Participants Categorized by Worst Value for Total Cholesterol During the Study [units: participants]	
Low	4
Normal	194
High	735

14. Secondary Outcome Measure:

Measure Title	Number of Participants Categorized by Worst Value for Neutrophil Count During the Study
Measure Description	Blood samples were collected for a Neutrophil Count every 12 weeks and at the follow-up visit in the Extension study and were sent to a central laboratory for analysis. The number of participants categorized by the worst value for Neutrophil Count during the study is reported: Low is below central lab reference range, Normal is within the central lab reference range and High is above central lab reference range.
Time Frame	108 Weeks
Safety Issue?	No

Analysis Population Description

Participants from the LTE Safety population (all participants who received study drug and had at least one assessment of safety in the long term extension) with data available for analysis.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	932
Number of Participants Categorized by Worst Value for Neutrophil Count During the Study	

	Tocilizumab
[units: participants]	
Low	321
Normal	608
High	3

15. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Clinically Meaningful Improvement in Disease Activity Score-28 (DAS28)
Measure Description	The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 0 to approximately 10. Scores below 2.6 indicate best disease control and scores above 5.1 indicate worse disease control. Clinical meaningful improvement was defined as a ≥ 1.2 unit reduction in DAS28.
Time Frame	Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

Long Term Extension Intent-to-treat (LTE ITT) population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available for both Baseline and the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Percentage of Participants With Clinically Meaningful Improvement in Disease Activity Score-28 (DAS28) [units: percentage of participants]	
Week 12 (n=889)	94.7
Week 24 (n=757)	94.8

	Tocilizumab
Week 36 (n=607)	96.4
Week 48 (n=440)	96.6
Week 60 (n=320)	97.8
Week 72 (n=216)	96.8
Week 84 (n=119)	95.8
Week 96 (n=54)	100.0
Week 108 (n=42)	100.0

16. Secondary Outcome Measure:

Measure Title	Percentage of Participants With DAS28 Low Disease Activity
Measure Description	The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 0 to approximately 10. Scores below 2.6 indicate best disease control and scores above 5.1 indicate worse disease control. Low Disease Activity was defined as a score of < 3.2.
Time Frame	Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available at the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934

	Tocilizumab
Percentage of Participants With DAS28 Low Disease Activity [units: percentage of participants]	
Week 12 (n=891)	75.3
Week 24 (n=759)	76.9
Week 36 (n=609)	77.3
Week 48 (n=440)	78.2
Week 60 (n=320)	80.6
Week 72 (n=216)	84.3
Week 84 (n=119)	83.2
Week 96 (n=54)	88.9
Week 108 (n=42)	83.3

17. Secondary Outcome Measure:

Measure Title	Percentage of Participants With DAS28 Remission
Measure Description	The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 0 to approximately 10. Scores below 2.6 indicate best disease control and scores above 5.1 indicate worse disease control. DAS28 Remission was defined as a DAS28 score < 2.6.
Time Frame	Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available at the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Percentage of Participants With DAS28 Remission [units: percentage of participants]	
Week 12 (n=891)	59.6
Week 24 (n=759)	61.9
Week 36 (n=609)	62.7
Week 48 (n=440)	62.7
Week 60 (n=320)	65.9
Week 72 (n=216)	69.9
Week 84 (n=119)	68.9
Week 96 (n=54)	70.4
Week 108 (n=42)	71.4

18. Secondary Outcome Measure:

Measure Title	Change From Baseline in DAS28
Measure Description	The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 0 to approximately 10. Scores below 2.6 indicate best disease control and scores above 5.1 indicate worse disease control. A negative change from Baseline indicated improvement.
Time Frame	Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available at both Baseline and the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Change From Baseline in DAS28 [units: score on a scale] Mean (Standard Deviation)	
Week 12 (n=889)	-3.58 (1.498)
Week 24 (n=757)	-3.62 (1.496)
Week 36 (n=607)	-3.74 (1.443)
Week 48 (n=440)	-3.80 (1.420)
Week 60 (n=320)	-3.91 (1.318)
Week 72 (n=216)	-3.93 (1.394)
Week 84 (n=119)	-3.94 (1.273)
Week 96 (n=54)	-4.14 (1.132)
Week 108 (n=42)	-4.12 (1.178)

19. Secondary Outcome Measure:

Measure Title	Change From Baseline in Tender Joint Count
Measure Description	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. A negative change from Baseline indicated improvement.
Time Frame	Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available at both Baseline and the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Change From Baseline in Tender Joint Count [units: joint count] Mean (Standard Deviation)	
Week 12 (n=927)	-17.45 (14.492)
Week 24 (n=789)	-18.07 (14.524)
Week 36 (n=627)	-18.592 (14.59)
Week 48 (n=457)	-18.77 (14.744)
Week 60 (n=334)	-19.16 (13.575)
Week 72 (n=223)	-18.30 (13.157)
Week 84 (n=121)	-17.45 (12.481)
Week 96 (n=55)	-17.47 (11.445)
Week 108 (n=43)	-17.35 (12.049)

20. Secondary Outcome Measure:

Measure Title	Change From Baseline in Swollen Joint Count
Measure Description	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. A negative change from Baseline indicated improvement.
Time Frame	Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available at both Baseline and the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Change From Baseline in Swollen Joint Count [units: joint count] Mean (Standard Deviation)	
Week 12 (n=927)	-10.16 (9.838)
Week 24 (n=789)	-10.17 (9.633)
Week 36 (n=627)	-10.55 (9.981)
Week 48 (n=457)	-10.78 (10.410)
Week 60 (n=334)	-10.83 (8.885)
Week 72 (n=223)	-10.91 (8.563)
Week 84 (n=121)	-9.90 (6.378)
Week 96 (n=55)	-8.62 (7.230)
Week 108 (n=43)	-8.58 (5.662)

21. Secondary Outcome Measure:

Measure Title	Change From Baseline in Patient Assessment of Pain Visual Analog Scale (VAS)
Measure Description	The patient assessed their pain using a 0 to 100 millimeter (mm) horizontal visual analogue scale (VAS). The left-hand extreme of the line equals 0 mm, and is described as "no pain" and the right-hand extreme equals 100 mm as "unbearable pain". A negative change from Baseline indicated improvement.
Time Frame	Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108

Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available at both Baseline and the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Change From Baseline in Patient Assessment of Pain Visual Analog Scale (VAS) [units: mm] Mean (Standard Deviation)	
Week 12 (n=900)	-32.52 (26.297)
Week 24 (n=772)	-32.59 (25.998)
Week 36 (n=612)	-33.04 (25.461)
Week 48 (n=445)	-32.69 (27.244)
Week 60 (n=326)	-35.35 (26.082)
Week 72 (n=219)	-35.24 (27.901)
Week 84 (n=119)	-35.71 (25.901)
Week 96 (n=55)	-43.40 (21.131)
Week 108 (n=42)	-45.48 (20.956)

22. Secondary Outcome Measure:

Measure Title	Change From Baseline in Patient Global Assessment of Disease Activity VAS

Measure Description	The patients global assessment of disease activity was assessed on a 0 to 100 millimeter (mm) horizontal visual analogue scale (VAS) by the patient. The left-hand extreme of the line equals 0 mm, and is described as "no disease activity" (symptom-free and no arthritis symptoms) and the right-hand extreme equals 100 mm, as "maximum disease activity" (maximum arthritis disease activity). A negative change from Baseline indicated improvement.
Time Frame	Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available at both Baseline and the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Change From Baseline in Patient Global Assessment of Disease Activity VAS [units: score on a scale] Mean (Standard Deviation)	
Week 12 (n=900)	-35.90 (25.964)
Week 24 (n=773)	-35.57 (25.368)
Week 36 (n=612)	-35.75 (25.853)
Week 48 (n=445)	-35.56 (27.475)
Week 60 (n=326)	-37.85 (26.723)
Week 72 (n=219)	-36.36 (26.828)
Week 84 (n=119)	-37.91 (27.628)
Week 96 (n=55)	-45.44 (21.766)
Week 108 (n=42)	-44.90 (28.689)

23. Secondary Outcome Measure:

Measure Title	Change From Baseline in Physician Global Assessment of Disease Activity VAS
Measure Description	The physician global assessment of disease activity was assessed using a 0 to 100 mm horizontal visual analogue scale (VAS) by the physician. The left-hand extreme of the line equals 0 mm, and is described as "no disease activity" (symptom-free and no arthritis symptoms) and the right-hand extreme equals 100 mm, as "maximum disease activity" (maximum arthritis disease activity). A negative change from Baseline indicated improvement.
Time Frame	Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available at both Baseline and the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Change From Baseline in Physician Global Assessment of Disease Activity VAS [units: mm] Mean (Standard Deviation)	
Week 12 (n=900)	-41.14 (21.221)
Week 24 (n=769)	-40.86 (21.114)
Week 36 (n=613)	-40.97 (21.244)
Week 48 (n=447)	-42.20 (21.551)
Week 60 (n=325)	-42.67 (21.656)
Week 72 (n=217)	-43.74 (20.941)
Week 84 (n=119)	-42.68 (21.307)
Week 96 (n=55)	-43.60 (17.828)

	Tocilizumab
Week 108 (n=42)	-44.38 (25.580)

24. Secondary Outcome Measure:

Measure Title	Change From Baseline in Erythrocyte Sedimentation Rate (ESR)
Measure Description	Blood was collected for Erythrocyte Sedimentation Rate (ESR) (a test that assesses tissue inflammation) and was analyzed at a local laboratory. ESR was measured in millimeters/hour (mm/hr). A reduction in the level is considered an improvement.
Time Frame	Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available at Baseline and the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Change From Baseline in Erythrocyte Sedimentation Rate (ESR) [units: mm/hr] Mean (Standard Deviation)	
Week 12 (n=903)	-30.59 (24.839)
Week 24 (n=764)	-29.96 (24.584)
Week 36 (n=615)	-31.56 (24.293)
Week 48 (n=443)	-31.09 (24.408)
Week 60 (n=320)	-31.61 (22.864)

	Tocilizumab
Week 72 (n=217)	-29.62 (21.904)
Week 84 (n=119)	-29.79 (19.525)
Week 96 (n=55)	-34.38 (18.865)
Week 108 (n=42)	-36.67 (17.167)

25. Secondary Outcome Measure:

Measure Title	Change From Baseline in C-Reactive Protein (CRP)
Measure Description	Blood was collected for C-Reactive Protein (CRP) (a test for analysis of inflammatory and infectious disorders) and was analyzed at a central laboratory. The serum concentration of CRP was measured in milligrams/deciliter (mg/dL). A reduction in the level is considered an improvement.
Time Frame	Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available at Baseline and the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Change From Baseline in C-Reactive Protein (CRP) [units: mg/dL] Mean (Standard Deviation)	
Week 12 (n=904)	-1.72 (2.785)
Week 24 (n=767)	-1.73 (2.620)
Week 36 (n=611)	-1.79 (2.756)

	Tocilizumab
Week 48 (n=445)	-1.73 (2.696)
Week 60 (n=319)	-1.82 (2.823)
Week 72 (n=208)	-1.54 (2.609)
Week 84 (n=112)	-1.56 (2.618)
Week 96 (n=54)	-1.24 (1.999)
Week 108 (n=43)	-0.98 (1.324)

26. Secondary Outcome Measure:

Measure Title	Percentage of Participants With American College of Rheumatology 20 (ACR20) Response
Measure Description	ACR20 response was defined as a ≥ 20 % improvement (reduction) compared with baseline for both total joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: Patient's Assessment of Pain over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain; Patient's Global Assessment of Disease Activity and Physician's Global Assessment of Disease Activity over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity; Health Assessment Questionnaire: 20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do; and acute-phase reactant [either C-reactive protein or Erythrocyte Sedimentation Rate].
Time Frame	Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available at both Baseline and the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934

	Tocilizumab
Percentage of Participants With American College of Rheumatology 20 (ACR20) Response [units: percentage of participants]	
Week 12	76.1
Week 24 (n=827)	75.1
Week 36 (n=685)	72.6
Week 48 (n=534)	69.1
Week 60 (n=419)	65.6
Week 72 (n=313)	60.7
Week 84 (n=217)	46.1
Week 96 (n=154)	31.8
Week 108 (n=142)	28.2

27. Secondary Outcome Measure:

Measure Title	Percentage of Participants With American College of Rheumatology 50 (ACR50) Response
Measure Description	ACR50 response is defined as a ≥ 50 % improvement (reduction) compared with baseline for both total joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: Patient's Assessment of Pain over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain; Patient's Global Assessment of Disease Activity and Physician's Global Assessment of Disease Activity over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity; Health Assessment Questionnaire: 20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do; and acute-phase reactant [either C-reactive protein or Erythrocyte Sedimentation Rate].
Time Frame	Core Baseline, Extension Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available at both Baseline and the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Percentage of Participants With American College of Rheumatology 50 (ACR50) Response [units: percentage of participants]	
Week 12	56.3
Week 24 (n=827)	53.9
Week 36 (n=685)	53.6
Week 48 (n=534)	48.5
Week 60 (n=419)	49.2
Week 72 (n=313)	46.0
Week 84 (n=217)	33.2
Week 96 (n=154)	26.6
Week 108 (n=142)	23.9

28. Secondary Outcome Measure:

Measure Title	Percentage of Participants With American College of Rheumatology 70 (ACR70) Response
Measure Description	ACR70 response is defined as a ≥ 70 % improvement (reduction) compared with baseline for both total joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: Patient's Assessment of Pain over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain; Patient's Global Assessment of Disease Activity and Physician's Global Assessment of Disease Activity over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity; Health Assessment Questionnaire: 20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do; and acute-phase reactant [either C-reactive protein or Erythrocyte Sedimentation Rate].

Time Frame	Core Baseline, Extension Weeks 12, 24, 36 ,48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available at both Baseline and the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Percentage of Participants With American College of Rheumatology 70 (ACR70) Response [units: percentage of participants]	
Week 12	31.4
Week 24 (n=827)	31.0
Week 36 (n=685)	32.6
Week 48 (n=534)	31.3
Week 60 (n=419)	28.2
Week 72 (n=313)	29.7
Week 84 (n=217)	23.5
Week 96 (n=154)	20.8
Week 108 (n=142)	17.6

29. Secondary Outcome Measure:

Measure Title	Percentage of Participants With American College of Rheumatology 90 (ACR90) Response

Measure Description	ACR90 response is defined as a ≥ 90 % improvement (reduction) compared with baseline for both total joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: Patient's Assessment of Pain over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain; Patient's Global Assessment of Disease Activity and Physician's Global Assessment of Disease Activity over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity; Health Assessment Questionnaire: 20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do; and acute-phase reactant [either C-reactive protein or Erythrocyte Sedimentation Rate].
Time Frame	Core Baseline, Extension Weeks 12, 24, 36 ,48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available at both Baseline and the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Percentage of Participants With American College of Rheumatology 90 (ACR90) Response [units: percentage of participants]	
Week 12	9.9
Week 24 (n=827)	10.5
Week 36 (n=685)	12.0
Week 48 (n=534)	11.2
Week 60 (n=419)	11.0
Week 72 (n=313)	11.2
Week 84 (n=217)	11.5
Week 96 (n=154)	9.7

	Tocilizumab
Week 108 (n=142)	9.2

30. Secondary Outcome Measure:

Measure Title	Change From Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) Response
Measure Description	The Stanford Health Assessment Questionnaire Disability Index (HAQ-DI) is a patient completed questionnaire specific for rheumatoid arthritis, consisting of 20 questions in 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. There are 4 possible responses for each question: 0=without any difficulty, 1=with some difficulty, 2=with much difficulty and 3=unable to do. The score for each of the domains is the highest (worst) score in each domain. A patient must have a domain score for at least 6 of 8 domains to calculate a valid HAQ-DI score which is the sum of domain scores, divided by the number of domains that have a score for a total possible score minimum/maximum 0 (best) to 3 (worst). A negative change from Baseline indicated improvement.
Time Frame	Core Baseline, Extension Weeks 12, 24, 36 ,48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available at both Baseline and the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Change From Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) Response [units: score on a scale] Mean (Standard Deviation)	
Week 12 (n=895)	-0.58 (0.605)
Week 24 (n=765)	-0.59 (0.611)
Week 36 (n=611)	-0.61 (0.607)

	Tocilizumab
Week 48 (n=446)	-0.63 (0.595)
Week 60 (n=327)	-0.65 (0.614)
Week 72 (n=218)	-0.64 (0.610)
Week 84 (n=119)	-0.68 (0.650)
Week 96 (n=55)	-0.82 (0.582)
Week 108 (n=42)	-0.87 (0.634)

31. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving Clinical Meaningful Health Assessment Questionnaire Disability Index (HAQ-DI) Response
Measure Description	The Stanford Health Assessment Questionnaire Disability Index (HAQ-DI) is a patient completed questionnaire specific for rheumatoid arthritis, consisting of 20 questions in 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. There are 4 possible responses for each question: 0=without any difficulty, 1=with some difficulty, 2=with much difficulty and 3=unable to do. The score for each of the domains is the highest (worst) score in each domain. A patient must have a domain score for at least 6 of 8 domains to calculate a valid HAQ-DI score which is the sum of domain scores, divided by the number of domains that have a score for a total possible score minimum/maximum 0 (best) to 3 (worst). Clinically meaningful improvement is defined as a reduction from Baseline in the HAQ-DI score ≥ 0.2.
Time Frame	Core Baseline, Extension Weeks 12, 24, 36 ,48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available at the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Percentage of Participants Achieving Clinical Meaningful Health Assessment Questionnaire Disability Index (HAQ-DI) Response [units: percentage of participants]	
Week 12 (n=895)	73.6
Week 24 (n=765)	73.9
Week 36 (n=611)	74.1
Week 48 (n=446)	76.5
Week 60 (n=327)	76.8
Week 72 (n=218)	77.5
Week 84 (n=119)	76.5
Week 96 (n=55)	89.1
Week 108 (n=42)	90.5

32. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving Health Assessment Questionnaire Disability Index (HAQ-DI) Clinical Remission
Measure Description	The Stanford Health Assessment Questionnaire Disability Index (HAQ-DI) is a patient completed questionnaire specific for rheumatoid arthritis, consisting of 20 questions in 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. There are 4 possible responses for each question: 0=without any difficulty, 1=with some difficulty, 2=with much difficulty and 3=unable to do. The score for each of the domains is the highest (worst) score in each domain. A patient must have a domain score for at least 6 of 8 domains to calculate a valid HAQ-DI score which is the sum of domain scores, divided by the number of domains that have a score for a total possible score minimum/maximum 0 (best) to 3 (worst). Clinical Remission is defined as a HAQ-DI score < 0.5.
Time Frame	Extension Weeks 12, 24, 36 ,48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available at the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Percentage of Participants Achieving Health Assessment Questionnaire Disability Index (HAQ-DI) Clinical Remission [units: percentage of participants]	
Week 12 (n=900)	32.1
Week 24 (n=770)	33.4
Week 36 (n=614)	34.5
Week 48 (n=446)	33.2
Week 60 (n=327)	37.0
Week 72 (n=218)	34.9
Week 84 (n=119)	38.7
Week 96 (n=55)	41.8
Week 108 (n=42)	50.0

33. Secondary Outcome Measure:

Measure Title	Change From Baseline in Quality of Life Short Form (SF-36): Physical Component Score
Measure Description	The SF-36 is a questionnaire used to assess physical functioning and is made up of eight domains: Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional and Mental Health. Transforming and standardizing these domains leads to the calculation of the Physical (PCS) and Mental (MCS) Component Summary measures. Scores ranging from 0 to 100, with 0=worst score (or quality of life) and 100=best score. A positive change from Baseline indicated improvement.
Time Frame	Core Baseline, Extension Weeks 12, 24, 36 ,48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available at both Baseline and the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Change From Baseline in Quality of Life Short Form (SF-36): Physical Component Score [units: score on a scale] Mean (Standard Deviation)	
Week 12 (n=885)	9.86 (10.548)
Week 24 (n=747)	9.30 (10.291)
Week 36 (n=607)	9.54 (10.580)
Week 48 (n=444)	9.82 (11.025)
Week 60 (n=324)	10.34 (10.837)
Week 72 (n=217)	10.38 (11.157)
Week 84 (n=117)	10.62 (10.378)
Week 96 (n=55)	13.06 (9.175)
Week 108 (n=42)	13.59 (9.932)

34. Secondary Outcome Measure:

Measure Title	Change From Baseline in Quality of Life Short Form (SF-36):Mental Component Score

Measure Description	The SF-36 is a questionnaire used to assess physical functioning and is made up of eight domains: Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional and Mental Health. Transforming and standardizing these domains leads to the calculation of the Physical (PCS) and Mental (MCS) Component Summary measures. Scores ranging from 0 to 100, with 0=worst score (or quality of life) and 100=best score. A positive change from Baseline indicated improvement.
Time Frame	Core Baseline, Extension Weeks 12, 24, 36 ,48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available for both Baseline and at the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Change From Baseline in Quality of Life Short Form (SF-36):Mental Component Score [units: score on a scale] Mean (Standard Deviation)	
Week 12 (n=885)	8.10 (14.426)
Week 24 (n=747)	8.37 (14.607)
Week 36 (n=607)	9.43 (14.311)
Week 48 (n=444)	8.27 (13.868)
Week 60 (n=324)	9.67 (13.91)
Week 72 (n=217)	8.30 (13.515)
Week 84 (n=117)	7.36 (14.466)
Week 96 (n=55)	10.57 (14.365)
Week 108 (n=42)	7.42 (12.272)

35. Secondary Outcome Measure:

Measure Title	Change From Baseline in FACIT-Fatigue Score
Measure Description	FACIT-F is a 13-item questionnaire. Patients scored each item on a 5-point scale: 0 (Not at all) to 4 (Very much). The larger the patient's response to the questions (with the exception of 2 negatively stated), the greater the patient'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 patient'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 patient's health status. A positive change from Baseline indicated improvement.
Time Frame	Core Baseline, Extension Weeks 12, 24, 36 ,48, 60, 72, 84, 96, 108
Safety Issue?	No

Analysis Population Description

LTE ITT population included all participants from the Core Study who received at least one dose of study drug in the Extension Study. "n" in each of the categories is the number of participants with data available for both Baseline and at the given time-point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Measured Values

	Tocilizumab
Number of Participants Analyzed	934
Change From Baseline in FACIT-Fatigue Score [units: score on a scale] Mean (Standard Deviation)	
Week 12 (n=900)	10.67 (11.287)
Week 24 (n=765)	10.70 (11.239)
Week 36 (n=613)	11.42 (11.826)
Week 48 (n=447)	11.02 (11.684)
Week 60 (n=326)	11.77 (11.660)
Week 72 (n=217)	10.71 (11.170)

	Tocilizumab
Week 84 (n=119)	10.63 (11.602)
Week 96 (n=55)	11.69 (10.374)
Week 108 (n=42)	10.56 (10.636)

Reported Adverse Events

Time Frame	108 Weeks
Additional Description	[Not specified]

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV, maximum dose not exceeding 800 mg in a single infusion, every 4 weeks for up to 104 weeks or up to 4 weeks after tocilizumab became commercially available in the respective country whichever occurred first.

Serious Adverse Events

	Tocilizumab
	Affected/At Risk (%)
Total	60/934 (6.42%)
Blood and lymphatic system disorders	
Thymus enlargement [A] †	1/934 (0.11%)
Cardiac disorders	
Atrial flutter [A] †	1/934 (0.11%)
Cardiac arrest [A] †	1/934 (0.11%)
Myocardial infarction [B] †	2/934 (0.21%)
Gastrointestinal disorders	
Colitis ischaemic [B] †	1/934 (0.11%)

	Tocilizumab
	Affected/At Risk (%)
Large intestine perforation [A] †	1/934 (0.11%)
Pancreatitis acute [A] †	1/934 (0.11%)
General disorders	
Asthenia [B] †	1/934 (0.11%)
Device breakage [A] †	1/934 (0.11%)
Device dislocation [A] †	1/934 (0.11%)
Non-cardiac chest pain [A] †	1/934 (0.11%)
Hepatobiliary disorders	
Cholecystitis [B] †	1/934 (0.11%)
Cholelithiasis [A] †	1/934 (0.11%)
Infections and infestations	
Abscess limb [A] †	1/934 (0.11%)
Appendicitis [A] †	1/934 (0.11%)
Campylobacter gastroenteritis [A] †	1/934 (0.11%)
Cellulitis [B] †	5/934 (0.54%)
Diverticulitis [A] †	2/934 (0.21%)
Epiglottitis [A] †	1/934 (0.11%)
Gastroenteritis [A] †	1/934 (0.11%)
Intervertebral discitis [A] †	1/934 (0.11%)
Periorbital cellulitis [A] †	1/934 (0.11%)
Pneumonia [A] †	5/934 (0.54%)
Postoperative wound infection [A] †	1/934 (0.11%)

	Tocilizumab
	Affected/At Risk (%)
Sepsis [A] †	1/934 (0.11%)
Staphylococcal infection [A] †	1/934 (0.11%)
Injury, poisoning and procedural complications	
Accidental Overdose [B] †	1/934 (0.11%)
Femur fracture [A] †	1/934 (0.11%)
Foreign body [A] †	1/934 (0.11%)
Joint dislocation [A] †	1/934 (0.11%)
Post procedural haemorrhage [A] †	1/934 (0.11%)
Metabolism and nutrition disorders	
Dehydration [A] †	1/934 (0.11%)
Musculoskeletal and connective tissue disorders	
Arthropathy [A] †	1/934 (0.11%)
Musculoskeletal chest pain [A] †	1/934 (0.11%)
Osteoarthritis [B] †	2/934 (0.21%)
Rheumatoid arthritis [A] †	1/934 (0.11%)
Spinal column stenosis [A] †	1/934 (0.11%)
Synovitis [A] †	1/934 (0.11%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Basal cell carcinoma [B] †	1/934 (0.11%)
Breast cancer [A] †	1/934 (0.11%)
Colon cancer [A] †	1/934 (0.11%)
Lung adenocarcinoma metastatic [A] †	1/934 (0.11%)
Pituitary tumour benign [A] †	1/934 (0.11%)

	Tocilizumab
	Affected/At Risk (%)
Renal oncocytoma [A] †	1/934 (0.11%)
Nervous system disorders	
Cerebral infarction [A] †	1/934 (0.11%)
Cerebrovascular accident [A] †	2/934 (0.21%)
Cognitive Disorder [A] †	1/934 (0.11%)
Demyelination [A] †	1/934 (0.11%)
Epilepsy [A] †	1/934 (0.11%)
Headache [A] †	1/934 (0.11%)
Intracranial aneurysm [A] †	1/934 (0.11%)
Syncope [A] †	1/934 (0.11%)
Transient Ischaemic attack [A] †	1/934 (0.11%)
Pregnancy, puerperium and perinatal conditions	
Abortion missed [A] †	1/934 (0.11%)
Respiratory, thoracic and mediastinal disorders	
Chronic obstructive pulmonary disease [B] †	1/934 (0.11%)
Dyspnoea [B] †	1/934 (0.11%)
Haemoptysis [A] †	1/934 (0.11%)
Hydrothorax [A] †	1/934 (0.11%)
Interstitial lung disease [A] †	1/934 (0.11%)
Surgical and medical procedures	
Central venous catheterisation [A] †	1/934 (0.11%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (15.0)
B Term from vocabulary, MedDRA (15,0)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Tocilizumab
	Affected/At Risk (%)
Total	141/934 (15.1%)
Infections and infestations	
Nasopharyngitis [A] †	89/934 (9.53%)
Upper respiratory tract infection [A] †	52/934 (5.57%)

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA (15.0)

Limitations and Caveats

[Not specified]

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 only after the first publication or presentation that involves the Overall Study. The 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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