ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 01/15/2015

A Study of Glucocorticoid Use to Evaluate Systematic Methylprednisolone Reduction in Patients With Rheumatoid Arthritis on Background RoActemra/Actemra (Tocilizumab) (ACT-ALONE)

This study has been completed.

Sponsor:	Hoffmann-La Roche
Collaborators:	
Information provided by (Responsible Party):	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT01219933

Purpose

This open-label, single-arm study will assess the use of glucocorticoids (GC) in daily clinical practice and will evaluate the dose reduction of glucocorticoids once low disease activity is achieved in patients with rheumatoid arthritis tre ated with GC and background RoActemra/Actemra (tocilizumab) 8mg/kg intravenously every 4 weeks. In the non-interventional phase, the use of GC in daily clinical Belgian practice will be evaluated and described. This period of maximum 6 mont hs will allow those patients to obtain the inclusion criteria for the secondary interventional phase. In the interventional phase, a systematic GC dose reductio n schedule will be evaluated in patients having achieved low disease activity wh ile receiving the same background therapy with RoActemra/Actemra 8 mg/kg. Methyl prednisolone will be given from a starting dose of >/= 1 mg to </=20 mg orally d aily and will be tapered down. The anticipated study duration is up to 13 months

Condition	Intervention	Phase
Rheumatoid Arthritis	Drug: methylprednisolone Drug: tocilizumab [RoActemra/Actemra]	Phase 4

Study Type: Interventional
Study Design: Treatment, Single Group Assignment, Open Label, Non-Randomized, Safety/Efficacy Study
Official Title: An Open-label, Single-arm Study to Describe Glucocorticoid Use in Rheumatoid Arthritis Patients Treated With Tocilizumab in Daily Clinical Practice and to Evaluate Systematic Glucocorticoid Dose Reduction Once Low Disease Activity is Reached (ACT-ALONE)

Further study details as provided by Hoffmann-La Roche:

Primary Outcome Measure:

- Median GC Dose Taken During the Noninterventional Phase [Time Frame: V1 and V2 (up to 6 months after V1)] [Designated as safety issue: No]
  During the noninterventional phase of the study participants received GC as prescribed by the physician. Doses of all GC administered are expressed as MP equivalents.
- Number of Participants With GC Switches During the Noninterventional Phase [Time Frame: V1 and V2 (up to 6 months after V1)] [Designated as safety issue: No]
  During the noninterventional phase of the study, once LDA was achieved, GC was switched to MP tablets.
- Type of GC Taken at the End of the Noninterventional Phase [Time Frame: V1 and V2 (up to 6 months after V1)] [Designated as safety issue: No]
  During the noninterventional phase of the study participants received GC as prescribed by the physician.
- Percentage of Participants in the Interventional Phase Who Achieved LDA and Discontinued Oral GC Within 20 Weeks [Time Frame: Visits 3 (7 months), 4 (8 months), 5 (9 months), 6 (10 months), 7 (11 months), and 8 (12 months)] [Designated as safety issue: No]
  The percentage of participants with rheumatoid arthritis (RA) with LDA was defined as DAS28 ≤3.2, able to discontinue oral GC within 20 weeks and at the latest at V8, confirmed at the Consolidation Visit without loss of clinical response defined as DAS28 (CRP) >3.2.

Secondary Outcome Measures:

- Percentage of Participants Able to Acheive LDA Assessed Using DAS28 While Receiving Oral GC on Background Tocilizumab Treatment During the Noninterventional Phase [Time Frame: V1 and V2 (up to 6 months after V1)] [Designated as safety issue: No]
  DAS28 was calculated from the number of swollen joints and tender joints using the 28-joint count, the CRP and Patient's Global Assessment (PtGA) of disease activity (participant rated arthritis activity assessment with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity). DAS28 ≤3.2 and oral GC intake with MP equivalent dose of ≥1 mg and ≤20 mg/day= LDA.
- Percentage of Participants Acheiving Remission Assessed Using DAS28 While Receiving Oral GC on Background TocilizumabTreatment During the Noninterventional Phase [Time Frame: V1 and V2 (up to 6 months after V1)] [Designated as safety issue: No]
  DAS28 was calculated from the number of swollen joints and tender joints using the 28-joint count, the CRP and PtGA of disease activity (participant rated arthritis activity assessment with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity). DAS28 <2.6 = remission.
- Percentage of Participants With Erosions During the NonInterventional Phase [Time Frame: V1 and V2 (up to 6 months after V1)] [Designated as safety issue: No]
  In RA, the presence, number and size of bone erosions and the number of joints with erosions on conventional radiographs (CRs) are hallmarks for diagnosis, staging and prediction of damage progression and are used for treatment monitoring in randomized controlled studies.
- Number of Erosions During the NonInterventional Phase [Time Frame: V1 and V2 (up to 6 months after V1)] [Designated as safety issue: No]
  In RA, the presence, number, and size of bone erosions and the number of joints with erosions on CRs are hallmarks for diagnosis, staging and prediction of damage progression and are used for treatment monitoring in randomized controlled studies.
- Percentage of Participants Positive for Rheumatoid Factor (RF) During the Noninterventional Phase [Time Frame: V1 and V2 (up to 6 months after V1)] [Designated as safety issue: No]
  RF is the auto antibody directed against immunoglobulin G (IgG) and its concentration is observed in human serum or plasma. RF value higher than 20 units per milliliter (U/mL) is considered positive.
- Percentage of Participants Positive for Anti-cyclic Citrullinated Peptide (Anti-CCP) Antibody During the Noninterventional Phase [Time Frame: V1 and V2 (up to 6 months after V1)] [Designated as safety issue: No]
  Anti-CCP antibodies are important markers of bone erosion in RA. Anti-CCP antibodies were classified as positive if >7 U/mL.
- Health Assessment Questionnaire Disability Index (HAQ-DI) During the Noninterventional Phase [Time Frame: V1 and V2 (up to 6 months after V1)] [Designated as safety issue: No]
  HAQ-DI is a self-reported, valid assessment of functional disability in RA. Assessed based on ability of participants to perform daily activities in 8 categories: dressing, arising, eating, walking, reaching, gripping, hygiene, and carrying out daily activities. HAQ-DI score range: 0-3: without any difficulty=0, with some difficulty=1, with much difficulty=2, unable to do=3. HAQ total scores expressed as overall mean score with range 0-3:

0-0.25=normal functioning; 0.25-0.5=mild functional limitation; 0.5-1=moderate functional limitation; more than 1=significant functional limitation. Timepoint was V2, or before V2 for participants withdrawn before V2.

- DAS28-CRP During the Noninterventional Phase [Time Frame: V1 and V2 (up to 6 months after V1)] [Designated as safety issue: No]
  DAS28-CRP was calculated from the swollen joint count (SJC) and tender joint count (TJC) using the 28-joint count and CRP (mg/L). Total score range: 0 to 10, higher score indicated more disease activity. DAS28-CRP ≤3.2=LDA and >3.2 to 5.1=moderate to high disease activity, and DAS28-CRP <2.6=remission. Timepoint was V2, or before V2 for participants withdrawn before V2; DAS28-CRP values indicated in the Case Report Form (CRF) were recalculated by the data manager. The recalculated values were used in the statistical analyses.
- DAS28-ESR During the Noninterventional Phase [Time Frame: V1 and V2 (up to 6 months after V1)] [Designated as safety issue: No]
  DAS28-ESR was calculated from the SJC and TJC using the 28 joints count and ESR (millimeters per hour [mm/hr]). Total score range: 0 to 9.4, higher score indicated more disease activity. DAS28-ESR ≤3.2=LDA and >3.2 to 5.1=moderate to high disease activity, and DAS28-ESR <2.6=remission. Timepoint was V2, or before V2 for participants withdrawn before V2; DAS28-ESR values indicated in the CRF were recalculated by the data manager. The recalculated values were used in the statistical analyses.
- Clinical Disease Activity Index (CDAI) During the Noninterventional Phase [Time Frame: V1 and V2 (up to 6 months after V1)] [Designated as safety issue: No]
  The CDAI is the numerical sum of 4 outcome parameters: TJC and SJC based on a 28-joint assessment, PtGA and Physician Global Assessment (PGA) of disease assessed on 0-100 mm Visual analog scale (VAS); higher scores=greater affection due to disease activity. CDAI total score=0-76. CDAI ≤2.8=disease remission, >2.8 to 10=LDA, >10 to 22=moderate disease activity, and >22=high disease activity.
- Median Time Interval Between V1 and V2 [Time Frame: V1 and V2 (up to 6 months after V1)] [Designated as safety issue: No]
  The noninterventional phase was planned to last for a maximum of 6 months per participant. The time between V1 and V2 was measured in months.
- Median Dose of Tocilizumab During the Noninterventional Phase [Time Frame: V1 and V2 (up to 6 months after V1)] [Designated as safety issue: No]
- Number of Participants With Changes in Tocilizumab Dose During the Noninterventional Phase [Time Frame: V1 and V2 (up to 6 months after V1)] [Designated as safety issue: No]
  The dose of tocilizumab could have been reduced from the recommended 8 mg/kg to 4 mg/kg in participants in the case of adverse events.
- Percentage of Participants With Changes in RA Treatment During the Noninterventional Phase [Time Frame: V1 and V2 (up to 6 months after V1)] [Designated as safety issue: No]
- Percentage of Participants Able to Start the GC Reduction Phase at V3 [Time Frame: V3 (7 months)] [Designated as safety issue: No]
  All participants who maintained LDA (defined as DAS28-CRP ≤3.2) from V2 to V3 were included in the interventional phase for reduction of GC.
- Percentage of Participants Able to Reduce Oral GCs by ≥50 Percent (%) During the Interventional Phase by V9 [Time Frame: V9 (24 weeks after V3)] [Designated as safety issue: No]
- Percentage of Participants Able to Discontinue GCs During the Interventional Phase by V9 [Time Frame: V9 (24 weeks after V3)] [Designated as safety issue: No]
- Time-Averaged GC Dose Changes During the Interventional Phase [Time Frame: V3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)] [Designated as safety issue: No]
  Area Under the Curve (AUC) of GC dose during the interventional phase was determined using the trapezoidal method and was calculated as: AUC = sigma(Ti+1 - Ti) x [(Di+1+Di)/2] With Di=dosage at time Ti It corresponds to the total GC dose received between Baseline (visit 3) and visit 9 and has been calculated only for the 30 patients achieving visit 9.
- DAS28-CRP During the Interventional Phase [Time Frame: V3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)] [Designated as safety issue: No]
  DAS28-CRP was calculated from the SJC and TJC using the 28-joint count and CRP (mg/L). Total score range: 0 to 10, higher score indicated more disease activity. DAS28-CRP) ≤3.2=LDA and >3.2 to 5.1=moderate to high disease activity, and DAS28-CRP <2.6=remission. DAS28-CRP values indicated in the CRF were recalculated by the data manager. The cumulative DAS28 (CRP) value (AUC method) was performed using the calculated DAS28. The recalculated values were used in the statistical analyses.
- HAQ-DI During the Interventional Phase [Time Frame: Visit 3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)] [Designated as safety issue: No]

HAQ-DI is a self-reported, valid assessment of functional disability in RA. Assessed based on ability of participants to perform daily activities in 8 categories: dressing, arising, eating, walking, reaching, gripping, hygiene, and carrying out daily activities. HAQ-DI score range: 0-3: without any difficulty=0, with some difficulty=1, with much difficulty=2, unable to do=3. HAQ total scores expressed as overall mean score with range 0-3: 0-0.25=normal functioning; 0.25-0.5=mild functional limitation; 0.5-1=moderate functional limitation; more than 1=significant functional limitation. V3, CV, and the change from V3 to CV was determined.

- VAS-Physician's Global Assessment of Disease Activity (GDA) During the Interventional Phase [Time Frame: V3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)] [Designated as safety issue: No]

  Physician's were asked to determine the overall GDA for each participant using a 100-mm VAS, where 0=no disease activity and 100=maximum disease activity. The physician marked the line corresponding to their assessment and the distance from the left edge was measured. V3, CV, and the change from V3 to CV was determined.
- VAS for Pain (VAS-Pain) During the Interventional Phase [Time Frame: V3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)] [Designated as safety issue: No]

  Participants were asked to mark the line corresponding to the intensity of their pain on a 100-mm VAS, where 0=no pain and 100=worst possible pain. The distance from the left edge was measured. Change = V3 mean minus CV mean.
- SJC and TJC During the Interventional Phase [Time Frame: V3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)] [Designated as safety issue: No]

  TJC and SJC were assessed for 28 joints. An assessment of 28 joints for swelling and tenderness was made. Joints were assessed and classified as swollen (1)/not swollen (0) and tender (1)/not tender (0) by pressure and joint manipulation on physical examination for a total score range of 0-28. Higher scores indicated greater disease activity (tenderness/swelling). V3, CV, and the change from V3 to CV was determined.
- Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Score During the Interventional Phase [Time Frame: V3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)] [Designated as safety issue: No]

  FACIT-F is a 13-item questionnaire. Participants scored each item on a 5-point scale: 0 (not at all) to 4 (very much). The larger the participant's response to the questions (with the exception of 2 negatively stated), the greater the participant's fatigue. For all questions, except for the 2 negatively stated ones, the code was reversed and a new score was calculated as (4 minus the participant's response). The sum of all responses resulted in the FACIT-F score for a total possible score of 0 (worse score) to 52 (better score). V3, CV, and the change from V3 to CV was determined.
- Short-Form 36 (SF-36) Mental Component Score (MCS) and Physical Component Score (PCS) During the Interventional Phase [Time Frame: V3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)] [Designated as safety issue: No]

  36-Item Short-Form Health Survey (SF-36) is a standardized survey evaluating 8 aspects of functional health and well-being: physical and social functioning, physical and emotional role limitations, bodily pain, general health, vitality, mental health. These 8 aspects can also be summarized as physical and mental component scores (PCS and MCS). Total of 11 variables were analyzed (8 subscales, 2 composite subscales and Question 2 "how would you rate your health in general now?" (range 1= better, 5= worst). The score for a section is an average of the individual question scores, which are scaled 0-100 (100=highest level of functioning). Higher scores reflect higher quality of life. V3, CV, and the change from V3 to CV was determined.
- SF-36 Subscale Scores During the Interventional Phase [Time Frame: V3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)] [Designated as safety issue: No]

  SF-36 is a standardized survey evaluating 8 aspects of functional health and well-being: physical and social functioning, physical and emotional role limitations, bodily pain, general health, vitality, mental health. These 8 aspects can also be summarized as physical and mental component scores (PCS and MCS). Total of 11 variables were analyzed (8 subscales, 2 composite subscales and Question 2 "how would you rate your health in general now?" (range 1= better, 5= worst). The score for a section is an average of the individual question scores, which are scaled 0-100 (100=highest level of functioning). Higher scores reflect higher quality of life. V3, CV, and the change from V3 to CV was determined.
- CDAI Score During the Interventional Phase [Time Frame: V3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)] [Designated as safety issue: No]

  The CDAI is the numerical sum of 4 outcome parameters: TJC and SJC based on a 28-joint assessment, PtGA and PGA assessed on 0-100 mm VAS; higher scores=greater affection due to disease activity. CDAI total score=0-76. CDAI ≤2.8=disease remission, >2.8 to 10=LDA, >10 to 22=moderate disease activity, and >22=high disease activity. V3, CV, and the change from V3 to CV was determined.

- Percentage of Participants With LDA or Remission During the Interventional Phase Assessed Using CDAI [Time Frame: Visits 3 (7 months), 4 (8 months), 5 (9 months), 6 (10 months), 7 (11 months), 8 (12 months), and 9 (24 weeks after V3) or CV (4 weeks after GC-free status, maximum of 24 weeks after V3)] [Designated as safety issue: No]
  The CDAI is the numerical sum of 4 outcome parameters: TJC and SJC based on a 28-joint assessment, PtGA and PGA assessed on 0-100 mm VAS; higher scores=greater affection due to disease activity. CDAI total score=0-76. CDAI ≤2.8=disease remission and >2.8 to 10=LDA.
- Percentage of Participants With LDA or Remission During the Interventional Phase Assessed Using DAS28-CRP [Time Frame: Visits 3 (7 months), 4 (8 months), 5 (9 months), 6 (10 months), 7 (11 months), 8 (12 months), 9 (24 weeks after V3) or CV (4 weeks after GC-free status, maximum of 24 weeks after V3)] [Designated as safety issue: No]
  DAS28 calculated from the number of swollen joints (SJC) and tender joints (TJC) using the 28 joint count, the CRP and PtGA of disease activity (participant rated arthritis activity assessment with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity). DAS28-CRP ≤3.2 and oral GC intake with MP equivalent dose of ≥1 mg and ≤20 mg/day=LDA; DAS28 <2.6 = remission.

Enrollment: 68
Study Start Date: January 2011
Primary Completion Date: March 2013
Study Completion Date: March 2013

Arms	Assigned Interventions
Experimental: 1	Drug: methylprednisolone starting dose >/= 1 mg and </= 20 mg orally daily, according to dose-reduction schedule Drug: tocilizumab [RoActemra/Actemra] background therapy: 8 mg/kg iv every 4 weeks

Eligibility

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

Criteria

Inclusion Criteria:

Non-interventional phase

- Adult patients, >/=18 years of age
- Moderate to severe active rheumatoid arthritis defined as Disease Activity Score using 28-joint count (DAS28) >/=5.1
- Patients with inadequate clinical response to a current treatment with 2 or more non-biologic disease-modifying anti-rheumatic drugs (DMARDs), one of them being methotrexate (MTX) optimally administered during a period of more than 3 months or inadequate response to a current anti-TNF therapy
- Current use of oral glucocorticoids started at least 4 weeks prior to enrolment Interventional phase
- Patients enrolled in the non-interventional phase
- Patients with low disease activity defined as DAS28 </=3.2 at Visit 2
- Use of oral glucocorticoids with methylprednisolone equivalent dose of >/=1mg and </=20mg/day at Visit 2

Exclusion Criteria:

Non-interventional & interventional phase

- Rheumatic autoimmune disease other than rheumatoid arthritis, or significant systemic involvement secondary to rheumatoid arthritis
- Functional class IV as defined by the American College of Rheumatology (ACR) Classification of Functional Status in rheumatoid arthritis
- Prior history or current inflammatory joint disease other than rheumatoid arthritis (e.g. gout)

Contacts and Locations

Locations

Belgium

Aalst, Belgium, 9300
Brugge, Belgium, 8000
Bruxelles, Belgium, 1070
Bruxelles, Belgium, 1020
Charleroi, Belgium, 6000
Edegem, Belgium, 2650
Genk, Belgium, 3600
Genk, Belgium, 3600
Gilly, Belgium, 6060
Godinne, Belgium, 5530
Haine-Saint-Paul, Belgium, 7100
Heusy, Belgium, 4802
Kortrijk, Belgium, 8500
La Louviere, Belgium, 7100
Liege, Belgium, 4000
Oostende, Belgium, 8400
Wilrijk, Belgium, 2610

Investigators

Study Director:	Clinical Trials	Hoffmann-La Roche

More Information

Responsible Party:	Hoffmann-La Roche
Study ID Numbers:	ML25252 2010-019694-15
Health Authority:	Belgium: Ministry of Health

Participant Flow

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 milligrams per kilogram (mg/kg) intravenously (IV) once every 4 weeks and methotrexate (MTX) 7.5 to 25 mg per week (mg/week; per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received an oral glucocorticoid (GC; no product/dose limitation) until low disease activity (LDA; defined as Disease Activity Score Based on 28-Joint Count and C-reactive protein [DAS28-CRP] less than or equal to [≤]3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to methylprednisolone (MP) tablets, by mouth (PO). MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be greater than or equal to [≥]1 mg and ≤20 mg per day [mg/day]), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment

Overall Study

	Tocilizumab
Started	68
Completed	30
Not Completed	38
Adverse Event	8
No LDA reached	5
No LDA maintained	7
Lost to Follow-up	3
GC free	1
Withdrawal by Subject	5
Protocol Violation	8
Lack of Efficacy	1

Baseline Characteristics

Analysis Population Description

Safety observational (obs): all participants included in the study who were eligible for the study at Visit (V) 1.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Baseline Measures

	Tocilizumab
Number of Participants	68
Age, Continuous [units: years] Mean (Standard Deviation)	58.0 (12.2)
Gender, Male/Female [units: participants]	
Female	47
Male	21

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Median GC Dose Taken During the Noninterventional Phase
Measure Description	During the noninterventional phase of the study participants received GC as prescribed by the physician. Doses of all GC administered are expressed as MP equivalents.
Time Frame	V1 and V2 (up to 6 months after V1)
Safety Issue?	No

Analysis Population Description

Safety obs population; n (number) equals (=) number of participants analyzed for a given parameter at a specified timepoint

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	68
Median GC Dose Taken During the Noninterventional Phase [units: mg] Median (Full Range)	
Start dose V1 (n=68)	6 (2 to 40)
Start dose (V1) for Interventional phase (n=50)	6 (2 to 32)
Stop dose (V2; n=50)	4 (1 to 16)
Change from start to stop (n=50)	0 (-24 to 2)
Cumulative dose from V1 to V2 (n=45)	320 (58 to 2688)

2. Primary Outcome Measure:

Measure Title	Number of Participants With GC Switches During the Noninterventional Phase
Measure Description	During the noninterventional phase of the study, once LDA was achieved, GC was switched to MP tablets.
Time Frame	V1 and V2 (up to 6 months after V1)
Safety Issue?	No

Analysis Population Description

Safety obs population; n=number of participants analyzed for a given parameter at a specified timepoint

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	50
Number of Participants With GC Switches During the Noninterventional Phase [units: participants]	0

3. Primary Outcome Measure:

Measure Title	Type of GC Taken at the End of the Noninterventional Phase
Measure Description	During the noninterventional phase of the study participants received GC as prescribed by the physician.
Time Frame	V1 and V2 (up to 6 months after V1)
Safety Issue?	No

Analysis Population Description

Safety obs population; n=number of participants analyzed for a given parameter at a specified timepoint

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	50
Type of GC Taken at the End of the Noninterventional Phase [units: percentage of participants]	
MP	70.0
Prednisolone	28.0
Prednisone	2.0

4. Primary Outcome Measure:

Measure Title	Percentage of Participants in the Interventional Phase Who Achieved LDA and Discontinued Oral GC Within 20 Weeks
Measure Description	The percentage of participants with rheumatoid arthritis (RA) with LDA was defined as DAS28 ≤3.2, able to discontinue oral GC within 20 weeks and at the latest at V8, confirmed at the Consolidation Visit without loss of clinical response defined as DAS28 (CRP) >3.2.
Time Frame	Visits 3 (7 months), 4 (8 months), 5 (9 months), 6 (10 months), 7 (11 months), and 8 (12 months)
Safety Issue?	No

Analysis Population Description

Intent-to-Treat (ITT) population: all participants included in the interventional GC reduction phase of the study.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	43

	Tocilizumab
Percentage of Participants in the Interventional Phase Who Achieved LDA and Discontinued Oral GC Within 20 Weeks [units: percentage of participants] Number (95% Confidence Interval)	58.1 (42.1 to 73.0)

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants Able to Acheive LDA Assessed Using DAS28 While Receiving Oral GC on Background Tocilizumab Treatment During the Noninterventional Phase
Measure Description	DAS28 was calculated from the number of swollen joints and tender joints using the 28-joint count, the CRP and Patient's Global Assessment (PtGA) of disease activity (participant rated arthritis activity assessment with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity). DAS28 ≤3.2 and oral GC intake with MP equivalent dose of ≥1 mg and ≤20 mg/day= LDA.
Time Frame	V1 and V2 (up to 6 months after V1)
Safety Issue?	No

Analysis Population Description

Safety Obs Population

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	68
Percentage of Participants Able to Acheive LDA Assessed Using DAS28 While Receiving Oral GC on Background Tocilizumab Treatment During the Noninterventional Phase	72.1

	Tocilizumab
[units: percentage of participants]	

6. Secondary Outcome Measure:

Measure Title	Percentage of Participants Acheiving Remission Assessed Using DAS28 While Receiving Oral GC on Background TocilizumabTreatment During the Noninterventional Phase
Measure Description	DAS28 was calculated from the number of swollen joints and tender joints using the 28-joint count, the CRP and PtGA of disease activity (participant rated arthritis activity assessment with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity). DAS28 <2.6 = remission.
Time Frame	V1 and V2 (up to 6 months after V1)
Safety Issue?	No

Analysis Population Description

Safety Obs population

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	68
Percentage of Participants Acheiving Remission Assessed Using DAS28 While Receiving Oral GC on Background TocilizumabTreatment During the Noninterventional Phase [units: percentage of participants]	41.2

7. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Erosions During the NonInterventional Phase
Measure Description	In RA, the presence, number and size of bone erosions and the number of joints with erosions on conventional radiographs (CRs) are hallmarks for diagnosis, staging and prediction of damage progression and are used for treatment monitoring in randomized controlled studies.
Time Frame	V1 and V2 (up to 6 months after V1)
Safety Issue?	No

Analysis Population Description

Safety Obs Population; n=number of participants analyzed for the given parameter at the specified timepoint.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	57
Percentage of Participants With Erosions During the NonInterventional Phase [units: percentage of participants]	
V1 (n=57)	47.4
Between V1 and V2 (n=36)	41.7

8. Secondary Outcome Measure:

Measure Title	Number of Erosions During the NonInterventional Phase
Measure Description	In RA, the presence, number, and size of bone erosions and the number of joints with erosions on CRs are hallmarks for diagnosis, staging and prediction of damage progression and are used for treatment monitoring in randomized controlled studies.

Time Frame	V1 and V2 (up to 6 months after V1)
Safety Issue?	No

Analysis Population Description

Safety Obs Population; n=number of participants analyzed for the given parameter at the specified timepoint.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	11
Number of Erosions During the NonInterventional Phase [units: erosions] Mean (Standard Deviation)	
V1 (n=11)	5.1 (6.0)
Between V1 and V2 (n=6)	3.2 (2.3)

9. Secondary Outcome Measure:

Measure Title	Percentage of Participants Positive for Rheumatoid Factor (RF) During the Noninterventional Phase
Measure Description	RF is the auto antibody directed against immunoglobulin G (IgG) and its concentration is observed in human serum or plasma. RF value higher than 20 units per milliliter (U/mL) is considered positive.
Time Frame	V1 and V2 (up to 6 months after V1)
Safety Issue?	No

Analysis Population Description

Safety Obs Population; n=number of participants analyzed for the given parameter at the specified timepoint.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	39
Percentage of Participants Positive for Rheumatoid Factor (RF) During the Noninterventional Phase [units: percentage of participants]	
V1 (n=39)	56.4
Between V1 and V2 (n=21)	52.4

10. Secondary Outcome Measure:

Measure Title	Percentage of Participants Positive for Anti-cyclic Citrullinated Peptide (Anti-CCP) Antibody During the Noninterventional Phase
Measure Description	Anti-CCP antibodies are important markers of bone erosion in RA. Anti-CCP antibodies were classified as positive if >7 U/mL.
Time Frame	V1 and V2 (up to 6 months after V1)
Safety Issue?	No

Analysis Population Description

Safety Obs Population; n=number of participants analyzed for the given parameter at the specified timepoint.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	20
Percentage of Participants Positive for Anti-cyclic Citrullinated Peptide (Anti-CCP) Antibody During the Noninterventional Phase [units: percentage of participants]	
V1 (n=20)	75.0
Between V1 and V2 (n=6)	83.3

11. Secondary Outcome Measure:

Measure Title	Health Assessment Questionnaire Disability Index (HAQ-DI) During the Noninterventional Phase
Measure Description	HAQ-DI is a self-reported, valid assessment of functional disability in RA. Assessed based on ability of participants to perform daily activities in 8 categories: dressing, arising, eating, walking, reaching, gripping, hygiene, and carrying out daily activities. HAQ-DI score range: 0-3: without any difficulty=0, with some difficulty=1, with much difficulty=2, unable to do=3. HAQ total scores expressed as overall mean score with range 0-3: 0-0.25=normal functioning; 0.25-0.5=mild functional limitation; 0.5-1=moderate functional limitation; more than 1=significant functional limitation. Timepoint was V2, or before V2 for participants withdrawn before V2.
Time Frame	V1 and V2 (up to 6 months after V1)
Safety Issue?	No

Analysis Population Description

Safety Obs Population; n=number of participants analyzed for the given parameter at the specified timepoint.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	66
Health Assessment Questionnaire Disability Index (HAQ-DI) During the Noninterventional Phase [units: units on a scale] Mean (Standard Deviation)	
V1 (n=66)	1.7 (0.6)
V2 (n=61)	1.2 (0.7)
Change from V1 to V2 (n=60)	-0.5 (0.6)

12. Secondary Outcome Measure:

Measure Title	DAS28-CRP During the Noninterventional Phase
Measure Description	DAS28-CRP was calculated from the swollen joint count (SJC) and tender joint count (TJC) using the 28-joint count and CRP (mg/L). Total score range: 0 to 10, higher score indicated more disease activity. DAS28-CRP ≤3.2=LDA and >3.2 to 5.1=moderate to high disease activity, and DAS28-CRP <2.6=remission. Timepoint was V2, or before V2 for participants withdrawn before V2; DAS28-CRP values indicated in the Case Report Form (CRF) were recalculated by the data manager. The recalculated values were used in the statistical analyses.
Time Frame	V1 and V2 (up to 6 months after V1)
Safety Issue?	No

Analysis Population Description

Safety Obs Population; n=number of participants analyzed for the given parameter at the specified timepoint.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	67
DAS28-CRP During the Noninterventional Phase [units: units on a scale] Mean (Standard Deviation)	
V1 (n=67)	5.4 (1.0)
V2 (n=66)	2.9 (1.1)
Change from V1 to V2 (n=65)	-2.5 (1.3)

13. Secondary Outcome Measure:

Measure Title	DAS28-ESR During the Noninterventional Phase
Measure Description	DAS28-ESR was calculated from the SJC and TJC using the 28 joints count and ESR (millimeters per hour [mm/hr]). Total score range: 0 to 9.4, higher score indicated more disease activity. DAS28-ESR ≤3.2=LDA and >3.2 to 5.1=moderate to high disease activity, and DAS28-ESR <2.6=remission. Timepoint was V2, or before V2 for participants withdrawn before V2; DAS28-ESR values indicated in the CRF were recalculated by the data manager. The recalculated values were used in the statistical analyses.
Time Frame	V1 and V2 (up to 6 months after V1)
Safety Issue?	No

Analysis Population Description

Safety Obs Population; n=number of participants analyzed for the given parameter at the specified timepoint.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	62
DAS28-ESR During the Noninterventional Phase [units: units on a scale] Mean (Standard Deviation)	
V1 (n=62)	5.8 (1.0)
V2 (n=52)	3.3 (1.4)
Change from V1 to V2 (n=50)	-2.7 (1.3)

14. Secondary Outcome Measure:

Measure Title	Clinical Disease Activity Index (CDAI) During the Noninterventional Phase
Measure Description	The CDAI is the numerical sum of 4 outcome parameters: TJC and SJC based on a 28-joint assessment, PtGA and Physician Global Assessment (PGA) of disease assessed on 0-100 mm Visual analog scale (VAS); higher scores=greater affection due to disease activity. CDAI total score=0-76. CDAI ≤2.8=disease remission, >2.8 to 10=LDA, >10 to 22=moderate disease activity, and >22=high disease activity.
Time Frame	V1 and V2 (up to 6 months after V1)
Safety Issue?	No

Analysis Population Description

Safety Obs Population; n=number of participants analyzed for the given parameter at the specified timepoint.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	62
Clinical Disease Activity Index (CDAI) During the Noninterventional Phase [units: units on a scale] Mean (Standard Deviation)	
V1 (n=62)	33.8 (12.2)
V2 (n=52)	14.6 (10.3)
Change from V1 to V2 (n=50)	-20.4 (13.7)

15. Secondary Outcome Measure:

Measure Title	Median Time Interval Between V1 and V2
Measure Description	The noninterventional phase was planned to last for a maximum of 6 months per participant. The time between V1 and V2 was measured in months.
Time Frame	V1 and V2 (up to 6 months after V1)
Safety Issue?	No

Analysis Population Description

Safety Obs Population

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	50
Median Time Interval Between V1 and V2 [units: months] Median (Full Range)	2.3 (0.8 to 5.9)

16. Secondary Outcome Measure:

Measure Title	Median Dose of Tocilizumab During the Noninterventional Phase
Measure Description	
Time Frame	V1 and V2 (up to 6 months after V1)
Safety Issue?	No

Analysis Population Description
Safety Obs Population

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	50
Median Dose of Tocilizumab During the Noninterventional Phase [units: mg/kg] Median (Full Range)	8.0 (8.0 to 8.0)

17. Secondary Outcome Measure:

Measure Title	Number of Participants With Changes in Tocilizumab Dose During the Noninterventional Phase
Measure Description	The dose of tocilizumab could have been reduced from the recommended 8 mg/kg to 4 mg/kg in participants in the case of adverse events.
Time Frame	V1 and V2 (up to 6 months after V1)
Safety Issue?	No

Analysis Population Description

Safety Obs Population

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	68
Number of Participants With Changes in Tocilizumab Dose During the Noninterventional Phase [units: participants]	1

18. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Changes in RA Treatment During the Noninterventional Phase
Measure Description	
Time Frame	V1 and V2 (up to 6 months after V1)
Safety Issue?	No

Analysis Population Description
Safety Obs Population

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	66
Percentage of Participants With Changes in RA Treatment During the Noninterventional Phase [units: percentage of participants]	15.2

19. Secondary Outcome Measure:

Measure Title	Percentage of Participants Able to Start the GC Reduction Phase at V3
Measure Description	All participants who maintained LDA (defined as DAS28-CRP ≤3.2) from V2 to V3 were included in the interventional phase for reduction of GC.
Time Frame	V3 (7 months)
Safety Issue?	No

Analysis Population Description

Safety Int (intervention) run-in: all participants eligible to enter the interventional phase at V2 and who had taken at least 1 dose of MP.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	49
Percentage of Participants Able to Start the GC Reduction Phase at V3 [units: percentage of participants] Number (95% Confidence Interval)	87.8 (75.2 to 95.4)

20. Secondary Outcome Measure:

Measure Title	Percentage of Participants Able to Reduce Oral GCs by ≥50 Percent (%) During the Interventional Phase by V9
Measure Description	
Time Frame	V9 (24 weeks after V3)
Safety Issue?	No

Analysis Population Description

Safety Int run-in; only those participants who completed the study at V9 were included in the analysis.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	30
Percentage of Participants Able to Reduce Oral GCs by ≥50 Percent (%) During the Interventional Phase by V9 [units: percentage of participants] Number (95% Confidence Interval)	93.3 (77.9 to 99.2)

21. Secondary Outcome Measure:

Measure Title	Percentage of Participants Able to Discontinue GCs During the Interventional Phase by V9
Measure Description	
Time Frame	V9 (24 weeks after V3)
Safety Issue?	No

Analysis Population Description

Safety Int run-in; pnly those participants who completed the study at V9 were included in analysis.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	30
Percentage of Participants Able to Discontinue GCs During the Interventional Phase by V9 [units: percentage of participants] Number (95% Confidence Interval)	3.3 (0.1 to 17.2)

22. Secondary Outcome Measure:

Measure Title	Time-Averaged GC Dose Changes During the Interventional Phase
Measure Description	Area Under the Curve (AUC) of GC dose during the interventional phase was determined using the trapezoidal method and was calculated as: AUC = sigma(Ti+1 - Ti) x [(Di+1+Di)/2] With Di=dosage at time Ti It corresponds to the total GC dose received between Baseline (visit 3) and visit 9 and has been calculated only for the 30 patients achieving visit 9.
Time Frame	V3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)
Safety Issue?	No

Analysis Population Description

Safety Int run-in; only participants who completed the study were included in the analysis.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	30
Time-Averaged GC Dose Changes During the Interventional Phase [units: mg] Mean (Standard Deviation)	341.8 (364.2)

23. Secondary Outcome Measure:

Measure Title	DAS28-CRP During the Interventional Phase
Measure Description	DAS28-CRP was calculated from the SJC and TJC using the 28-joint count and CRP (mg/L). Total score range: 0 to 10, higher score indicated more disease activity. DAS28-CRP) ≤3.2=LDA and >3.2 to 5.1=moderate to high disease activity, and DAS28-CRP <2.6=remission. DAS28-CRP values indicated in the CRF were recalculated by the data manager. The cumulative DAS28 (CRP) value (AUC method) was performed using the calculated DAS28. The recalculated values were used in the statistical analyses.
Time Frame	V3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)
Safety Issue?	No

Analysis Population Description

Safety Obs Population; n=number of participants analyzed for the given parameter at the specified timepoint.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	42
DAS28-CRP During the Interventional Phase [units: units on a scale] Mean (Standard Deviation)	
V3 (n=42)	2.2 (0.7)
CV (n=27)	2.3 (0.8)
Change from V3 to CV (n=27)	0.2 (0.8)

24. Secondary Outcome Measure:

Measure Title	HAQ-DI During the Interventional Phase
Measure Description	HAQ-DI is a self-reported, valid assessment of functional disability in RA. Assessed based on ability of participants to perform daily activities in 8 categories: dressing, arising, eating, walking, reaching, gripping, hygiene, and carrying out daily activities. HAQ-DI score range: 0-3: without any difficulty=0, with some difficulty=1, with much difficulty=2, unable to do=3. HAQ total scores expressed as overall mean score with range 0-3: 0-0.25=normal functioning; 0.25-0.5=mild functional limitation; 0.5-1=moderate functional limitation; more than 1=significant functional limitation. V3, CV, and the change from V3 to CV was determined.
Time Frame	Visit 3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)
Safety Issue?	No

Analysis Population Description

Safety Obs Population; n=number of participants analyzed for the given parameter at the specified timepoint.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	41
HAQ-DI During the Interventional Phase [units: units on a scale] Mean (Standard Deviation)	
V3 (n=41)	1.0 (0.7)
CV (n=28)	0.8 (0.7)
Change from V3 to CV (n=26)	0.0 (0.4)

25. Secondary Outcome Measure:

Measure Title	VAS-Physician's Global Assessment of Disease Activity (GDA) During the Interventional Phase
Measure Description	Physician's were asked to determine the overall GDA for each participant using a 100-mm VAS, where 0=no disease activity and 100=maximum disease activity. The physician marked the line corresponding to their assessment and the distance from the left edge was measured. V3, CV, and the change from V3 to CV was determined.
Time Frame	V3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)
Safety Issue?	No

Analysis Population Description

Safety Int run-in; n=number of participants analyzed for the given parameter at the specified timepoint. Only participants with values at both visits were included in the analysis.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	40
VAS-Physician's Global Assessment of Disease Activity (GDA) During the Interventional Phase [units: mm] Mean (Standard Deviation)	
V3 (n=40)	16.6 (12.5)
CV (n=28)	16.7 (15.9)
Change from V3 to CV (n=26)	3.1 (15.4)

26. Secondary Outcome Measure:

Measure Title	VAS for Pain (VAS-Pain) During the Interventional Phase
Measure Description	Participants were asked to mark the line corresponding to the intensity of their pain on a 100-mm VAS, where 0=no pain and 100=worst possible pain. The distance from the left edge was measured. Change = V3 mean minus CV mean.
Time Frame	V3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)
Safety Issue?	No

Analysis Population Description

Safety Int run-in; n=number of participants analyzed for the given parameter at the specified timepoint. Only participants with values at both visits were included in the analysis.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	43
VAS for Pain (VAS-Pain) During the Interventional Phase [units: mm] Mean (Standard Deviation)	
V3 (n=43)	19.9 (16.5)
CV (n=28)	24.9 (19.0)
Change from V3 to CV (n=28)	6.9 (22.4)

27. Secondary Outcome Measure:

Measure Title	SJC and TJC During the Interventional Phase
Measure Description	TJC and SJC were assessed for 28 joints. An assessment of 28 joints for swelling and tenderness was made. Joints were assessed and classified as swollen (1)/not swollen (0) and tender (1)/not tender (0) by pressure and joint manipulation on physical examination for a total score range of 0-28. Higher scores indicated greater disease activity (tenderness/swelling). V3, CV, and the change from V3 to CV was determined.
Time Frame	V3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)
Safety Issue?	No

Analysis Population Description

Safety Int run-in; n=number of participants analyzed for the given parameter at the specified timepoint.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	43
SJC and TJC During the Interventional Phase [units: joints] Mean (Standard Deviation)	
SJC V3 (n=43)	0.9 (1.3)
SJC CV (n=29)	0.4 (0.9)
SJC Change from V3 to CV (n=29)	-0.3 (0.8)
TJC V3 (n=43)	0.9 (1.2)
TJC CV (n=29)	1.8 (2.7)
TJC Change from V3 to CV (n=29)	1.0 (2.6)

28. Secondary Outcome Measure:

Measure Title	Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Score During the Interventional Phase
Measure Description	FACIT-F is a 13-item questionnaire. Participants scored each item on a 5-point scale: 0 (not at all) to 4 (very much). The larger the participant’s response to the questions (with the exception of 2 negatively stated), the greater the participant’s fatigue. For all questions, except for the 2 negatively stated ones, the code was reversed and a new score was calculated as (4 minus the participant’s response). The sum of all responses resulted in the FACIT-F score for a total possible score of 0 (worse score) to 52 (better score). V3, CV, and the change from V3 to CV was determined.
Time Frame	V3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)
Safety Issue?	No

Analysis Population Description

Safety Int run-in; n=number of participants analyzed for the given parameter at the specified timepoint.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	37
Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Score During the Interventional Phase [units: units on a scale] Mean (Standard Deviation)	
V3 (n=37)	37.5 (9.9)
CV (n=26)	35.6 (10.8)
Change from V3 to CV (n=22)	8.8 (19.0)

29. Secondary Outcome Measure:

Measure Title	Short-Form 36 (SF-36) Mental Component Score (MCS) and Physical Component Score (PCS) During the Interventional Phase
Measure Description	36-Item Short-Form Health Survey (SF-36) is a standardized survey evaluating 8 aspects of functional health and well-being: physical and social functioning, physical and emotional role limitations, bodily pain, general health, vitality, mental health. These 8 aspects can also be summarized as physical and mental component scores (PCS and MCS). Total of 11 variables were analyzed (8 subscales, 2 composite subscales and Question 2 “how would you rate your health in general now?” (range 1= better, 5= worst). The score for a section is an average of the individual question scores, which are scaled 0-100 (100=highest level of functioning). Higher scores reflect higher quality of life. V3, CV, and the change from V3 to CV was determined.
Time Frame	V3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)

Safety Issue?	No

Analysis Population Description

Safety Int run-in; n=number of participants analyzed for the given parameter at the specified timepoint.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	37
Short-Form 36 (SF-36) Mental Component Score (MCS) and Physical Component Score (PCS) During the Interventional Phase [units: units on a scale] Mean (Standard Deviation)	
MCS V3 (n=37)	47.0 (9.9)
MCS CV (n=26)	46.2 (9.0)
MCS: Change from V3 to CV (n=22)	-4.4 (10.6)
PCS V3 (n=36)	42.5 (7.6)
PCS CV (n=26)	41.8 (8.8)
PCS: Change from V3 to CV (n=22)	-2.1 (6.4)

30. Secondary Outcome Measure:

Measure Title	SF-36 Subscale Scores During the Interventional Phase

Measure Description	SF-36 is a standardized survey evaluating 8 aspects of functional health and well-being: physical and social functioning, physical and emotional role limitations, bodily pain, general health, vitality, mental health. These 8 aspects can also be summarized as physical and mental component scores (PCS and MCS). Total of 11 variables were analyzed (8 subscales, 2 composite subscales and Question 2 “how would you rate your health in general now?” (range 1= better, 5= worst). The score for a section is an average of the individual question scores, which are scaled 0-100 (100=highest level of functioning). Higher scores reflect higher quality of life. V3, CV, and the change from V3 to CV was determined.
Time Frame	V3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)
Safety Issue?	No

Analysis Population Description

ITT Population; n=number of participants analyzed for the given parameter at the specified time point.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	37
SF-36 Subscale Scores During the Interventional Phase [units: units on a scale] Mean (Standard Deviation)	
Physical functioning V3 (n=36)	41.52 (10.37)
Physical functioning CV (n=26)	41.92 (10.44)
Change in physical functioning V3 to CV (n=22)	-1.80 (6.77)
Physical sub-score V3 (n=37)	40.61 (7.53)
Physical sub-score CV (n=26)	39.85 (8.23)
Change in physical sub-score V3 to CV (n=22)	-2.79 (7.68)
Bodily pain V3 (n=37)	45.88 (8.35)

	Tocilizumab
Bodily pain CV (n=26)	44.65 (9.70)
Change in bodily pain V3 to CV (n=22)	-3.21 (8.67)
General health V3 (n=37)	43.11 (9.42)
General health CV (n=26)	40.82 (8.77)
Change in general health V3 to CV (n=22)	-3.78 (7.35)
Vitality V3 (n=37)	50.51 (8.74)
Vitality CV (n=26)	48.91 (9.13)
Change in vitality V3 to CV (n=22)	-4.37 (9.98)
Social functioning V3 (n=37)	45.42 (9.63)
Social functioning CV (n=26)	45.58 (9.29)
Change in social functioning V3 to CV (n=22)	-2.73 (9.63)
Emotional sub-score V3 (n=37)	40.59 (9.98)
Emotional sub-score CV (n=26)	40.37 (10.53)
Change in emotional sub-score V3 to CV (n=22)	-2.45 (10.29)
Mental health V3 (n=37)	47.14 (10.00)
Mental health CV (n=26)	45.94 (10.37)
Change in Mental health V3 to CV (n=22)	-5.47 (10.98)

31. Secondary Outcome Measure:

Measure Title	CDAI Score During the Interventional Phase
Measure Description	The CDAI is the numerical sum of 4 outcome parameters: TJC and SJC based on a 28-joint assessment, PtGA and PGA assessed on 0-100 mm VAS; higher scores=greater affection due to disease activity. CDAI total score=0-76. CDAI ≤2.8=disease remission, >2.8 to 10=LDA, >10 to 22=moderate disease activity, and >22=high disease activity. V3, CV, and the change from V3 to CV was determined.
Time Frame	V3 (7 months) and CV (4 weeks after GC-free status, maximum of 24 weeks after V3)
Safety Issue?	No

Analysis Population Description

Safety Int run-in; n=number of participants analyzed for the given parameter at the specified timepoint.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	40
CDAI Score During the Interventional Phase [units: units on a scale] Mean (Standard Deviation)	
V3 (n=40)	5.6 (3.8)
CV (n=27)	6.5 (5.4)
Change from V3 to CV (n=25)	1.4 (5.2)

32. Secondary Outcome Measure:

Measure Title	Percentage of Participants With LDA or Remission During the Interventional Phase Assessed Using CDAI
Measure Description	The CDAI is the numerical sum of 4 outcome parameters: TJC and SJC based on a 28-joint assessment, PtGA and PGA assessed on 0-100 mm VAS; higher scores=greater affection due to disease activity. CDAI total score=0-76. CDAI ≤2.8=disease remission and >2.8 to 10=LDA.
Time Frame	Visits 3 (7 months), 4 (8 months), 5 (9 months), 6 (10 months), 7 (11 months), 8 (12 months), and 9 (24 weeks after V3) or CV (4 weeks after GC-free status, maximum of 24 weeks after V3)
Safety Issue?	No

Analysis Population Description

Safety Int run-in; n=number of participants analyzed for the given parameter at the specified timepoint.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	41
Percentage of Participants With LDA or Remission During the Interventional Phase Assessed Using CDAI [units: percentage of participants]	
V3 LDA (n=40)	85.0
V3 Remission (n=40)	27.5
V4 LDA (n=41)	82.9
V4 Remission (n=41)	39.0
V5 LDA (n=38)	81.6
V5 Remission (n=38)	47.4
V6 LDA (n=35)	71.4
V6 Remission (n=35)	37.1
V7 LDA (n=33)	75.8
V7 Remission (n=33)	33.3
V8 LDA (n=31)	80.6
V8 Remission (n=31)	38.7
V9 LDA (n=29)	69.0
V9 Remission (n=29)	31.0
CV LDA (n=27)	77.8
CV Remission (n=27)	33.3

33. Secondary Outcome Measure:

Measure Title	Percentage of Participants With LDA or Remission During the Interventional Phase Assessed Using DAS28-CRP
Measure Description	DAS28 calculated from the number of swollen joints (SJC) and tender joints (TJC) using the 28 joint count, the CRP and PtGA of disease activity (participant rated arthritis activity assessment with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity). DAS28-CRP ≤3.2 and oral GC intake with MP equivalent dose of ≥1 mg and ≤20 mg/day=LDA; DAS28 <2.6 = remission.
Time Frame	Visits 3 (7 months), 4 (8 months), 5 (9 months), 6 (10 months), 7 (11 months), 8 (12 months), 9 (24 weeks after V3) or CV (4 weeks after GC-free status, maximum of 24 weeks after V3)
Safety Issue?	No

Analysis Population Description

Safety Int run-in; n=number of participants analyzed for the given parameter at the specified timepoint.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week per investigator's discretion, or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Measured Values

	Tocilizumab
Number of Participants Analyzed	42
Percentage of Participants With LDA or Remission During the Interventional Phase Assessed Using DAS28-CRP [units: percentage of participants]	
V3 LDA (n=42)	90.5
V3 Remission (n=42)	73.8
V4 LDA (n=41)	85.4
V4 Remission (n=41)	73.2

	Tocilizumab
V5 LDA (n=35)	88.6
V5 Remission (n=35)	71.4
V6 LDA (n=35)	82.9
V6 Remission (n=35)	62.9
V7 LDA (n=33)	90.9
V7 Remission (n=33)	57.6
V8 LDA (n=32)	87.5
V8 Remission (n=32)	62.5
V9 LDA (n=30)	73.3
V9 Remission (n=30)	56.7
CV LDA (n=27)	88.9
CV Remission (n=27)	59.3

Reported Adverse Events

Time Frame	Adverse events were recorded throughout the study from V1, 6 months before Interventional phase to CV
Additional Description	[Not specified]

Reporting Groups

	Description
Noninterventional Phase	Participants received tocilizumab 8 mg/kg IV once every 4 weeks and MTX 7.5 to 25 mg/week according to local standard of care and at the investigator's discretion (or without MTX if intolerant) for up to 13 months. Participants also received GC (no product/dose limitation) until LDA (defined as DAS28-CRP ≤3.2), up to a maximum of 6 months.
Interventional Phase	All participants who maintained LDA from V2 to V3 were included in the interventional phase for reduction of GC. Once LDA achieved, GC was switched to MP tablets, PO. MP dose determined by recalculating original GC dose to obtain an equivalent MP dose (had to be ≥1 mg and ≤20 mg/day), which was administered for 4 weeks. If LDA continued after 4 weeks, MP dose was reduced over the following 6 months per protocol-defined dose reduction schedule to reach 0 mg within 6 months for a maximum duration of 7 months of MP treatment.

Serious Adverse Events

	Noninterventional Phase	Interventional Phase
	Affected/At Risk (%)	Affected/At Risk (%)
Total	4/68 (5.88%)	1/43 (2.33%)
Cardiac disorders		
Atrial fibrillation [A] *	1/68 (1.47%)	0/43 (0%)
Infections and infestations		
Cellulitis [A] *	1/68 (1.47%)	0/43 (0%)
Osteitis [A] *	1/68 (1.47%)	0/43 (0%)
Musculoskeletal and connective tissue disorders		
Neck pain [A] *	1/68 (1.47%)	0/43 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Breast cancer [A] *	0/68 (0%)	1/43 (2.33%)
Psychiatric disorders		
Attempted to commit suicide [A] *	1/68 (1.47%)	0/43 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (16.0)

Other Adverse Events

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

	Noninterventional Phase	Interventional Phase
	Affected/At Risk (%)	Affected/At Risk (%)
Total	36/68 (52.94%)	26/43 (60.47%)
Blood and lymphatic system disorders		
Leukopenia [A] *	1/68 (1.47%)	3/43 (6.98%)
Neutropenia [A] *	0/68 (0%)	1/43 (2.33%)
Thrombocytopenia [A] *	1/68 (1.47%)	0/43 (0%)
Cardiac disorders		

	Noninterventional Phase	Interventional Phase
	Affected/At Risk (%)	Affected/At Risk (%)
Atrial fibrillation [A] *	1/68 (1.47%)	0/43 (0%)
Palpitations [A] *	2/68 (2.94%)	0/43 (0%)
Ear and labyrinth disorders		
Otosalpingitis [A] *	1/68 (1.47%)	0/43 (0%)
Vertigo [A] *	2/68 (2.94%)	1/43 (2.33%)
Eye disorders		
Cataract [A] *	1/68 (1.47%)	0/43 (0%)
Conjunctivitis [A] *	1/68 (1.47%)	0/43 (0%)
Gastrointestinal disorders		
Abdominal pain [A] *	2/68 (2.94%)	0/43 (0%)
Abdominal pain upper [A] *	0/68 (0%)	1/43 (2.33%)
Diarrhoea [A] *	2/68 (2.94%)	1/43 (2.33%)
Diverticulum intestinal [A] *	0/68 (0%)	1/43 (2.33%)
Dyspepsia [A] *	1/68 (1.47%)	0/43 (0%)
Gastritis [A] *	2/68 (2.94%)	0/43 (0%)
Nausea [A] *	2/68 (2.94%)	0/43 (0%)
Umbilical hernia [A] *	1/68 (1.47%)	0/43 (0%)
Vomiting [A] *	1/68 (1.47%)	1/43 (2.33%)
General disorders		
Asthenia [A] *	1/68 (1.47%)	0/43 (0%)
Face oedema [A] *	1/68 (1.47%)	0/43 (0%)
Fatigue [A] *	4/68 (5.88%)	0/43 (0%)
Influenza like illness [A] *	1/68 (1.47%)	0/43 (0%)

	Noninterventional Phase	Interventional Phase
	Affected/At Risk (%)	Affected/At Risk (%)
Local swelling [A] *	1/68 (1.47%)	0/43 (0%)
Oedema peripheral [A] *	0/68 (0%)	3/43 (6.98%)
Pain [A] *	0/68 (0%)	2/43 (4.65%)
Pyrexia [A] *	1/68 (1.47%)	1/43 (2.33%)
Hepatobiliary disorders		
Hepatocellular injury [A] *	1/68 (1.47%)	0/43 (0%)
Infections and infestations		
Arthritis infective [A] *	1/68 (1.47%)	0/43 (0%)
Body tinea [A] *	0/68 (0%)	1/43 (2.33%)
Bronchitis [A] *	6/68 (8.82%)	3/43 (6.98%)
Bronchopneumonia [A] *	0/68 (0%)	1/43 (2.33%)
Cellulitis [A] *	1/68 (1.47%)	0/43 (0%)
Cystitis [A] *	1/68 (1.47%)	0/43 (0%)
Ear infection [A] *	0/68 (0%)	1/43 (2.33%)
Erysipelas [A] *	0/68 (0%)	1/43 (2.33%)
Gastroenteritis [A] *	1/68 (1.47%)	0/43 (0%)
Herpes virus infection [A] *	0/68 (0%)	1/43 (2.33%)
Infection [A] *	0/68 (0%)	1/43 (2.33%)
Laryngitis [A] *	0/68 (0%)	2/43 (4.65%)
Lung infection [A] *	1/68 (1.47%)	0/43 (0%)
Nasopharyngitis [A] *	0/68 (0%)	1/43 (2.33%)
Pharyngitis [A] *	1/68 (1.47%)	0/43 (0%)

	Noninterventional Phase	Interventional Phase
	Affected/At Risk (%)	Affected/At Risk (%)
Rhinitis [A] *	1/68 (1.47%)	0/43 (0%)
Sinusitis [A] *	1/68 (1.47%)	0/43 (0%)
Tinea pedis [A] *	1/68 (1.47%)	0/43 (0%)
Upper respiratory tract infection [A] *	1/68 (1.47%)	0/43 (0%)
Urinary tract infection [A] *	1/68 (1.47%)	0/43 (0%)
Vulvovaginal mycotic infection [A] *	1/68 (1.47%)	0/43 (0%)
Injury, poisoning and procedural complications		
Spinal fracture [A] *	0/68 (0%)	1/43 (2.33%)
Wound [A] *	1/68 (1.47%)	0/43 (0%)
Investigations		
Alanine aminotransferase increased [A] *	1/68 (1.47%)	0/43 (0%)
Blood bilirubin increased [A] *	1/68 (1.47%)	0/43 (0%)
Hepatic enzyme increased [A] *	1/68 (1.47%)	0/43 (0%)
Weight increased [A] *	0/68 (0%)	1/43 (2.33%)
Metabolism and nutrition disorders		
Diabetes mellitus [A] *	0/68 (0%)	1/43 (2.33%)
Folate deficiency [A] *	0/68 (0%)	1/43 (2.33%)
Glucose tolerance impaired [A] *	0/68 (0%)	1/43 (2.33%)
Hypercholesterolaemia [A] *	5/68 (7.35%)	1/43 (2.33%)
Hyperglycaemia [A] *	1/68 (1.47%)	0/43 (0%)
Hyperlipidaemia [A] *	0/68 (0%)	1/43 (2.33%)
Hypertriglyceridaemia [A] *	0/68 (0%)	1/43 (2.33%)

	Noninterventional Phase	Interventional Phase
	Affected/At Risk (%)	Affected/At Risk (%)
Vitamin D deficiency [A] *	0/68 (0%)	1/43 (2.33%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] *	1/68 (1.47%)	1/43 (2.33%)
Back pain [A] *	1/68 (1.47%)	3/43 (6.98%)
Muscle spasms [A] *	2/68 (2.94%)	1/43 (2.33%)
Musculoskeletal pain [A] *	0/68 (0%)	1/43 (2.33%)
Neck pain [A] *	2/68 (2.94%)	1/43 (2.33%)
Osteitis [A] *	1/68 (1.47%)	0/43 (0%)
Osteoarthritis [A] *	1/68 (1.47%)	0/43 (0%)
Osteoporosis [A] *	1/68 (1.47%)	0/43 (0%)
Rheumatoid arthritis [A] *	1/68 (1.47%)	0/43 (0%)
Tendonitis [A] *	1/68 (1.47%)	0/43 (0%)
Tenosynovitis [A] *	1/68 (1.47%)	0/43 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Basal cell carcinoma [A] *	0/68 (0%)	1/43 (2.33%)
Breast cancer [A] *	0/68 (0%)	1/43 (2.33%)
Nervous system disorders		
Dizziness [A] *	0/68 (0%)	1/43 (2.33%)
Headache [A] *	3/68 (4.41%)	0/43 (0%)
Presyncope [A] *	0/68 (0%)	1/43 (2.33%)
Psychiatric disorders		
Anxiety [A] *	2/68 (2.94%)	1/43 (2.33%)
Depression [A] *	1/68 (1.47%)	0/43 (0%)

	Noninterventional Phase	Interventional Phase
	Affected/At Risk (%)	Affected/At Risk (%)
Insomnia [A] *	1/68 (1.47%)	1/43 (2.33%)
Suicide attempt [A] *	1/68 (1.47%)	0/43 (0%)
Renal and urinary disorders		
Renal cyst [A] *	1/68 (1.47%)	0/43 (0%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] *	3/68 (4.41%)	2/43 (4.65%)
Oropharyngeal pain [A] *	1/68 (1.47%)	1/43 (2.33%)
Rhinorrhoea [A] *	0/68 (0%)	2/43 (4.65%)
Sneezing [A] *	0/68 (0%)	1/43 (2.33%)
Skin and subcutaneous tissue disorders		
Acne [A] *	0/68 (0%)	1/43 (2.33%)
Alopecia [A] *	1/68 (1.47%)	1/43 (2.33%)
Pruritus [A] *	2/68 (2.94%)	1/43 (2.33%)
Psoriasis [A] *	1/68 (1.47%)	0/43 (0%)
Rash [A] *	1/68 (1.47%)	1/43 (2.33%)
Skin exfoliation [A] *	1/68 (1.47%)	0/43 (0%)
Skin reaction [A] *	1/68 (1.47%)	0/43 (0%)
Surgical and medical procedures		
Hip surgery [A] *	1/68 (1.47%)	0/43 (0%)
Skin neoplasm excision [A] *	0/68 (0%)	1/43 (2.33%)
Surgery [A] *	0/68 (0%)	1/43 (2.33%)
Vascular disorders		
Hot flush [A] *	0/68 (0%)	1/43 (2.33%)

	Noninterventional Phase	Interventional Phase
	Affected/At Risk (%)	Affected/At Risk (%)
Hypertension [A] *	1/68 (1.47%)	0/43 (0%)
Phlebitis [A] *	0/68 (0%)	1/43 (2.33%)
Rheumatoid vasculitis [A] *	0/68 (0%)	1/43 (2.33%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (16.0)

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 after the first publication or presentation that involves the overall study. Sponsor may request that confidential information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

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