ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 01/22/2015

ClinicalTrials.gov ID: NCT01034397

Study Identification

Unique Protocol ID:	ML22648
Brief Title:	A Study of Tocilizumab Plus Non-biological DMARD in Patients With Moderate to Severe Rheumatoid Arthritis and an Inadequate Response to Non-biological DMARDs
Official Title:	A Randomized, Double-blind, Placebo-controlled Study to Assess Efficacy of Tocilizumab+Non-biological DMARD in Reducing Synovitis as Measured by MRI at 12 Weeks After Initiation of Treatment in Patients With Moderate to Severe Rheumatoid Arthritis With Inadequate Response to Non-biological DMARDs
Secondary IDs:	2009-012218-30

Study Status

Record Verification:	January 2015
Overall Status:	Completed
Study Start:	March 2010
Primary Completion:	September 2011 [Actual]
Study Completion:	September 2011 [Actual]

Sponsor/Collaborators

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

Oversight

FDA Regulated?:	No
IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: 0907A336 Board Name: Comissão de Ética para Investigação Clìnica Board Affiliation: unknown Phone: (351) 217 985 340 Email: ceic@ceic.pt
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Portugal: National Pharmacy and Medicines Institute

Study Description

Brief Summary:	This randomized, double-blind, placebo-controlled study will use Magnetic Resonance Imaging (MRI) to assess the efficacy of tocilizumab plus non-biological DMARD in patients with moderate to severe rheumatoid arthritis who have had an inadequate response to non-biological DMARDS. Patients will be randomized to receive either intravenous tocilizumab at 8mg/kg (minimal dose 480mg, maximum dose 800mg) or placebo every 4 weeks, in addition to their stable dose of non-biological DMARD. Anticipated time on study treatment is 24 weeks, and target sample size is <100.
Detailed Description:	

Conditions

Conditions:	Rheumatoid Arthritis
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 4
Intervention Model:	Parallel Assignment
Number of Arms:	2

Masking:	Double Blind (Subject, Investigator)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	54 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1	Drug: tocilizumab [RoActemra/Actemra] 8mg/kg (minimal dose 480mg, maximum dose 800mg) iv infusion every 4 weeks for 24 weeks Drug: non-biological DMARDs stable dose at investigator's prescription
Placebo Comparator: 2	Drug: placebo iv every 4 weeks for 24 weeks Drug: non-biological DMARDs stable dose at investigator's prescription

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	
Gender:	Both
Accepts Healthy Volunteers?:	No
Criteria:	Inclusion Criteria:

- adult patients, >/=18 years of age
- moderate to severe rheumatoid arthritis of >/=6 months duration
- synovitis (swollen and tender joint) in the wrist of the dominant hand
- non-biologic DMARDs at stable dose for >/=12 weeks prior to baseline
- oral corticosteroids at stable dose for at least 25 out of 28 days prior to baseline

Exclusion Criteria:

- rheumatic autoimmune disease other than RA
- history of or current inflammatory joint disease other than RA

- functional class IV (ACR classification)
- intraarticular or parenteral corticosteroids within 6 weeks prior to baseline
- previous treatment with a biologic agent for RA

Contacts/Locations

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: Portugal
Coimbra, Portugal, 3000-075

Lisboa, Portugal, 1349-019

Almada, Portugal, 2801-951

Lisboa, Portugal, 1649-035

Porto, Portugal, 4200-319

Lisboa, Portugal, 1069-639

Coimbra, Portugal, 3041-801

Vila Nova de Gaia, Portugal, 4400-129

Lisboa, Portugal, 1050-34

Ponte do Lima, Portugal, 4990-041

Porto, Portugal, 4099-001

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Reporting Groups

	Description
Tocilizumab 8 Milligrams Per Kilogram (mg/kg)	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) intravenously (IV) once every 4 weeks for 24 weeks.
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 24 weeks. At 12 weeks, participants who did not respond to treatment (those who did not show improvement of greater than or equal to [≥]20 percent [%] in tender joint count and swollen joint count) were offered rescue therapy with open-label tocilizumab 8 mg/kg every 4 weeks through Week 24.

Overall Study

	Tocilizumab 8 Milligrams Per Kilogram (mg/kg)	Placebo
Started	35	19
Completed	28	17
Not Completed	7	2
Lack of compliance	0	1
Lack of Efficacy	3	0
Adverse Event	4	0
Not specified	0	1

Baseline Characteristics

Analysis Population Description

Intent-to Treat (ITT) population: all participants randomized who had at least one efficacy measurement performed.

Reporting Groups

	Description
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 24 weeks. At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in tender joint count and swollen joint count) were offered rescue therapy with open-label tocilizumab 8 mg/kg every 4 weeks through Week 24.

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 24 weeks.

Baseline Measures

	Placebo	Tocilizumab 8 mg/kg	Total
Number of Participants	19	35	54
Age, Continuous [units: years] Median (Full Range)	54 (45 to 69)	54 (28 to 79)	54 (28 to 79)
Gender, Male/Female [units: participants]			
Female	17	29	46
Male	2	6	8

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 12 in Synovitis Measured by Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) Rheumatoid Arthritis Magnetic Resonance Image Scoring System (RAMRIS) Score
Measure Description	Synovitis is defined as an area in the synovial compartment that shows above normal postgadolinium enhancement of a thickness greater than the width of the normal synovium. T1-weighted images were acquired before and after the administration of intravenous contrast agent containing gadolinium. Intravenous contrast was required to demonstrate enhancing synovitis. Three wrist regions (distal radioulnar joint, radiocarpal joint, the intercarpal and intermetacarpal joint) and the 2nd to 5th metacarpophalangeal (MCP) were assessed for synovitis via magnetic resonance imaging (MRI) and scored using a scale ranging from 0-3 where 0 is normal and scores 1-3 (mild, moderate, severe) are by thirds of the presumed volume of enhancing tissue in the synovial compartment. These values were then summed yielding scores of 0-9 in the wrist region, 0-12 for MCP joints, and 0-22 on the aggregate. A negative value in synovitis change from Baseline score indicates an improvement.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population; n (number) equals (=) number of participants assessed for the specified parameter

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in tender joint count [TJC] and swollen joint count [SJC]) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	30	17
Percent Change From Baseline to Week 12 in Synovitis Measured by Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) Rheumatoid Arthritis Magnetic Resonance Image Scoring System (RAMRIS) Score [units: percent change] Median (Full Range)		
Wrist region (n=30,17)	-20.0 (-100.0 to 200.0)	-37.5 (-100.0 to 40.0)
2nd to 5th MCP joints (n=25,14)	-25.0 (-91.7 to 100.0)	0.0 (-100.0 to 100.0)
Total synovitis score (n=30,17)	-23.6 (-80.0 to 1200.0)	-25.0 (-69.2 to 60.0)

Statistical Analysis 1 for Percent Change From Baseline to Week 12 in Synovitis Measured by Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) Rheumatoid Arthritis Magnetic Resonance Image Scoring System (RAMRIS) Score

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	1.00
	Comments	Wrist region: Tocilizumab versus placebo; Since one-sided t-test was used all effects in the opposite direction of what was predicted have a p-value=1.
	Method	t-test, 1 sided

	Comments	[Not specified]

Statistical Analysis 2 for Percent Change From Baseline to Week 12 in Synovitis Measured by Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) Rheumatoid Arthritis Magnetic Resonance Image Scoring System (RAMRIS) Score

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.026
	Comments	2nd and 5th MCP joints: Tocilizumab versus placebo
	Method	t-test, 1 sided
	Comments	[Not specified]

Statistical Analysis 3 for Percent Change From Baseline to Week 12 in Synovitis Measured by Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) Rheumatoid Arthritis Magnetic Resonance Image Scoring System (RAMRIS) Score

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	1.00
	Comments	Total synovitis score: Tocilizumab versus placebo; Since one-sided t-test was used all effects in the opposite direction of what was predicted have a p-value=1.
	Method	t-test, 1 sided
	Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 12 in OMERACT RAMRIS Score

Measure Description	RAMRIS score is the sum of its core components: Synovitis Score, Edema Score, and Erosion Score. Synovitis scored from 0 (normal) to 9 (maximum distension of synovial cavity). Edema scored 0 (normal) to 69 (maximum articular bone involvement). Erosion scored from 0 (normal) to 230 (maximum erosion of articular bone). RAMRIS=Synovial Score plus (+) Edema Score + Erosion Score. Minimum RAMRIS score=0 (normal), maximum RAMRIS score=308 (severe structural damage). For Synovial Score, Edema Score, Erosion Score, and RAMRIS score, increasing number=increasing severity.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	30	17
Percent Change From Baseline to Week 12 in OMERACT RAMRIS Score [units: percent change] Median (Full Range)	-10.6 (-80.9 to 127.8)	-15.4 (-59.7 to 41.7)

Statistical Analysis 1 for Percent Change From Baseline to Week 12 in OMERACT RAMRIS Score

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.421
	Comments	Percentage Change in OMERACT RAMRIS global score; Tocilizumab versus placebo.
	Method	t-test, 1 sided
	Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Absolute Change From Baseline to Week 12 in OMERACT RAMRIS Score
Measure Description	RAMRIS score is the sum of its core components: Synovitis Score, Edema Score, and Erosion Score. Synovitis scored from 0 (normal) to 9 (maximum distension of synovial cavity). Edema scored 0 (normal) to 69 (maximum articular bone involvement). Erosion scored from 0 (normal) to 230 (maximum erosion of articular bone). RAMRIS=Synovial Score plus (+) Edema Score + Erosion Score. Minimum RAMRIS score=0 (normal), maximum RAMRIS score=308 (severe structural damage). For Synovial Score, Edema Score, Erosion Score, and RAMRIS score, increasing number=increasing severity.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	30	17
Absolute Change From Baseline to Week 12 in OMERACT RAMRIS Score [units: units on a scale] Median (Full Range)	-5.5 (-38.0 to 23.0)	-7.0 (-43.0 to 15.0)

Statistical Analysis 1 for Absolute Change From Baseline to Week 12 in OMERACT RAMRIS Score

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.434
	Comments	Absolute change in OMERACT RAMRIS global score; Placebo versus Tocilizumab
	Method	t-test, 1 sided
	Comments	[Not specified]

4. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 24 in OMERACT RAMRIS Score
Measure Description	RAMRIS score is the sum of its core components: Synovitis Score, Edema Score, and Erosion Score. Synovitis scored from 0 (normal) to 9 (maximum distension of synovial cavity). Edema scored 0 (normal) to 69 (maximum articular bone involvement). Erosion scored from 0 (normal) to 230 (maximum erosion of articular bone). RAMRIS=Synovial Score + Edema Score + Erosion Score. Minimum RAMRIS score=0 (normal), maximum RAMRIS score=308 (severe structural damage). For Synovial Score, Edema Score, Erosion Score, and RAMRIS score, increasing number=increasing severity.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population; participants from the placebo group who did not show an improvement of ≥20% in TJC and SJC were offered recovery therapy with tocilizumab 8 mg/kg and were placed in Placebo-Tocilizumab 8 mg/kg group.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).

	Description
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	24	7	9
Percent Change From Baseline to Week 24 in OMERACT RAMRIS Score [units: percent change] Median (Full Range)	-24.2 (-70.0 to 83.3)	-17.3 (-33.3 to -4.2)	-36.8 (-73.7 to 11.8)

5. Secondary Outcome Measure:

Measure Title	Absolute Change From Baseline to Week 24 in OMERACT RAMRIS Score
Measure Description	RAMRIS score is the sum of its core components: Synovitis Score, Edema Score, and Erosion Score. Synovitis scored from 0 (normal) to 9 (maximum distension of synovial cavity). Edema scored 0 (normal) to 69 (maximum articular bone involvement). Erosion scored from 0 (normal) to 230 (maximum erosion of articular bone). RAMRIS=Synovial Score + Edema Score + Erosion Score. Minimum RAMRIS score=0 (normal), maximum RAMRIS score=308 (severe structural damage). For Synovial Score, Edema Score, Erosion Score, and RAMRIS score, increasing number=increasing severity.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population; participants from the placebo group who did not show an improvement of ≥20% in TJC and SJC were offered recovery therapy with tocilizumab 8 mg/kg and were placed in Placebo-Tocilizumab 8 mg/kg group.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).

	Description
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	24	7	9
Absolute Change From Baseline to Week 24 in OMERACT RAMRIS Score [units: units on a scale] Median (Full Range)	-13.0 (-34.0 to 15.0)	-3.0 (-24.0 to -1.0)	-14.0 (-46.0 to 4.0)

6. Secondary Outcome Measure:

Measure Title	Absolute Change From Baseline to Week 12 in OMERACT-RAMRIS Synovitis Score
Measure Description	Synovitis is defined as an area in the synovial compartment that shows above normal postgadolinium enhancement of a thickness greater than the width of the normal synovium. T1-weighted images were acquired before and after the administration of intravenous contrast agent containing gadolinium. Intravenous contrast was required to demonstrate enhancing synovitis. Three wrist regions (distal radioulnar joint, radiocarpal joint, the intercarpal and intermetacarpal joint) and the 2nd to 5th MCP were assessed for synovitis via MRI and scored using a scale ranging from 0-3 where 0 is normal and scores 1-3 (mild, moderate, severe) are by thirds of the presumed volume of enhancing tissue in the synovial compartment. These values were then summed yielding scores of 0-9 in the wrist region, 0-12 for MCP joints, and 0-22 on the aggregate. A negative value in synovitis change from Baseline score indicates an improvement.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).

	Description
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	30	17
Absolute Change From Baseline to Week 12 in OMERACT-RAMRIS Synovitis Score [units: units on a scale] Median (Full Range)		
Wrist region	-1.0 (-6.0 to 3.0)	-2.0 (-8.0 to 2.0)
2nd to 5th MCP joints	-1.0 (-11.0 to 10.0)	0.0 (-4.0 to 6.0)
Total synovitis score	-2.0 (-14.0 to 12.0)	-2.0 (-9.0 to 5.0)

Statistical Analysis 1 for Absolute Change From Baseline to Week 12 in OMERACT-RAMRIS Synovitis Score

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	1.00
	Comments	Change in Wrist region; Tocilizumab versus placebo. Since one-sided t-test was used all effects in the opposite direction of what was predicted have a p-value=1.
	Method	t-test, 1 sided
	Comments	[Not specified]

Statistical Analysis 2 for Absolute Change From Baseline to Week 12 in OMERACT-RAMRIS Synovitis Score

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.065
	Comments	Change in 2nd to 5th MCP; Tocilizumab versus placebo.
	Method	t-test, 1 sided
	Comments	[Not specified]

Statistical Analysis 3 for Absolute Change From Baseline to Week 12 in OMERACT-RAMRIS Synovitis Score

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	1.00
	Comments	Change in Total synovitis; Tocilizumab versus placebo. Since one-sided t-test was used all effects in the opposite direction of what was predicted have a p-value=1.
	Method	t-test, 1 sided
	Comments	[Not specified]

7. Secondary Outcome Measure:

Measure Title	Absolute Change From Baseline to Week 24 in OMERACT-RAMRIS Synovitis Score
Measure Description	Synovitis is defined as an area in the synovial compartment that shows above normal postgadolinium enhancement of a thickness greater than the width of the normal synovium. T1-weighted images were acquired before and after the administration of intravenous contrast agent containing gadolinium. Intravenous contrast was required to demonstrate enhancing synovitis. Three wrist regions (distal radioulnar joint, radiocarpal joint, the intercarpal and intermetacarpal joint) and the 2nd to 5th MCP were assessed for synovitis via MRI and scored using a scale ranging from 0-3 where 0 is normal and scores 1-3 (mild, moderate, severe) are by thirds of the presumed volume of enhancing tissue in the synovial compartment. These values were then summed yielding scores of 0-9 in the wrist region, 0-12 for MCP joints, and 0-22 on the aggregate. A negative value in synovitis change from Baseline score indicates an improvement.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description
ITT population.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	24	7	9
Absolute Change From Baseline to Week 24 in OMERACT-RAMRIS Synovitis Score [units: units on a scale] Median (Full Range)			
Wrist region	-1.0 (-7.0 to 2.0)	-2.0 (-5.0 to -1.0)	-2.0 (-5.0 to -1.0)
2nd to 5th MCP joints	-1.0 (-9.0 to 7.0)	0.0 (-1.0 to 6.0)	-1.0 (-9.0 to 3.0)
Total synovitis score	-3.0 (-9.0 to 9.0)	-1.0 (-5.0 to 3.0)	-3.0 (-10.0 to 0.0)

8. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 12 in OMERACT RAMRIS Bone Erosion Score
Measure Description	Bones from the wrist regions (carpal bones, distal radius, distal ulna and metacarpal bases) and the MCP joints (metacarpal heads and phalangeal bases) were assessed for erosion via MRI and scored separately based on the proportion of eroded bone compared to the 'assessed bone volume' judged from all available images. Scoring ranges from 0 (no erosion) to 10 (91-100%). For long bones, the 'assessed bone volume' is from the articular surface to a depth of 1 centimeter (cm) (if the articular surface is absent its best estimated position is used), and in carpal bones it is the whole bone. Results were summed, resulting in scores from 0 to 80 for the wrist region, 0 to 150 for the MCP joints, and 0 to 230 on aggregate. A negative value in change from Baseline score indicates an improvement.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	30	17
Percent Change From Baseline to Week 12 in OMERACT RAMRIS Bone Erosion Score [units: percent change] Median (Full Range)	-3.7 (-72.7 to 180.0)	0.0 (-60.6 to 41.7)

Statistical Analysis 1 for Percent Change From Baseline to Week 12 in OMERACT RAMRIS Bone Erosion Score

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	1.00
	Comments	Absolute Change in Bone erosion; Tocilizumab versus placebo. Since one-sided t-test was used all effects in the opposite direction of what was predicted have a p-value=1.
	Method	t-test, 1 sided
	Comments	[Not specified]

9. Secondary Outcome Measure:

Measure Title	Absolute Change From Baseline to Week 12 in OMERACT RAMRIS Bone Erosion Score

Measure Description	Bones from the wrist regions (carpal bones, distal radius, distal ulna and metacarpal bases) and the MCP joints (metacarpal heads and phalangeal bases) were assessed for erosion via MRI and scored separately based on the proportion of eroded bone compared to the 'assessed bone volume' judged from all available images. Scoring ranges from 0 (no erosion) to 10 (91-100%). For long bones, the 'assessed bone volume' is from the articular surface to a depth of 1 centimeter (cm) (if the articular surface is absent its best estimated position is used), and in carpal bones it is the whole bone. Results were summed, resulting in scores from 0 to 80 for the wrist region, 0 to 150 for the MCP joints, and 0 to 230 on aggregate. A negative value in change from Baseline score indicates an improvement.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	30	17
Absolute Change From Baseline to Week 12 in OMERACT RAMRIS Bone Erosion Score [units: units on a scale] Median (Full Range)	-0.5 (-16.0 to 10.0)	0.0 (-20.0 to 5.0)

Statistical Analysis 1 for Absolute Change From Baseline to Week 12 in OMERACT RAMRIS Bone Erosion Score

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	1.00
	Comments	Percentage Change in Bone erosion; Tocilizumab versus placebo. Since one-sided t-test was used all effects in the opposite direction of what was predicted have a p-value=1.
	Method	t-test, 1 sided
	Comments	[Not specified]

10. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 24 in OMERACT RAMRIS Bone Erosion Score
Measure Description	Bones from the wrist regions (carpal bones, distal radius, distal ulna and metacarpal bases) and the MCP joints (metacarpal heads and phalangeal bases) were assessed for erosion via MRI and scored separately based on the proportion of eroded bone compared to the 'assessed bone volume' judged from all available images. Scoring ranges from 0 (no erosion) to 10 (91-100%). For long bones, the 'assessed bone volume' is from the articular surface to a depth of 1 cm (if the articular surface is absent its best estimated position is used), and in carpal bones it is the whole bone. Results were summed, resulting in scores from 0 to 80 for the wrist region, 0 to 150 for the MCP joints, and 0 to 230 on aggregate. A negative value in change from Baseline score indicates an improvement.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	24	7	9
Percent Change From Baseline to Week 24 in OMERACT RAMRIS Bone Erosion Score [units: percent change]	-6.6 (-66.7 to 140.0)	-12.0 (-51.5 to 10.0)	-5.0 (-80.3 to 33.3)

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Median (Full Range)			

11. Secondary Outcome Measure:

Measure Title	Absolute Change From Baseline to Week 24 in OMERACT RAMRIS Bone Erosion Score
Measure Description	Bones from the wrist regions (carpal bones, distal radius, distal ulna and metacarpal bases) and the MCP joints (metacarpal heads and phalangeal bases) were assessed for erosion via MRI and scored separately based on the proportion of eroded bone compared to the 'assessed bone volume' judged from all available images. Scoring ranges from 0 (no erosion) to 10 (91-100%). For long bones, the 'assessed bone volume' is from the articular surface to a depth of 1 cm (if the articular surface is absent its best estimated position is used), and in carpal bones it is the whole bone. Results were summed, resulting in scores from 0 to 80 for the wrist region, 0 to 150 for the MCP joints, and 0 to 230 on aggregate. A negative value in change from Baseline score indicates an improvement.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population; participants from the placebo group who did not show an improvement of ≥ 20% in TJC and SJC were offered recovery therapy with tocilizumab 8mg/kg and were placed in Placebo-Tocilizumab 8mg/kg group.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	24	7	9
Absolute Change From Baseline to Week 24 in OMERACT RAMRIS Bone Erosion Score [units: units on a scale] Median (Full Range)	-1.5 (-9.0 to 7.0)	-2.0 (-17.0 to 1.0)	-2.0 (-15.0 to 4.0)

12. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 12 in OMERACT RAMRIS Bone Edema Score
Measure Description	Bones from the wrist regions (carpal bones, distal radius, distal ulna and metacarpal bases) and the MCP joints (metacarpal heads and phalangeal bases) were assessed for edema via MRI and scored separately based on the proportion of bone with edema. Scoring ranged from 0 to 3 as follows: 0: no edema; 1: 1-33% of bone edematous; 2: 34-66% of bone edematous; 3: 67-100%. Summing these values yielded a scale from 0-45 for the wrist region, 0-24 for the MCP joints, and 0-69 on aggregate.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	30	17
Percent Change From Baseline to Week 12 in OMERACT RAMRIS Bone Edema Score [units: percent change] Median (Full Range)	-17.1 (-100.0 to 66.7)	-15.0 (-83.3 to 137.5)

Statistical Analysis 1 for Percent Change From Baseline to Week 12 in OMERACT RAMRIS Bone Edema Score

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.266
	Comments	Percentage Change in Bone oedema; Tocilizumab versus placebo.
	Method	t-test, 1 sided
	Comments	[Not specified]

13. Secondary Outcome Measure:

Measure Title	Absolute Change From Baseline to Week 12 in OMERACT RAMRIS Bone Edema Score
Measure Description	Bones from the wrist regions (carpal bones, distal radius, distal ulna and metacarpal bases) and the MCP joints (metacarpal heads and phalangeal bases) were assessed for edema via MRI and scored separately based on the proportion of bone with edema. Scoring ranged from 0 to 3 as follows: 0: no edema; 1: 1-33% of bone edematous; 2: 34-66% of bone edematous; 3: 67-100%. Summing these values yielded a scale from 0-45 for the wrist region, 0-24 for the MCP joints, and 0-69 on aggregate.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	30	17

	Tocilizumab 8 mg/kg	Placebo
Absolute Change From Baseline to Week 12 in OMERACT RAMRIS Bone Edema Score [units: units on a scale] Median (Full Range)	-3.0 (-19.0 to 7.0)	-2.0 (-25.0 to 11.0)

Statistical Analysis 1 for Absolute Change From Baseline to Week 12 in OMERACT RAMRIS Bone Edema Score

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.337
	Comments	Absolute Change in Bone edema; Tocilizumab versus placebo.
	Method	t-test, 1 sided
	Comments	[Not specified]

14. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 24 in OMERACT RAMRIS Bone Edema Score
Measure Description	Bones from the wrist regions (carpal bones, distal radius, distal ulna and metacarpal bases) and the MCP joints (metacarpal heads and phalangeal bases) were assessed for edema via MRI and scored separately based on the proportion of bone with edema. Scoring ranged from 0 to 3 as follows: 0: no edema; 1: 1-33% of bone edematous; 2: 34-66% of bone edematous; 3: 67-100%. Summing these values yielded a scale from 0-45 for the wrist region, 0-24 for the MCP joints, and 0-69 on aggregate.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population; participants from the placebo group who did not show an improvement of ≥ 20% in TJC and SJC were offered recovery therapy with tocilizumab 8mg/kg and were placed in Placebo-Tocilizumab 8mg/kg group.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	22	7	9
Percent Change From Baseline to Week 24 in OMERACT RAMRIS Bone Edema Score [units: percent change] Median (Full Range)	-37.5 (-100.0 to 6.7)	-37.5 (-100.0 to 10.7)	-51.9 (-85.2 to 116.7)

15. Secondary Outcome Measure:

Measure Title	Absolute Change From Baseline to Week 24 in OMERACT RAMRIS Bone Edema Score
Measure Description	Bones from the wrist regions (carpal bones, distal radius, distal ulna and metacarpal bases) and the MCP joints (metacarpal heads and phalangeal bases) were assessed for edema via MRI and scored separately based on the proportion of bone with edema. Scoring ranged from 0 to 3 as follows: 0: no edema; 1: 1-33% of bone edematous; 2: 34-66% of bone edematous; 3: 67-100%. Summing these values yielded a scale from 0-45 for the wrist region, 0-24 for the MCP joints, and 0-69 on aggregate.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population; participants from the placebo group who did not show an improvement of ≥ 20% in TJC and SJC were offered recovery therapy with tocilizumab 8mg/kg and were placed in Placebo-Tocilizumab 8mg/kg group.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).

	Description
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	24	7	9
Absolute Change From Baseline to Week 24 in OMERACT RAMRIS Bone Edema Score [units: percent change] Median (Full Range)	-5.5 (-29.0 to 1.0)	-3.0 (-9.0 to 3.0)	-10.0 (-23.0 to 7.0)

16. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 12 in Dynamic Contrast Enhanced (DCE)-MRI Early Enhancement Rate (EER) Global Score
Measure Description	Contrast enhancement was quantified in terms of initial rate of enhancement (IRE) and number of voxels (Nvox), which are extracted by examining individual signal intensity vs time curves derived from defined regions of interest (ROIs). A volume ROI was manually drawn around wrist and MCP 2-5 joints at each visit representative of size/volume of enhancement and underlying inflammation. Maximum enhancement (ME)=mean of ME and Nplateau+Nwashout (Nvoxels) are number of voxels that have a plateau and washout, used to assess volume of enhancing voxels within drawn ROIs. IRE=percentage increase of signal intensity (SI) until I ME is reached calculated as maximum increase in post-contrast SI divided by baseline SI; IRE=increase in SI in %/s from time of onset of enhancement to ME. EER reflects the IRE parameter and the output is the mean from all the assessed ROIs (range=between 0 and 1; 0=no change/enhancement, 1=maximum change/enhancement. Negative change from Baseline score=improvement.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).

	Description
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	12	9
Percent Change From Baseline to Week 12 in Dynamic Contrast Enhanced (DCE)-MRI Early Enhancement Rate (EER) Global Score [units: percent change] Median (Full Range)	-38.7 (-55.3 to -18.4)	-12.1 (-78.3 to 31.0)

Statistical Analysis 1 for Percent Change From Baseline to Week 12 in Dynamic Contrast Enhanced (DCE)-MRI Early Enhancement Rate (EER) Global Score

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.114
	Comments	Percentage change in DCE-MRI EER (global); Placebo versus Tocilizumab
	Method	t-test, 1 sided
	Comments	[Not specified]

17. Secondary Outcome Measure:

Measure Title	Absolute Change From Baseline to Week 12 in Dynamic Contrast Enhanced (DCE)-MRI Early Enhancement Rate (EER) Global Score

Measure Description	Contrast enhancement was quantified in terms of IRE and Nvox, which are extracted by examining individual signal intensity vs time curves derived from defined ROIs. A volume ROI was manually drawn around wrist and MCP 2-5 joints at each visit representative of size/volume of enhancement and underlying inflammation. ME=mean of ME and Nplateau+Nwashout (Nvoxels) are number of voxels that have a plateau and washout, used to assess volume of enhancing voxels within drawn ROIs. IRE=percentage increase of SI until I ME is reached calculated as maximum increase in post-contrast SI divided by baseline SI; IRE=increase in SI in %/s from time of onset of enhancement to ME. EER reflects the IRE parameter and the output is the mean from all the assessed ROIs (range=between 0 and 1; 0=no change/enhancement, 1=maximum change/enhancement. Negative change from Baseline score=improvement.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	12	9
Absolute Change From Baseline to Week 12 in Dynamic Contrast Enhanced (DCE)-MRI Early Enhancement Rate (EER) Global Score [units: units on a scale] Median (Full Range)	-0.002 (-0.004 to 0.001)	-0.001 (-0.01 to 0.002)

Statistical Analysis 1 for Absolute Change From Baseline to Week 12 in Dynamic Contrast Enhanced (DCE)-MRI Early Enhancement Rate (EER) Global Score

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.239
	Comments	Absolute Change in DCE-MRI EER; Tocilizumab versus placebo.
	Method	t-test, 1 sided
	Comments	[Not specified]

18. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 24 in DCE-MRI EER Global Score
Measure Description	Contrast enhancement was quantified in terms of IRE and Nvox, which are extracted by examining individual signal intensity vs time curves derived from defined ROIs. A volume ROI was manually drawn around wrist and MCP 2-5 joints at each visit representative of size/volume of enhancement and underlying inflammation. ME=mean of ME and Nplateau+Nwashout (Nvoxels) are number of voxels that have a plateau and washout, used to assess volume of enhancing voxels within drawn ROIs. IRE=percentage increase of SI until I ME is reached calculated as maximum increase in post-contrast SI divided by baseline SI; IRE=increase in SI in %/s from time of onset of enhancement to ME. EER reflects the IRE parameter and the output is the mean from all the assessed ROIs (range=between 0 and 1; 0=no change/enhancement, 1=maximum change/enhancement. Negative change from Baseline score=improvement.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	10	4	5

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Percent Change From Baseline to Week 24 in DCE-MRI EER Global Score [units: percent change] Median (Full Range)	-45.4 (-68.6 to -11.8)	23.0 (-37.5 to 76.5)	-32.7 (-57.6 to -3.5)

19. Secondary Outcome Measure:

Measure Title	Absolute Change From Baseline to Week 24 in DCE-MRI EER Global Score
Measure Description	Contrast enhancement was quantified in terms of IRE and Nvox, which are extracted by examining individual signal intensity vs time curves derived from defined ROIs. A volume ROI was manually drawn around wrist and MCP 2-5 joints at each visit representative of size/volume of enhancement and underlying inflammation. ME=mean of ME and Nplateau+Nwashout (Nvoxels) are number of voxels that have a plateau and washout, used to assess volume of enhancing voxels within drawn ROIs. IRE=percentage increase of SI until I ME is reached calculated as maximum increase in post-contrast SI divided by baseline SI; IRE=increase in SI in %/s from time of onset of enhancement to ME. EER reflects the IRE parameter and the output is the mean from all the assessed ROIs (range=between 0 and 1; 0=no change/enhancement, 1=maximum change/enhancement. Negative change from Baseline score=improvement.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description
ITT population;

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	10	4	5
Absolute Change From Baseline to Week 24 in DCE-MRI EER Global Score	-0.003 (-0.01 to 0.00)	0.0002 (0.00 to 0.01)	-0.002 (-0.01 to 0.00)

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
[units: units on a scale] Median (Full Range)			

20. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 12 in DCE-MRI EER MCP Score
Measure Description	Contrast enhancement was quantified in terms of IRE and Nvox, which are extracted by examining individual signal intensity vs time curves derived from defined ROIs. A volume ROI was manually drawn around wrist and MCP 2-5 joints at each visit representative of size/volume of enhancement and underlying inflammation. ME=mean of ME and Nplateau+Nwashout (Nvoxels) are number of voxels that have a plateau and washout, used to assess volume of enhancing voxels within drawn ROIs. IRE=percentage increase of SI until I ME is reached calculated as maximum increase in post-contrast SI divided by baseline SI; IRE=increase in SI in %/s from time of onset of enhancement to ME. EER reflects the IRE parameter and the output is the mean from the MCP ROIs (range=between 0 and 1; 0=no change/ enhancement, 1=maximum change/enhancement. Negative change from Baseline score=improvement.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	15	10
Percent Change From Baseline to Week 12 in DCE-MRI EER MCP Score [units: percent change] Median (Full Range)	-29.8 (-83.9 to 471.7)	-10.9 (-88.0 to 91.1)

Statistical Analysis 1 for Percent Change From Baseline to Week 12 in DCE-MRI EER MCP Score

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.271
	Comments	Percentage change in DCE-MRI EER (MCP); Placebo versus Tocilizumab
	Method	t-test, 1 sided
	Comments	[Not specified]

21. Secondary Outcome Measure:

Measure Title	Absolute Change From Baseline to Week 12 in DCE-MRI EER MCP Score
Measure Description	Contrast enhancement was quantified in terms of IRE and Nvox, which are extracted by examining individual signal intensity vs time curves derived from defined ROIs. A volume ROI was manually drawn around wrist and MCP 2-5 joints at each visit representative of size/volume of enhancement and underlying inflammation. ME=mean of ME and Nplateau+Nwashout (Nvoxels) are number of voxels that have a plateau and washout, used to assess volume of enhancing voxels within drawn ROIs. IRE=percentage increase of SI until I ME is reached calculated as maximum increase in post-contrast SI divided by baseline SI; IRE=increase in SI in %/s from time of onset of enhancement to ME. EER reflects the IRE parameter and the output is the mean from the MCP ROIs (range=between 0 and 1; 0=no change/ enhancement, 1=maximum change/enhancement. Negative change from Baseline score=improvement.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).

	Description
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	15	10
Absolute Change From Baseline to Week 12 in DCE-MRI EER MCP Score [units: units on a scale] Median (Full Range)	-0.002 (-0.01 to 0.00)	-0.001 (-0.02 to 0.00)

Statistical Analysis 1 for Absolute Change From Baseline to Week 12 in DCE-MRI EER MCP Score

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.370
	Comments	Absolute change in DCE-MRI EER (MCP); Placebo versus Tocilizumab
	Method	t-test, 1 sided
	Comments	[Not specified]

22. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 24 in DCE-MRI EER MCP Score

Measure Description	Contrast enhancement was quantified in terms of IRE and Nvox, which are extracted by examining individual signal intensity vs time curves derived from defined ROIs. A volume ROI was manually drawn around wrist and MCP 2-5 joints at each visit representative of size/volume of enhancement and underlying inflammation. ME=mean of ME and Nplateau+Nwashout (Nvoxels) are number of voxels that have a plateau and washout, used to assess volume of enhancing voxels within drawn ROIs. IRE=percentage increase of SI until I ME is reached calculated as maximum increase in post-contrast SI divided by baseline SI; IRE=increase in SI in %/s from time of onset of enhancement to ME. EER reflects the IRE parameter and the output is the mean from the MCP ROIs (range=between 0 and 1; 0=no change/ enhancement, 1=maximum change/enhancement. Negative change from Baseline score=improvement.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description
ITT population;

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	12	5	5
Percent Change From Baseline to Week 24 in DCE-MRI EER MCP Score [units: percent change] Median (Full Range)	-32.3 (-100.0 to 40.0)	15.0 (-56.9 to 45.7)	-29.1 (-66.8 to 7.5)

23. Secondary Outcome Measure:

Measure Title	Absolute Change From Baseline to Week 24 in DCE-MRI EER MCP Score

Measure Description	Contrast enhancement was quantified in terms of IRE and Nvox, which are extracted by examining individual signal intensity vs time curves derived from defined ROIs. A volume ROI was manually drawn around wrist and MCP 2-5 joints at each visit representative of size/volume of enhancement and underlying inflammation. ME=mean of ME and Nplateau+Nwashout (Nvoxels) are number of voxels that have a plateau and washout, used to assess volume of enhancing voxels within drawn ROIs. IRE=percentage increase of SI until I ME is reached calculated as maximum increase in post-contrast SI divided by baseline SI; IRE=increase in SI in %/s from time of onset of enhancement to ME. EER reflects the IRE parameter and the output is the mean from the MCP ROIs (range=between 0 and 1; 0=no change/ enhancement, 1=maximum change/enhancement. Negative change from Baseline score=improvement.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description
ITT population;

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	12	5	5
Absolute Change From Baseline to Week 24 in DCE-MRI EER MCP Score [units: units on a scale] Median (Full Range)	-0.002 (-0.01 to 0.00)	0.001 (0.00 to 0.01)	-0.001 (-0.01 to 0.00)

24. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 12 in DCE-MRI EER Wrist Score

Measure Description	Contrast enhancement was quantified in terms of IRE and Nvox, which are extracted by examining individual signal intensity vs time curves derived from defined ROIs. A volume ROI was manually drawn around wrist and MCP 2-5 joints at each visit representative of size/volume of enhancement and underlying inflammation. ME=mean of ME and Nplateau+Nwashout (Nvoxels) are number of voxels that have a plateau and washout, used to assess volume of enhancing voxels within drawn ROIs. IRE=percentage increase of SI until I ME is reached calculated as maximum increase in post-contrast SI divided by baseline SI; IRE=increase in SI in %/s from time of onset of enhancement to ME. EER reflects the IRE parameter and the output is the mean from the wrist ROIs (range=between 0 and 1; 0=no change/ enhancement, 1=maximum change/enhancement. Negative change from Baseline score=improvement.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	15	10
Percent Change From Baseline to Week 12 in DCE-MRI EER Wrist Score [units: percent change] Median (Full Range)	-24.8 (-81.6 to 102.1)	-19.1 (-84.3 to 111.4)

Statistical Analysis 1 for Percent Change From Baseline to Week 12 in DCE-MRI EER Wrist Score

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	1.00
	Comments	Percentage and absolute change in DCE-MRI EER (wrist); Placebo versus Tocilizumab
	Method	t-test, 1 sided
	Comments	[Not specified]

25. Secondary Outcome Measure:

Measure Title	Absolute Change From Baseline to Week 12 in DCE-MRI EER Wrist Score
Measure Description	Contrast enhancement was quantified in terms of IRE and Nvox, which are extracted by examining individual signal intensity vs time curves derived from defined ROIs. A volume ROI was manually drawn around wrist and MCP 2-5 joints at each visit representative of size/volume of enhancement and underlying inflammation. ME=mean of ME and Nplateau+Nwashout (Nvoxels) are number of voxels that have a plateau and washout, used to assess volume of enhancing voxels within drawn ROIs. IRE=percentage increase of SI until I ME is reached calculated as maximum increase in post-contrast SI divided by baseline SI; IRE=increase in SI in %/s from time of onset of enhancement to ME. EER reflects the IRE parameter and the output is the mean from the wrist ROIs (range=between 0 and 1; 0=no change/ enhancement, 1=maximum change/enhancement. Negative change from Baseline score=improvement.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	15	10

	Tocilizumab 8 mg/kg	Placebo
Absolute Change From Baseline to Week 12 in DCE-MRI EER Wrist Score [units: units on a scale] Median (Full Range)	-0.002 (-0.01 to 0.00)	-0.001 (-0.01 to 0.00)

26. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 24 in DCE-MRI EER Wrist Score
Measure Description	Contrast enhancement was quantified in terms of IRE and Nvox, which are extracted by examining individual signal intensity vs time curves derived from defined ROIs. A volume ROI was manually drawn around wrist and MCP 2-5 joints at each visit representative of size/volume of enhancement and underlying inflammation. ME=mean of ME and Nplateau+Nwashout (Nvoxels) are number of voxels that have a plateau and washout, used to assess volume of enhancing voxels within drawn ROIs. IRE=percentage increase of SI until I ME is reached calculated as maximum increase in post-contrast SI divided by baseline SI; IRE=increase in SI in %/s from time of onset of enhancement to ME. EER reflects the IRE parameter and the output is the mean from the wrist ROIs (range=between 0 and 1; 0=no change/ enhancement, 1=maximum change/enhancement. Negative change from Baseline score=improvement.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	12	5	5
Percent Change From Baseline to Week 24 in DCE-MRI EER Wrist Score	-27.0 (-80.0 to 59.1)	1.4 (-4.9 to 102.4)	-54.8 (-67.5 to -30.5)

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
[units: percent change] Median (Full Range)			

27. Secondary Outcome Measure:

Measure Title	Absolute Change From Baseline to Week 24 in DCE-MRI EER Wrist Score
Measure Description	Contrast enhancement was quantified in terms of IRE and Nvox, which are extracted by examining individual signal intensity vs time curves derived from defined ROIs. A volume ROI was manually drawn around wrist and MCP 2-5 joints at each visit representative of size/volume of enhancement and underlying inflammation. ME=mean of ME and Nplateau+Nwashout (Nvoxels) are number of voxels that have a plateau and washout, used to assess volume of enhancing voxels within drawn ROIs. IRE=percentage increase of SI until I ME is reached calculated as maximum increase in post-contrast SI divided by baseline SI; IRE=increase in SI in %/s from time of onset of enhancement to ME. EER reflects the IRE parameter and the output is the mean from the wrist ROIs (range=between 0 and 1; 0=no change/ enhancement, 1=maximum change/enhancement. Negative change from Baseline score=improvement.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	12	5	5
Absolute Change From Baseline to Week 24 in DCE-MRI EER Wrist Score [units: units on a scale] Median (Full Range)	-0.002 (-0.01 to 0.00)	0.0001 (0.00 to 0.02)	-0.004 (-0.01 to 0.00)

28. Secondary Outcome Measure:

Measure Title	Disease Activity Score Based on 28-Joint Count (DAS28)
Measure Description	DAS28 was calculated from the number of swollen joints and tender joints (SJC and TJC) using the 28-joint count, the erythrocyte sedimentation rate (ESR) (millimeters per hour [mm/hr]) and global health assessment (participant rated global assessment of disease activity using 10-mm visual analog scale [VAS]); DAS28 score ranged from 0 to 10, where higher scores correspond to greater disease activity.
Time Frame	Baseline, Weeks 12 and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for a 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	32	17	10
Disease Activity Score Based on 28-Joint Count (DAS28) [units: units on a scale] Median (Full Range)			
Baseline (n=32,17,0)	5.7 (3.4 to 8.0)	6.2 (4.1 to 8.2)	NA (NA to NA) [1]
Week 12 (n=30,17,0)	2.6 (1.1 to 5.8)	5.6 (1.8 to 8.0)	NA (NA to NA) [1]
Week 24 (n=24,7,10)	2.1 (0.8 to 4.1)	3.9 (3.2 to 6.6)	3.2 (1.5 to 5.1)

[1] Data for the Placebo group with recovery therapy were collected only at Weeks 16, 20, and 24.

29. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 12 in DAS28 Global Score
Measure Description	DAS28 was calculated from the number of swollen joints and tender joints (SJC and TJC) using the 28-joint count, the ESR (mm/hr) and global health assessment (participant rated global assessment of disease activity using 10-mm VAS); DAS28 score ranged from 0 to 10, where higher scores correspond to greater disease activity. Change in DAS28 global score was determined as the difference in the scores at baseline and Week 12. A negative number indicated improvement.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	30	15
Change From Baseline to Week 12 in DAS28 Global Score [units: units on a scale] Median (Full Range)	-2.99 (-5.23 to -0.40)	0.22 (-3.88 to 1.54)

Statistical Analysis 1 for Change From Baseline to Week 12 in DAS28 Global Score

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	t-test, 1 sided
	Comments	[Not specified]

30. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in DAS28 Global Score
Measure Description	DAS28 was calculated from the number of swollen joints and tender joints (SJC and TJC) using the 28-joint count, the ESR (mm/hr) and global health assessment (participant rated global assessment of disease activity using 10-mm VAS); DAS28 score ranged from 0 to 10, where higher scores correspond to greater disease activity. Change in DAS28 global score was determined as the difference in the scores at baseline and Week 24. A negative number indicated improvement.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	24	6	9

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Change From Baseline to Week 24 in DAS28 Global Score [units: units on a scale] Median (Full Range)	-3.4 (-6.5 to -1.8)	-1.2 (-5.0 to 0.6)	-2.9 (-4.1 to -1.5)

31. Secondary Outcome Measure:

Measure Title	Tender and Swollen Joint Counts
Measure Description	TJC and SJC were determined using the 28 joint counts. Joints were classified as tender/not tender and swollen/not swollen and counted. The scores ranged from 0 to 28. Higher scores indicated higher disease activity.
Time Frame	Weeks 12 and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	32	19	10
Tender and Swollen Joint Counts [units: joints] Median (Full Range)			
TJC, Week 12 (n=30,17,0)	3.5 (0.0 to 28.0)	8.0 (2.0 to 28.0)	NA (NA to NA) [1]
TJC, Week 24 (n=26,7,10)	1.0 (0.0 to 7.0)	7.0 (3.0 to 12.0)	5.5 (0.0 to 12.0)

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
SJC, Week 12 (n=30,17,0)	1.5 (0.0 to 12.0)	8.0 (0.0 to 24.0)	NA (NA to NA) [1]
SJC, Week 24 (n=26,7,10)	0.0 (0.0 to 4.0)	5.0 (1.0 to 17.0)	2.5 (1.0 to 9.0)

[1] Data for the Placebo group with recovery therapy were collected only at Weeks, 16, 20 and 24

32. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 12 in TJC
Measure Description	Change in TJC was determined as the difference in the number of tender joints at baseline and the number at Week 12. A negative number indicated improvement.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	30	17
Change From Baseline to Week 12 in TJC [units: tender joints] Median (Full Range)	-6.5 (-17.0 to 0.0)	-2.0 (-16.0 to 10.0)

Statistical Analysis 1 for Change From Baseline to Week 12 in TJC

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.067
	Comments	[Not specified]
	Method	t-test, 1 sided
	Comments	[Not specified]

33. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in TJC
Measure Description	Change in TJC was determined as the difference in the number of tender joints at baseline and the number at Week 24. A negative number indicated improvement.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	26	7	10

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Change From Baseline to Week 24 in TJC [units: tender joints] Median (Full Range)	-8.5 (-26.0 to 0.0)	-5.0 (-21.0 to 0.0)	-7.5 (-22.0 to 0.0)

34. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 12 in SJC
Measure Description	Change in SJC was determined as the difference in the number of swollen joints at baseline and the number at Week 12. A negative number indicated improvement.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	30	17
Change From Baseline to Week 12 in SJC [units: swollen joints] Median (Full Range)	-7.0 (-19.0 to -1.0)	-1.0 (-13.0 to 10.0)

Statistical Analysis 1 for Change From Baseline to Week 12 in SJC

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.001
	Comments	[Not specified]
	Method	t-test, 1 sided
	Comments	[Not specified]

35. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in SJC
Measure Description	Change in SJC was determined as the difference in the number of swollen joints at baseline and the number at Week 24. A negative number indicated improvement.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	26	7	10

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Change From Baseline to Week 24 in SJC [units: swollen joints] Median (Full Range)	-8.5 (-23.0 to -2.0)	-7.0 (-21.0 to 1.0)	-5.0 (-8.0 to 0.0)

36. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 12 in Patient Global Assessment of Disease Activity
Measure Description	General health was assessed using the Patient Global Assessment of Disease Activity, a 0 to 10 mm VAS, where 0 mm = very well and 10 mm = extremely bad. Participants were asked to answer the following question: “In general how would you rate your health over the last 2-3 weeks?”. Participants responded by marking the line and the distance from the left edge was recorded.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	30	17
Change From Baseline to Week 12 in Patient Global Assessment of Disease Activity [units: mm] Median (Full Range)	-3.8 (-9.4 to 2.0)	0.2 (-6.6 to 6.8)

Statistical Analysis 1 for Change From Baseline to Week 12 in Patient Global Assessment of Disease Activity

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.002
	Comments	[Not specified]
	Method	t-test, 1 sided
	Comments	[Not specified]

37. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in Patient Global Assessment of Disease Activity
Measure Description	General health was assessed using the Patient Global Assessment of Disease Activity, a 0 to 10 mm VAS, where 0 mm = very well and 10 mm = extremely bad. Participants were asked to answer the following question: “In general how would you rate your health over the last 2-3 weeks?”. Participants responded by marking the line and the distance from the left edge was recorded.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	26	7	10
Change From Baseline to Week 24 in Patient Global Assessment of Disease Activity [units: mm] Median (Full Range)	-4.4 (-9.5 to 2.6)	-1.5 (-7.1 to 3.7)	-1.4 (-5.4 to 1.0)

38. Secondary Outcome Measure:

Measure Title	Patient Global Assessment of Pain
Measure Description	Patient's Global Assessment of Pain was assessed using a 10-mm horizontal VAS (0 to 10 mm) where 0=pain absent and 10=intolerable pain. Participants responded by placing a mark on the line to indicate their current level of pain; the distance from the left edge to the mark was recorded.
Time Frame	Baseline, Weeks 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specific parameter at a given visit. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	32	19	10
Patient Global Assessment of Pain [units: mm] Median (Full Range)			

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Baseline (n=32,19,0)	5.2 (2.6 to 10.0)	5.1 (1.1 to 10.0)	NA (NA to NA) [1]
Week 4 (n= 31,18,0)	3.2 (0.4 to 7.4)	5.1 (1.3 to 10.0)	NA (NA to NA) [1]
Week 8 (n=31,17,0)	2.8 (0.0 to 8.6)	4.9 (1.9 to 8.3)	NA (NA to NA) [1]
Week 12 (n=30,17,0)	2.2 (0.0 to 8.0)	4.8 (1.0 to 8.6)	NA (NA to NA) [1]
Week 16 (n=26,7,10)	2.4 (0.0 to 6.6)	3.8 (0.4 to 8.2)	5.2 (1.5 to 8.8)
Week 20 (n=26,7,10)	1.5 (0.0 to 6.7)	5.0 (2.0 to 6.5)	3.8 (0.9 to 7.2)
Week 24 (n=26,7,10)	1.2 (0.0 to 8.0)	5.3 (1.5 to 6.6)	3.1 (0.7 to 6.2)

[1] Data for the Placebo group with recovery therapy were collected only at Weeks 16, 20, and 24.

Statistical Analysis 1 for Patient Global Assessment of Pain

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	Change from Baseline to Week 12
	Method	Other [Friedman's T test]
	Comments	[Not specified]

Statistical Analysis 2 for Patient Global Assessment of Pain

Statistical Analysis Overview	Comparison Groups	Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.500
	Comments	Change from Baseline to Week 12
	Method	Other [Friedman's T test]
	Comments	[Not specified]

39. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 12 in Patient Global Assessment of Pain
Measure Description	Patient's Global Assessment of Pain was assessed using a 10-mm horizontal VAS (0 to 10 mm) where 0=pain absent and 10=intolerable pain. Participants responded by placing a mark on the line to indicate their current level of pain; the distance from the left edge to the mark was recorded. Change in Patient Global Assessment of Pain was determined as the difference in the scores at baseline and Week 12. A negative number indicated improvement.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	30	17
Change From Baseline to Week 12 in Patient Global Assessment of Pain [units: mm] Median (Full Range)	-3.3 (-9.1 to 3.0)	-0.3 (-8.2 to 5.3)

Statistical Analysis 1 for Change From Baseline to Week 12 in Patient Global Assessment of Pain

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.007
	Comments	[Not specified]
	Method	t-test, 1 sided
	Comments	[Not specified]

40. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in Patient Global Assessment of Pain
Measure Description	Patient's Global Assessment of Pain was assessed using a 10-mm horizontal VAS (0 to 10 mm) where 0=pain absent and 10=intolerable pain. Participants responded by placing a mark on the line to indicate their current level of pain; the distance from the left edge to the mark was recorded. Change in Patient Global Assessment of Pain was determined as the difference in the scores at baseline and Week 24. A negative number indicated improvement.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	26	7	10
Change From Baseline to Week 24 in Patient Global Assessment of Pain [units: mm] Median (Full Range)	-3.7 (-9.4 to 2.8)	-3.4 (-4.4 to 3.2)	-1.5 (-5.9 to 1.9)

41. Secondary Outcome Measure:

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

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	32	19	10

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Health Assessment Questionnaire - Disease Index (HAQ-DI) Scores [units: units on a scale] Median (Full Range)			
Global score, Baseline (n=30,16,0)	2.1 (1.3 to 2.9)	2.3 (1.4 to 2.9)	NA (NA to NA) [1]
Global score, Week 12 (n=28,13,0)	1.5 (1.0 to 2.5)	2.3 (1.4 to 3.0)	NA (NA to NA) [1]
Global score, Week 24 (n=26,7,10)	1.3 (1.0 to 2.8)	2.1 (1.6 to 2.5)	2.1 (1.4 to 2.7)
Dressing/grooming, Baseline (n=31,18,0)	2.0 (1.0 to 3.0)	2.0 (1.0 to 3.0)	NA (NA to NA) [1]
Dressing/grooming, Week 12 (n=30,16,0)	1.0 (0.0 to 3.0)	2.0 (1.0 to 3.0)	NA (NA to NA) [1]
Dressing/grooming, Week 24 (n=26,7,10)	1.0 (1.0 to 3.0)	2.0 (1.0 to 3.0)	2.0 (1.0 to 3.0)
Arising, Baseline (n=32,19,0)	2.0 (1.0 to 3.0)	2.0 (1.0 to 3.0)	NA (NA to NA) [1]
Arising, Week 12 (n=30,17,0)	1.0 (1.0 to 3.0)	2.0 (0.0 to 3.0)	NA (NA to NA) [1]
Arising, Week 24 (n=26,7,10)	1.0 (1.0 to 3.0)	2.0 (1.0 to 2.0)	2.0 (1.0 to 3.0)
Eating, Baseline (n=26,14,0)	2.0 (1.0 to 3.0)	3.0 (1.0 to 3.0)	NA (NA to NA) [1]
Eating, Week 12 (n=27,10,0)	2.0 (1.0 to 3.0)	3.0 (2.0 to 3.0)	NA (NA to NA) [1]
Eating, Week 24 (n=24,7,9)	1.0 (1.0 to 3.0)	3.0 (2.0 to 3.0)	2.0 (2.0 to 3.0)
Walking, Baseline (n=32,19,0)	2.0 (1.0 to 3.0)	2.0 (1.0 to 3.0)	NA (NA to NA) [1]
Walking, Week 12 (n=30,17,0)	1.0 (0.0 to 3.0)	2.0 (1.0 to 3.0)	NA (NA to NA) [1]
Walking, Week 24 (n=26,7,10)	1.0 (1.0 to 3.0)	2.0 (2.0 to 3.0)	2.0 (1.0 to 3.0)
Hygiene, Baseline (n=31,18,0)	2.0 (1.0 to 3.0)	2.0 (1.0 to 3.0)	NA (NA to NA) [1]
Hygiene, Week 12 (n=30,17,0)	1.0 (0.0 to 3.0)	2.0 (0.0 to 3.0)	NA (NA to NA) [1]
Hygiene, Week 24 (n=26,7,10)	1.0 (1.0 to 3.0)	2.0 (1.0 to 2.0)	2.0 (1.0 to 2.0)
Reach, Baseline (n=24,12,0)	2.0 (1.0 to 3.0)	3.0 (1.0 to 3.0)	NA (NA to NA) [1]
Reach, Week 12 (n=26,10,0)	2.0 (0.0 to 3.0)	2.0 (0.0 to 3.0)	NA (NA to NA) [1]
Reach, Week 24 (n=23,7,8)	2.0 (1.0 to 3.0)	2.0 (2.0 to 2.0)	2.5 (1.0 to 3.0)
Grip, Baseline (n=29,18,0)	2.0 (1.0 to 3.0)	2.0 (1.0 to 3.0)	NA (NA to NA) [1]

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Grip, Week 12 (n=29,14,0)	1.0 (0.0 to 3.0)	2.0 (0.0 to 3.0)	NA (NA to NA) [1]
Grip, Week 24 (n=26,7,9)	1.0 (1.0 to 3.0)	2.0 (2.0 to 3.0)	2.0 (2.0 to 3.0)
Activity, Baseline (n=31,15,0)	2.0 (1.0 to 3.0)	2.0 (2.0 to 3.0)	NA (NA to NA) [1]
Activity, Week 12 (n=29,14,0)	2.0 (0.0 to 3.0)	2.0 (0.0 to 3.0)	NA (NA to NA) [1]
Activity, Week 24 (n=25,7,8)	1.0 (1.0 to 3.0)	2.0 (2.0 to 2.0)	2.0 (2.0 to 3.0)

[1] Data for the Placebo group with recovery therapy were collected only at Week 24.

42. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 12 in Erythrocyte Sedimentation Rate (ESR)
Measure Description	ESR is an inflammatory marker and is used to assess disease activity in rheumatoid arthritis (RA). A reduction in ESR indicates improvement.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	30	15
Change From Baseline to Week 12 in Erythrocyte Sedimentation Rate (ESR) [units: mm/hr]	-19.0 (-93.0 to 0.0)	2.0 (-49.0 to 39.0)

	Tocilizumab 8 mg/kg	Placebo
Median (Full Range)		

Statistical Analysis 1 for Change From Baseline to Week 12 in Erythrocyte Sedimentation Rate (ESR)

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.001
	Comments	[Not specified]
	Method	t-test, 1 sided
	Comments	[Not specified]

43. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in ESR
Measure Description	ESR is an inflammatory marker and is used to assess disease activity in RA. A reduction in ESR indicates improvement.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	24	6	9
Change From Baseline to Week 24 in ESR [units: mm/hr] Median (Full Range)	-20.0 (-95.0 to 5.0)	-9.0 (-47.0 to 3.0)	-27.0 (-75.0 to -7.0)

44. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 12 in C-Reactive Protein (CRP)
Measure Description	The test for CRP is a laboratory measurement for evaluation of an acute phase reactant of inflammation through the use of an ultrasensitive assay. A decrease in the level of CRP indicates reduction in inflammation and therefore improvement. CRP was measured in milligrams per deciliter (mg/dL).
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population. After Week 12, participants receiving placebo could have been switched to tocilizumab.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	29	15
Change From Baseline to Week 12 in C-Reactive Protein (CRP) [units: mg/dL] Median (Full Range)	-0.9 (-8.0 to 0.0)	-0.1 (-3.9 to 2.5)

Statistical Analysis 1 for Change From Baseline to Week 12 in C-Reactive Protein (CRP)

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.002
	Comments	[Not specified]
	Method	t-test, 1 sided
	Comments	[Not specified]

45. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in CRP
Measure Description	The test for CRP is a laboratory measurement for evaluation of an acute phase reactant of inflammation through the use of an ultrasensitive assay. A decrease in the level of CRP indicates reduction in inflammation and therefore improvement.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	24	5	5
Change From Baseline to Week 24 in CRP [units: mg/dL] Median (Full Range)	-1.2 (-8.0 to 0.0)	-0.2 (-2.9 to -0.02)	-0.6 (-9.7 to 0.0)

46. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 12 in Serum Cortisol
Measure Description	Change in serum cortisol was determined as the difference in the scores at Baseline and Week 12.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	29	16
Change From Baseline to Week 12 in Serum Cortisol [units: mg/dL] Median (Full Range)	-1.4 (-53.0 to 102.3)	2.5 (-31.6 to 119.3)

Statistical Analysis 1 for Change From Baseline to Week 12 in Serum Cortisol

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.118
	Comments	[Not specified]
	Method	t-test, 1 sided
	Comments	[Not specified]

47. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in Serum Cortisol
Measure Description	Change in serum cortisol was determined as the difference in the scores at Baseline and Week 24.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population;

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 24 weeks
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 24 weeks. At 12 weeks, participants who did not respond to treatment (those who did not show improvement of at least 20% in tender joint count and swollen joint count) were offered rescue therapy with open-label tocilizumab 8 mg/kg every 4 weeks.
Placebo-Tocilizumab	At 12 Weeks participants who did not show an improvement of ≥20% in tender and swollen joint counts were offered a rescue therapy with open-label tocilizumab 8mg/kg every 4 weeks

Measured Values

	Tocilizumab	Placebo	Placebo-Tocilizumab
Number of Participants Analyzed	25	7	10

	Tocilizumab	Placebo	Placebo-Tocilizumab
Change From Baseline to Week 24 in Serum Cortisol [units: mg/dL] Median (Full Range)	-2.5 (-40.1 to 51.8)	-5.2 (-32.0 to 6.0)	-5.1 (-63.2 to 106.2)

48. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 12 in Plasma Adrenocorticotrophic Hormone (ACTH)
Measure Description	Change in Plasma ACTH was determined as the difference in the scores at Baseline and Week 12.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	28	15
Change From Baseline to Week 12 in Plasma Adrenocorticotrophic Hormone (ACTH) [units: mg/dL] Median (Full Range)	0.00 (-10.27 to 7.41)	0.00 (-7.62 to 4.67)

Statistical Analysis 1 for Change From Baseline to Week 12 in Plasma Adrenocorticotrophic Hormone (ACTH)

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	1.00
	Comments	[Not specified]
	Method	t-test, 1 sided
	Comments	[Not specified]

49. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in Plasma ACTH
Measure Description	Change in plasma ACTH was determined as the difference in the scores at baseline and Week 24.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Patient's Global Assessment of Pain was assessed using a 10-mm horizontal VAS (0 to 10 mm) where 0=pain absent and 10=intolerable pain. Participants responded by placing a mark on the line to indicate their current level of pain; the distance from the left edge to the mark was recorded. Change in Patient Global Assessment of Pain was determined as the difference in the scores at baseline and Week 12. A negative number indicated improvement.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	24	6	10
Change From Baseline to Week 24 in Plasma ACTH [units: mg/dL] Median (Full Range)	-0.4 (-13.7 to 12.7)	-0.3 (-2.0 to 0.0)	0.8 (-1.9 to 4.1)

50. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 12 in Serum Androstenedione
Measure Description	Change in serum androstenedione was determined as the difference in the scores at Baseline and Week 12.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	28	16
Change From Baseline to Week 12 in Serum Androstenedione [units: mg/dL] Median (Full Range)	0.01 (-0.57 to 0.29)	0.01 (-0.12 to 0.18)

Statistical Analysis 1 for Change From Baseline to Week 12 in Serum Androstenedione

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.437
	Comments	[Not specified]
	Method	t-test, 1 sided
	Comments	[Not specified]

51. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 12 in 17 Hydroxy Progesterone (17OHP)
Measure Description	Change in 17OHP was determined as the difference in the scores at Baseline and Week 12.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	28	15
Change From Baseline to Week 12 in 17 Hydroxy Progesterone (17OHP)	-0.01 (-1.90 to 1.86)	-0.03 (-0.60 to 0.12)

	Tocilizumab 8 mg/kg	Placebo
[units: mg/dL] Median (Full Range)		

Statistical Analysis 1 for Change From Baseline to Week 12 in 17 Hydroxy Progesterone (17OHP)

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	1.00
	Comments	[Not specified]
	Method	t-test, 1 sided
	Comments	[Not specified]

52. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in Serum Androstenedione
Measure Description	Change in serum androstenedione was determined as the difference in the scores at Baseline and Week 24.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	25	6	10
Change From Baseline to Week 24 in Serum Androstenedione [units: mg/dL] Median (Full Range)	0.02 (-1.56 to 0.70)	0.01 (-0.10 to 0.06)	-0.002 (-0.71 to 0.36)

53. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in 17OHP
Measure Description	Change in 17OHP was determined as the difference in the scores at Baseline and Week 24.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	23	6	10
Change From Baseline to Week 24 in 17OHP [units: mg/dL] Median (Full Range)	-0.01 (-1.97 to 1.03)	-0.07 (-0.86 to 0.46)	-0.02 (-0.50 to 0.20)

54. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 12 in Serum Dehydroepiandrosterone (DHEA)
Measure Description	Change in DHEA was determined as the difference in the scores at Baseline and Week 12.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	28	15
Change From Baseline to Week 12 in Serum Dehydroepiandrosterone (DHEA) [units: mg/dL] Median (Full Range)	-0.07 (-6.09 to 2.90)	0.00 (-5.87 to 4.03)

Statistical Analysis 1 for Change From Baseline to Week 12 in Serum Dehydroepiandrosterone (DHEA)

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.190
	Comments	[Not specified]
	Method	t-test, 1 sided
	Comments	[Not specified]

55. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in Serum DHEA
Measure Description	Change in DHEA was determined as the difference in the scores at Baseline and Week 24.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	24	6	10
Change From Baseline to Week 24 in Serum DHEA [units: mg/dL] Median (Full Range)	0.17 (-5.67 to 4.07)	-0.73 (-3.45 to 2.50)	0.40 (-10.43 to 3.38)

56. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 12 in Neuropeptide Y

Measure Description	Change in Neuropeptide Y was determined as the difference in the scores at Baseline and Week 12.
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo
Number of Participants Analyzed	29	16
Change From Baseline to Week 12 in Neuropeptide Y [units: mg/dL] Median (Full Range)	-13.3 (-91.4 to 60.3)	-0.7 (-45.4 to 51.2)

Statistical Analysis 1 for Change From Baseline to Week 12 in Neuropeptide Y

Statistical Analysis Overview	Comparison Groups	Tocilizumab 8 mg/kg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.051
	Comments	[Not specified]
	Method	t-test, 1 sided
	Comments	[Not specified]

57. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in Neuropeptide Y
Measure Description	Change in Neuropeptide Y was determined as the difference in the scores at Baseline and Week 24.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions).
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Measured Values

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
Number of Participants Analyzed	24	6	9
Change From Baseline to Week 24 in Neuropeptide Y [units: mg/dL] Median (Full Range)	-11.1 (-80.8 to 80.6)	-2.5 (-44.5 to 58.4)	-13.9 (-52.8 to 28.2)

Reported Adverse Events

Time Frame	Adverse events were recorded from the day of screening until the end of study at Week 24.
Additional Description	[Not specified]

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 mg/kg (minimum dose of 480 mg, maximum dose of 800 mg) IV once every 4 weeks for 20 weeks (total of 6 infusions).
Placebo	Participants received placebo IV once every 4 weeks for a maximum of 20 weeks (total of 6 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) were offered rescue therapy with open-label tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.
Placebo-Tocilizumab 8 mg/kg	Participants received placebo IV once every 4 weeks for 12 weeks (total of 3 infusions). At 12 weeks, participants who did not respond to treatment (those who did not show improvement of ≥20% in TJC and SJC) received tocilizumab 8 mg/kg IV once every 4 weeks through Week 20.

Serious Adverse Events

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	2/35 (5.71%)	0/10 (0%)	0/9 (0%)
Infections and infestations			
Cellulitis [A] *	1/35 (2.86%)	0/10 (0%)	/
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gluteal cleft cyst [A] *	1/35 (2.86%)	0/10 (0%)	/

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

Other Adverse Events

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

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	29/35 (82.86%)	7/10 (70%)	6/9 (66.67%)
Blood and lymphatic system disorders			
Anemia [A] *	0/35 (0%)	1/10 (10%)	0/9 (0%)
Hematoma cyclid of the right eye [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Neutropenia [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Urine Leukocyte elevation [A] *	0/35 (0%)	1/10 (10%)	0/9 (0%)
Varicose vein rupture [A] *	0/35 (0%)	1/10 (10%)	0/9 (0%)
Gastrointestinal disorders			
Blood Diarrhea [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Diarrhea [A] *	0/35 (0%)	0/10 (0%)	1/9 (11.11%)
Dyspepsia [A] *	0/35 (0%)	0/10 (0%)	1/9 (11.11%)
Epigastric pain [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Gastroenteritis [A] *	0/35 (0%)	0/10 (0%)	1/9 (11.11%)
Vomiting [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
General disorders			
Back pain [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Cough [A] *	1/35 (2.86%)	0/10 (0%)	1/9 (11.11%)
Fall [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Finger cut [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Flu-like syndrome [A] *	0/35 (0%)	1/10 (10%)	1/9 (11.11%)
Gingivorrhagea in patient with low platelets [A] *	0/35 (0%)	0/10 (0%)	1/9 (11.11%)
Hoarseness [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Inter-digital wound [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Left leg cellulitis [A] *	1/35 (2.86%)	1/10 (10%)	0/9 (0%)
Nausea [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Odynophagia [A] *	0/35 (0%)	1/10 (10%)	0/9 (0%)
Sputum [A] *	0/35 (0%)	0/10 (0%)	1/9 (11.11%)

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Tooth ache [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Hepatobiliary disorders			
Hepatic toxicity [A] *	2/35 (5.71%)	2/10 (20%)	0/9 (0%)
Hepatotoxicity [A] *	2/35 (5.71%)	2/10 (20%)	0/9 (0%)
Infections and infestations			
Flu [A] *	2/35 (5.71%)	0/10 (0%)	0/9 (0%)
Herpes simplex in the lips [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Impetigo [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Infected traumatic right leg ulcer [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Mouth mucositis [A] *	0/35 (0%)	0/10 (0%)	1/9 (11.11%)
Oral candidiasis [A] *	0/35 (0%)	1/10 (10%)	0/9 (0%)
Pharyngitis [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Upper airways infection [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Urinary Tract infection [A] *	4/35 (11.43%)	1/10 (10%)	0/9 (0%)
Vaginal labial folliculitis [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Investigations			
Abnormal liver function tests [A] *	0/35 (0%)	1/10 (10%)	0/9 (0%)
Bilirubin Elevation [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Dislipidemia [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Elevated ALT [A] *	2/35 (5.71%)	0/10 (0%)	0/9 (0%)
Hypercholesterolemia [A] *	3/35 (8.57%)	1/10 (10%)	1/9 (11.11%)
Hypertriglyceridemia [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)

	Tocilizumab 8 mg/kg	Placebo	Placebo-Tocilizumab 8 mg/kg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Liver Enzyme Elevation [A] *	2/35 (5.71%)	0/10 (0%)	0/9 (0%)
Nitritis Elevation [A] *	0/35 (0%)	1/10 (10%)	0/9 (0%)
Transaminase Elevation [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Leg ulcer [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Oral aftosis [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Nervous system disorders			
Facial paralysis on the right side [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Renal and urinary disorders			
Mild renal failure [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Skin and subcutaneous tissue disorders			
Eczema [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)
Malar rash [A] *	0/35 (0%)	1/10 (10%)	0/9 (0%)
Rash [A] *	1/35 (2.86%)	0/10 (0%)	0/9 (0%)

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

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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