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A Study of RoActemra/Actemra (Tocilizumab) Versus Adalimumab in Combination With Methotrexate (MTX) in Patients With Moderate to Severe Active Rheumatoid Arthritis And an Inadequate Response to Treatment With Only One Tumor Necrosis Factor (TNF)-Inhibitor

This study has been terminated.
(The study was closed due to the slow enrollment rate.)

Sponsor:	Hoffmann-La Roche
Collaborators:	
Information provided by (Responsible Party):	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT01283971

Purpose

This randomized, parallel-group study will assess the efficacy and safety of RoActemra/Actemra (tocilizumab) versus adalimumab, both in combination with methotrexate (MTX) in patients with moderate to severe active rheumatoid arthritis. Patients, already treated with MTX at stable doses, will be randomized to receive either RoActemra/Actemra 8 mg/kg intravenously (IV) every 4 weeks or adalimumab 40 mg subcutaneous (SC) every 2 weeks. All patients will receive methotrexate (10-25 mg weekly) and folate (at least 5 mg weekly). The anticipated time on study treatment is 24 weeks.

Condition	Intervention	Phase
Rheumatoid Arthritis	Drug: tocilizumab [RoActemra/Actemra] Drug: adalimumab Drug: placebo to tocilizumab Drug: placebo to adalimumab Drug: methotrexate Drug: folate	Phase 4

Study Type: Interventional

Study Design: Treatment, Parallel Assignment, Open Label, Randomized, Safety/Efficacy Study
Official Title: A Randomized, Open-label, Parallel-group Study of the Reduction of Signs and Symptoms During Treatment With Tocilizumab Versus Adalimumab, Both in Combination With MTX, in Patients With Moderate to Severe Active Rheumatoid Arthritis and an Inadequate Response to Treatment With Only One TNF Inhibitor

Further study details as provided by Hoffmann-La Roche:

Primary Outcome Measure:

- Percentage of Participants With Disease Activity Score 28 Joints (DAS28) Remission at Week 24 [Time Frame: Week 24] [Designated as safety issue: No]
  The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 2 to 10. DAS28 Remission is defined as a DAS28 score <2.6.

Secondary Outcome Measures:

- Percentage of Participants With American College of Rheumatology (ACR20) Response at Week 24 [Time Frame: Baseline, Week 24] [Designated as safety issue: No]
  ACR20 response is defined as a ≥ 20% improvement (reduction) compared with baseline for both total joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: Patient's Assessment of Pain over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain; Patient's Global Assessment of Disease Activity and Physician's Global Assessment of Disease Activity over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity; Health Assessment Questionnaire: 20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do; and acute-phase reactant Erythrocyte Sedimentation Rate.
- Percentage of Participants With ACR50 Response at Week 24 [Time Frame: Baseline, Week 24] [Designated as safety issue: No]
  ACR50 response is defined as a ≥ 50% improvement (reduction) compared with baseline for both total joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: Patient's Assessment of Pain over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain; Patient's Global Assessment of Disease Activity and Physician's Global Assessment of Disease Activity over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity; Health Assessment Questionnaire: 20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do; and acute-phase reactant Erythrocyte Sedimentation Rate.
- Percentage of Participants With ACR70 Response at Week 24 [Time Frame: Baseline, Week 24] [Designated as safety issue: No]
  ACR70 response is defined as a ≥ 70% improvement (reduction) compared with baseline for both total joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: Patient's Assessment of Pain over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain; Patient's Global Assessment of Disease Activity and Physician's Global Assessment of Disease Activity over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity; Health Assessment Questionnaire: 20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do; and acute-phase reactant Erythrocyte Sedimentation Rate.
- Percentage of Participants With Good or Moderate European League Against Rheumatism (EULAR) DAS28 Responses at Week 24 [Time Frame: Baseline, Week 24] [Designated as safety issue: No]
  The DAS28 score is a measure of the subject's disease activity. It is based on the tender joint count (28 joints), swollen joint count (28 joints), patient's global assessment of disease activity (mm), and ESR. DAS28 total score ranges from 0 (best) to 10 (worst). A negative change from Baseline indicated improvement. European League Against Rheumatism (EULAR) Good response: DAS28 ≤ 3.2 or a change from Baseline < -1.2. EULAR Moderate response: DAS28 >3.2 to ≤ 5.1 or a change from Baseline < -0.6 to ≥ -1.2.
- Percentage of Participants With DAS28 Low Disease Activity (LDAS) at Week 24 [Time Frame: Week 24] [Designated as safety issue: No]
  The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 2 to 10. LDAS is defined as DAS28 ≤3.2.

- Change From Baseline in DAS28 Score at Week 24 [Time Frame: Baseline, Week 24] [Designated as safety issue: No]
  The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 2 to 10. A higher value indicated higher disease activity. A negative change from Baseline indicated improvement.
- Change From Baseline in Swollen Joint Count (SJC) at Week 24 [Time Frame: Baseline, Week 24] [Designated as safety issue: No]
  66 joints were assessed for swelling and joints are classified as swollen/not swollen giving a total possible swollen joint count score of 0 to 66. A negative change from Baseline indicated improvement.
- Change From Baseline in Tender Joint Count (TJC) at Week 24 [Time Frame: Baseline, Week 24] [Designated as safety issue: No]
  68 joints are assessed for tenderness and joints are classified as tender/not tender giving a total possible tender joint count score of 0 to 68. A negative change from Baseline indicated improvement.
- Change From Baseline in Patient Assessment of Pain Visual Analog Scale (VAS) at Week 24 [Time Frame: Baseline, Week 24] [Designated as safety issue: No]
  The patient assessed their pain using a 0 to 100 millimeter (mm) horizontal visual analogue scale (VAS). The left-hand extreme of the line equals 0 mm, and is described as "no pain" and the right-hand extreme equals 100 mm as "unbearable pain". A negative change from Baseline indicated improvement.
- Change From Baseline in the Patient Global Assessment of Disease Activity VAS at Week 24 [Time Frame: Baseline, Week 24] [Designated as safety issue: No]
  The patient's global assessment of disease activity is assessed on a 0 to 100 millimeter (mm) horizontal visual analogue scale (VAS) by the patient. The left-hand extreme of the line equals 0 mm, and is described as "no disease activity" (symptom-free and no arthritis symptoms) and the right-hand extreme equals 100 mm, as "maximum disease activity" (maximum arthritis disease activity). A negative change from Baseline indicated improvement.
- Change From Baseline in the Physician Global Assessment of Disease Activity VAS at Week 24 [Time Frame: Baseline, Week 24] [Designated as safety issue: No]
  The physician global assessment of disease activity was assessed using a 0 to 100 mm horizontal visual analogue scale (VAS) by the physician. The left-hand extreme of the line equals 0 mm, and is described as "no disease activity" (symptom-free and no arthritis symptoms) and the right-hand extreme equals 100 mm, as "maximum disease activity" (maximum arthritis disease activity). A negative change from Baseline indicated improvement.
- Change From Baseline in High Sensitivity C-Reactive Protein (hsCRP) at Week 24 [Time Frame: Baseline, Week 24] [Designated as safety issue: No]
  Blood was collected for C-Reactive Protein (CRP) (a test for analysis of inflammatory and infectious disorders) and was analyzed at a central laboratory. The concentration of CRP was measured in milligram/liter (mg/L). A reduction in the level is considered an improvement
- Change From Baseline in Erythrocyte Sedimentation Rate (ESR) at Week 24 [Time Frame: Baseline, Week 24] [Designated as safety issue: No]
  Blood was collected for Erythrocyte Sedimentation Rate (ESR) (a test that assesses tissue inflammation) and was analyzed at a local laboratory. ESR was measured in millimeter/hour (mm/hr). A reduction in the level is considered an improvement.
- Change From Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) Score at Week 24 [Time Frame: Baseline, Week 24] [Designated as safety issue: No]
  The Stanford Health Assessment Questionnaire Disability Index (HAQ-DI) is a patient completed questionnaire specific for rheumatoid arthritis, consisting of 20 questions in 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. There are 4 possible responses for each question: 0=without any difficulty, 1=with some difficulty, 2=with much difficulty and 3=unable to do. The score for each of the domains is the highest (worst) score in each domain. A patient must have a domain score for at least 6 of 8 domains to calculate a valid HAQ-DI score which is the sum of domain scores, divided by the number of domains that have a score for a total possible score minimum/maximum 0 (best) to 3 (worst). A negative change from Baseline indicated improvement.
- Change From Baseline in the Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-Fatigue) Score at Week 24 [Time Frame: Baseline, Week 24] [Designated as safety issue: No]
  FACIT-F is a 13-item questionnaire. Patients scored each item on a 5-point scale: 0 (Not at all) to 4 (Very much). The larger the patient's response to the questions (with the exception of 2 negatively stated), the greater the patient's fatigue. For all questions, except for the 2 negatively stated ones, the code was reversed and a new score was calculated as (4 minus the patient's response). The sum of all responses resulted in the FACIT-Fatigue score

for a total possible score of 0 (worse score) to 52 (better score). A higher score reflects an improvement in the patient's health status. A positive change from Baseline indicates improvement.

- Change From Baseline in Quality of Life Short Form (SF-36) Score at Week 24 [Time Frame: Baseline, Week 24] [Designated as safety issue: No]
  The SF-36 is a questionnaire used to assess physical functioning and is made up of eight domains: Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional and Mental Health. Transforming and standardizing these domains leads to the calculation of the Physical (PCS) and Mental (MCS) Component Summary measures. Scores ranging from 0 to 100, with 0=worst score (or quality of life) and 100=best score. A positive change from baseline indicates improvement.
- Change From Baseline in Routine Assessment of Patient Index Data 3 (RAPID3) Score at Week 24 [Time Frame: Baseline, Week 24] [Designated as safety issue: No]
  RAPID3 is a patient self reported assessment that combines the HAQ-DI [20 questions referring to 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip; common daily activities. Each domain has at least 2 component questions answered on a 4-point scale where 0=without any difficulty to 3=unable to do} converted to a score of 0-10, the Patients Assessment of Pain [Over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain] converted to a score of 0-10 and the Patient's Global Assessment of Disease Activity [over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity] converted to a score of 0-10. The 3 individual scales are summed for a raw score of 0-30 which is divided by 3 to achieve a total possible adjusted score of 0-10. A negative change from Baseline indicates improvement.
- Change From Baseline in Hemoglobin at Week 24 [Time Frame: Baseline, Week 24] [Designated as safety issue: No]
  Blood was collected at Baseline and Week 24. The samples were sent to a central laboratory for Hemoglobin analysis reported in gram/deciliter (g/dL). A positive number change from Baseline (a higher hemoglobin level compared to Baseline) indicated improvement
- Number of Participants With Serious Adverse Events (SAEs), Adverse Events (AEs), Discontinuation Due to AEs and Deaths [Time Frame: 32 weeks] [Designated as safety issue: No]
  An adverse event was considered any unfavorable and unintended sign, symptom, or disease associated with the use of the study drug, whether or not considered related to the study drug. Preexisting conditions that worsened during the study were reported as adverse events. A serious adverse event is any experience that suggests a significant hazard, contraindication, side effect or precaution that: results in death, is life-threatening, required in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect or is medically significant.

Enrollment: 96
Study Start Date: May 2011
Primary Completion Date: August 2012
Study Completion Date: August 2012

Arms	Assigned Interventions
Experimental: Tocilizumab + Methotrexate Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.	Drug: tocilizumab [RoActemra/Actemra] Tocilizumab 8 mg/kg IV every 4 weeks for 24 weeks. Other Names: RoActemra/Actemra Drug: placebo to adalimumab Placebo to adalimumab SC every 2 weeks for 24 weeks. Drug: methotrexate Methotrexate 10-25 mg weekly.

Arms	Assigned Interventions
	Drug: folate Folate at least 5 mg weekly.
Active Comparator: Adalimumab + Methotrexate Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.	Drug: adalimumab Adalimumab 40 mg SC every 2 weeks. Drug: placebo to tocilizumab Placebo to tocilizumab IV every 4 weeks for 24 weeks. Drug: methotrexate Methotrexate 10-25 mg weekly. Drug: folate Folate at least 5 mg weekly.

Eligibility

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

Criteria

Inclusion Criteria:

- Adult patients, >/= 18 years of age
- Rheumatoid arthritis of >/= 6 months duration (according to American College of Rheumatology (ACR) criteria)(according to ACR criteria)
- Inadequate response due to inefficacy of treatment (for at least 3 months) with only one approved Tumor Necrosis Factor (TNF)-agent other than adalimumab Depending on the TNF-inhibitor, last dose of TNF-inhibitor should have been 1 to 8 weeks before randomization to the study
- On methotrexate treatment for >/=12 weeks immediately prior to baseline, with stable dose (10-25 mg/week) for the last 8 weeks
- Disease Activity Score (DAS28) >3.2 at baseline
- Oral corticosteroids (</=10 mg/day prednisone or equivalent) and non-steroidal anti-inflammatory drugs (NSAIDs) are permitted if the dose has been stable for >/=6 weeks prior to baseline.

Exclusion Criteria:

- Major surgery (including joint surgery) within 8 weeks prior to screening or planned surgery within 6 months following randomization
- Rheumatic autoimmune disease other than rheumatoid arthritis
- Prior history of or current inflammatory joint disease other than rheumatoid arthritis
- Functional class IV (ACR criteria)
- History of severe allergic reaction to human, humanized or murine monoclonal antibodies
- Known active current or history of recurrent infection (including tuberculosis)
- Primary or secondary immunodeficiency (history of or currently active)
- Body weight >150 kg
- Previous treatment with any cell-depleting therapies

- Previous treatment with tocilizumab
- Intra-articular or parenteral corticosteroids within 6 weeks prior to baseline.

Contacts and Locations

Locations

United States, Alabama
Huntsville, Alabama, United States, 35801
Huntsville, Alabama, United States, 35801

United States, Arizona
Phoenix, Arizona, United States, 85027
Tucson, Arizona, United States, 85712

United States, California
Covina, California, United States, 91723
Escondido, California, United States, 92025
Huntington Beach, California, United States, 92646
La Mesa, California, United States, 91942
Lakewood, California, United States, 90712
Long Beach, California, United States, 90806
Los Angeles, California, United States, 90048
Los Angeles, California, United States, 90048
Sacramento, California, United States, 95816-5119
San Diego, California, United States, 92108
Westlake Village, California, United States, 91361
Whittier, California, United States, 90603
Whittier, California, United States, 90606
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Bridgeport, Connecticut, United States, 06606
Hamden, Connecticut, United States, 06518
Norwich, Connecticut, United States, 06360

United States, Delaware
Newark, Delaware, United States, 19713

United States, Florida
Aventura, Florida, United States, 33180
Fort Lauderdale, Florida, United States, 33334
Jupiter, Florida, United States, 33458
Melbourne, Florida, United States, 32901
Naples, Florida, United States, 34102
Ocala, Florida, United States, 34474
Orlando, Florida, United States, 32806
Ormond Beach, Florida, United States, 32174
Palm Habor, Florida, United States, 34684
Palm Harbor, Florida, United States, 34684

Sarasota, Florida, United States, 34239
Tamarac, Florida, United States, 33321
Tampa, Florida, United States, 33609
United States, Georgia
Atlanta, Georgia, United States, 30342
Valdosta, Georgia, United States, 31602
United States, Idaho
Idaho Falls, Idaho, United States, 83404
United States, Illinois
Chicago, Illinois, United States, 60611
Maywood, Illinois, United States, 60153
Moline, Illinois, United States, 61265
Springfield, Illinois, United States, 62704
United States, Indiana
Fort Wayne, Indiana, United States, 46804
South Bend, Indiana, United States, 46601
United States, Kentucky
Lexington, Kentucky, United States, 40515
United States, Louisiana
Baton Rouge, Louisiana, United States, 70808
Monroe, Louisiana, United States, 71203
United States, Maryland
Annapolis, Maryland, United States, 21401
Cumberland, Maryland, United States, 21502
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Tupelo, Mississippi, United States, 38802
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Saint Louis, Missouri, United States, 63117
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Washington, North Carolina, United States, 27889
United States, Ohio
Cleveland, Ohio, United States, 44195
Middleburg Heights, Ohio, United States, 44130
Toledo, Ohio, United States, 43606
United States, Oklahoma
Oklahoma City, Oklahoma, United States, 73109
United States, Oregon
Lake Oswego, Oregon, United States, 97035
United States, Pennsylvania
Duncansville, Pennsylvania, United States, 16635
Philadelphia, Pennsylvania, United States, 19152
Pittsburgh, Pennsylvania, United States, 15237
Pittsburgh, Pennsylvania, United States, 15261
Willow Grove, Pennsylvania, United States, 19090
Wynnewood, Pennsylvania, United States, 19096
Wyomissing, Pennsylvania, United States, 19610
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Investigators

Study Director:	Clinical Trials	Hoffmann-La Roche

More Information

Responsible Party: Hoffmann-La Roche
Study ID Numbers: MA25522
2010-023587-40 [EudraCT Number]
Health Authority: United States: Food and Drug Administration

Study Results

Participant Flow

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Overall Study

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Started	48	48
Intent to Treat Population	46	48
Completed	33	36
Not Completed	15	12
Adverse Event	3	5
Insufficient therapeutic responses	3	3
Protocol Violation	5	1
Refused treatment	3	1
Failure to return	0	1
Administrative reasons	1	1

Baseline Characteristics

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Baseline Measures

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate	Total
Number of Participants	48	48	96
Age, Continuous [units: years] Mean (Standard Deviation)	54.3 (11.89)	51.3 (12.51)	52.8 (12.2)
Age, Customized [units: Participants]			
<50 years	16	20	36
50 to 64 years	22	18	40
≥65 to 75 years	9	10	19
>75 years	1	0	1
Gender, Male/Female [units: participants]			
Female	40	38	78
Male	8	10	18

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With Disease Activity Score 28 Joints (DAS28) Remission at Week 24
Measure Description	The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 2 to 10. DAS28 Remission is defined as a DAS28 score <2.6.

Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat population, all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment, with data available at Baseline and Week 24. Last observation carried forward was used to impute missing tender and swollen joint counts. All other ACR components were used as observed.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	33	36
Percentage of Participants With Disease Activity Score 28 Joints (DAS28) Remission at Week 24 [units: Percentage of participants]	30.3	36.1

2. Secondary Outcome Measure:

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

Analysis Population Description

Participants from the Intent-to-treat population, all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment, with ACR score data available. Last observation carried forward was used to impute missing tender and swollen joint counts. All other ACR components were used as observed.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	33	35
Percentage of Participants With American College of Rheumatology (ACR20) Response at Week 24 [units: Percentage of participants]	66.7	62.9

3. Secondary Outcome Measure:

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

Analysis Population Description

Participants from the Intent-to-treat population, all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment, with ACR score data available. Last observation carried forward was used to impute missing tender and swollen joint counts. All other ACR components were used as observed.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	33	35
Percentage of Participants With ACR50 Response at Week 24 [units: Percentage of participants]	24.2	42.9

4. Secondary Outcome Measure:

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

Analysis Population Description

Participants from the Intent-to-treat population, all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment, with ACR score data available. Last observation carried forward was used to impute missing tender and swollen joint counts. All other ACR components were used as observed.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

	Description
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	33	35
Percentage of Participants With ACR70 Response at Week 24 [units: Percentage of participants]	18.2	22.9

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Good or Moderate European League Against Rheumatism (EULAR) DAS28 Responses at Week 24
Measure Description	The DAS28 score is a measure of the subject's disease activity. It is based on the tender joint count (28 joints), swollen joint count (28 joints), patient's global assessment of disease activity (mm), and ESR. DAS28 total score ranges from 0 (best) to 10 (worst). A negative change from Baseline indicated improvement. European League Against Rheumatism (EULAR) Good response: DAS28 ≤ 3.2 or a change from Baseline < -1.2. EULAR Moderate response: DAS28 >3.2 to ≤ 5.1 or a change from Baseline < -0.6 to ≥ -1.2.
Time Frame	Baseline, Week 24
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat population, all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment, with data available at Week 24. Last observation carried forward was used to impute missing tender and swollen joint counts. All other EULAR components were used as observed.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	33	36
Percentage of Participants With Good or Moderate European League Against Rheumatism (EULAR) DAS28 Responses at Week 24 [units: Percentage of participants]		
Moderate Response	39.4	27.8
Good Response	30.3	58.3

6. Secondary Outcome Measure:

Measure Title	Percentage of Participants With DAS28 Low Disease Activity (LDAS) at Week 24
Measure Description	The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 2 to 10. LDAS is defined as DAS28 ≤3.2.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat population, all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment, with data available at Baseline and Week 24. Last observation carried forward was used to impute missing tender and swollen joint counts. All other DAS28 components were used as observed.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	33	36

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Percentage of Participants With DAS28 Low Disease Activity (LDAS) at Week 24 [units: Percentage of participants]	30.3	58.3

7. Secondary Outcome Measure:

Measure Title	Change From Baseline in DAS28 Score at Week 24
Measure Description	The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 2 to 10. A higher value indicated higher disease activity. A negative change from Baseline indicated improvement.
Time Frame	Baseline, Week 24
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat population, all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment, with data available at Baseline and Week 24. Last observation carried forward was used to impute missing tender and swollen joint counts. All other DAS28 components were used as observed.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	33	36
Change From Baseline in DAS28 Score at Week 24 [units: Score on a scale] Mean (Standard Deviation)	-1.65 (1.541)	-2.80 (1.553)

8. Secondary Outcome Measure:

Measure Title	Change From Baseline in Swollen Joint Count (SJC) at Week 24
Measure Description	66 joints were assessed for swelling and joints are classified as swollen/not swollen giving a total possible swollen joint count score of 0 to 66. A negative change from Baseline indicated improvement.
Time Frame	Baseline, Week 24
Safety Issue?	No

Analysis Population Description

Intent-to-treat population included all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment. Last observation was used to impute missing swollen joint counts.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	46	48
Change From Baseline in Swollen Joint Count (SJC) at Week 24 [units: Joint count] Mean (Standard Deviation)	-5.7 (7.56)	-11.3 (15.84)

9. Secondary Outcome Measure:

Measure Title	Change From Baseline in Tender Joint Count (TJC) at Week 24
Measure Description	68 joints are assessed for tenderness and joints are classified as tender/not tender giving a total possible tender joint count score of 0 to 68. A negative change from Baseline indicated improvement.
Time Frame	Baseline, Week 24
Safety Issue?	No

Analysis Population Description

Intent-to-treat population included all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment. Last observation carried forward was used to impute missing tender joint counts.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	46	48
Change From Baseline in Tender Joint Count (TJC) at Week 24 [units: Joint count] Mean (Standard Deviation)	-8.0 (14.62)	-13.9 (16.50)

10. Secondary Outcome Measure:

Measure Title	Change From Baseline in Patient Assessment of Pain Visual Analog Scale (VAS) at Week 24
Measure Description	The patient assessed their pain using a 0 to 100 millimeter (mm) horizontal visual analogue scale (VAS). The left-hand extreme of the line equals 0 mm, and is described as "no pain" and the right-hand extreme equals 100 mm as "unbearable pain". A negative change from Baseline indicated improvement.
Time Frame	Baseline, Week 24
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat population, all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment, with data available at Baseline and Week 24.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

	Description
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	33	36
Change From Baseline in Patient Assessment of Pain Visual Analog Scale (VAS) at Week 24 [units: Score on a scale] Mean (Standard Deviation)	-30.1 (20.57)	-23.8 (29.28)

11. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Patient Global Assessment of Disease Activity VAS at Week 24
Measure Description	The patient's global assessment of disease activity is assessed on a 0 to 100 millimeter (mm) horizontal visual analogue scale (VAS) by the patient. The left-hand extreme of the line equals 0 mm, and is described as "no disease activity" (symptom-free and no arthritis symptoms) and the right-hand extreme equals 100 mm, as "maximum disease activity" (maximum arthritis disease activity). A negative change from Baseline indicated improvement.
Time Frame	Baseline, Week 24
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat population, all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment, with data available at Baseline and Week 24.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	33	36

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Change From Baseline in the Patient Global Assessment of Disease Activity VAS at Week 24 [units: Score on a scale] Mean (Standard Deviation)	-30.2 (22.17)	-21.5 (28.89)

12. Secondary Outcome Measure:

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

Analysis Population Description

Participants from the Intent-to-treat population, all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment, with data available at Baseline and Week 24.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	33	36
Change From Baseline in the Physician Global Assessment of Disease Activity VAS at Week 24 [units: Score on a scale] Mean (Standard Deviation)	-37.0 (23.20)	-36.8 (32.34)

13. Secondary Outcome Measure:

Measure Title	Change From Baseline in High Sensitivity C-Reactive Protein (hsCRP) at Week 24
Measure Description	Blood was collected for C-Reactive Protein (CRP) (a test for analysis of inflammatory and infectious disorders) and was analyzed at a central laboratory. The concentration of CRP was measured in milligram/liter (mg/L). A reduction in the level is considered an improvement
Time Frame	Baseline, Week 24
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat population, all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment, with data available at Baseline and Week 24 for this outcome measure.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	33	35
Change From Baseline in High Sensitivity C-Reactive Protein (hsCRP) at Week 24 [units: mg/L] Mean (Standard Deviation)	-1.127 (11.1261)	-7.474 (10.8446)

14. Secondary Outcome Measure:

Measure Title	Change From Baseline in Erythrocyte Sedimentation Rate (ESR) at Week 24
Measure Description	Blood was collected for Erythrocyte Sedimentation Rate (ESR) (a test that assesses tissue inflammation) and was analyzed at a local laboratory. ESR was measured in millimeter/hour (mm/hr). A reduction in the level is considered an improvement.
Time Frame	Baseline, Week 24
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat population, all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment, with data available at Baseline and Week 24 for this outcome measure.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	33	36
Change From Baseline in Erythrocyte Sedimentation Rate (ESR) at Week 24 [units: mm/hr] Mean (Standard Deviation)	-1.2 (16.78)	-25.7 (25.52)

15. Secondary Outcome Measure:

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

Analysis Population Description

Participants from the Intent-to-treat population, all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment, with data available at Baseline and Week 24.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	30	35
Change From Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) Score at Week 24 [units: Score on a scale] Mean (Standard Deviation)	-0.19 (0.437)	-0.36 (0.543)

16. Secondary Outcome Measure:

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

Analysis Population Description

Participants from the Intent-to-treat population, all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment, with data available at Baseline and Week 24.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

	Description
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	32	34
Change From Baseline in the Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-Fatigue) Score at Week 24 [units: Score on a scale] Mean (Standard Deviation)	5.6 (9.60)	8.0 (9.33)

17. Secondary Outcome Measure:

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

Analysis Population Description

Participants from the Intent-to-treat population, all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment, with data available at Baseline and Week 24 for this outcome measure.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	29	33
Change From Baseline in Quality of Life Short Form (SF-36) Score at Week 24 [units: Score on a scale] Mean (Standard Deviation)		
Physical Component Summary Score	4.39 (6.110)	5.84 (7.980)
Mental Component Summary Score	6.07 (12.171)	6.84 (11.907)

18. Secondary Outcome Measure:

Measure Title	Change From Baseline in Routine Assessment of Patient Index Data 3 (RAPID3) Score at Week 24
Measure Description	RAPID3 is a patient self reported assessment that combines the HAQ-DI [20 questions referring to 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip; common daily activities. Each domain has at least 2 component questions answered on a 4-point scale where 0=without any difficulty to 3=unable to do} converted to a score of 0-10, the Patients Assessment of Pain [Over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain] converted to a score of 0-10 and the Patient's Global Assessment of Disease Activity [over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity] converted to a score of 0-10. The 3 individual scales are summed for a raw score of 0-30 which is divided by 3 to achieve a total possible adjusted score of 0-10. A negative change from Baseline indicates improvement.
Time Frame	Baseline, Week 24
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat population, all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment, with data available at Baseline and Week 24 for this outcome measure.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	30	35
Change From Baseline in Routine Assessment of Patient Index Data 3 (RAPID3) Score at Week 24 [units: Score on a scale] Mean (Standard Deviation)	-2.17 (1.611)	-1.83 (2.257)

19. Secondary Outcome Measure:

Measure Title	Change From Baseline in Hemoglobin at Week 24
Measure Description	Blood was collected at Baseline and Week 24. The samples were sent to a central laboratory for Hemoglobin analysis reported in gram/deciliter (g/dL). A positive number change from Baseline (a higher hemoglobin level compared to Baseline) indicated improvement
Time Frame	Baseline, Week 24
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat population, all randomized participants who received study drug and had at least 1 post-baseline efficacy assessment, with hemoglobin data available at Baseline and Week 24.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	32	35
Change From Baseline in Hemoglobin at Week 24 [units: g/dL] Mean (Standard Deviation)	1.2 (8.70)	6.5 (12.01)

20. Secondary Outcome Measure:

Measure Title	Number of Participants With Serious Adverse Events (SAEs), Adverse Events (AEs), Discontinuation Due to AEs and Deaths
Measure Description	An adverse event was considered any unfavorable and unintended sign, symptom, or disease associated with the use of the study drug, whether or not considered related to the study drug. Preexisting conditions that worsened during the study were reported as adverse events. A serious adverse event is any experience that suggests a significant hazard, contraindication, side effect or precaution that: results in death, is life-threatening, required in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect or is medically significant.
Time Frame	32 weeks
Safety Issue?	No

Analysis Population Description

Safety Population included all participants who received study drug and who had at least 1 post-dose safety assessment.

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Measured Values

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
Number of Participants Analyzed	48	48
Number of Participants With Serious Adverse Events (SAEs), Adverse Events (AEs), Discontinuation Due to AEs and Deaths [units: Participants]		
Any Adverse Event (AE)	35	33
Any Serious Adverse Event	2	8
AE leading to withdrawal	3	5
Death	0	0

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
Adalimumab + Methotrexate	Adalimumab 40 mg SC every 2 weeks + Placebo to tocilizumab IV every 4 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.
Tocilizumab + Methotrexate	Tocilizumab 8 mg/kg intravenous (IV) every 4 weeks + Placebo to adalimumab subcutaneous (SC) every 2 weeks for 24 weeks. All participants received methotrexate 10-25 mg and folate at least 5 mg/kg weekly.

Serious Adverse Events

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
	Affected/At Risk (%)	Affected/At Risk (%)
Total	2/48 (4.17%)	8/48 (16.67%)
Cardiac disorders		
Ventricular tachycardia [A] †	0/48 (0%)	1/48 (2.08%)
Infections and infestations		
Appendicitis [A] †	0/48 (0%)	1/48 (2.08%)
Bursitis infective [A] †	0/48 (0%)	1/48 (2.08%)
Pneumonia [A] †	1/48 (2.08%)	1/48 (2.08%)
Urinary tract infection [A] †	0/48 (0%)	1/48 (2.08%)
Injury, poisoning and procedural complications		
Hip fracture [A] †	0/48 (0%)	1/48 (2.08%)
Tibia fracture [A] †	0/48 (0%)	1/48 (2.08%)
Investigations		
Alanine aminotransferase increased [A] †	1/48 (2.08%)	0/48 (0%)

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
	Affected/At Risk (%)	Affected/At Risk (%)
Transaminases increased [A] †	0/48 (0%)	1/48 (2.08%)
Musculoskeletal and connective tissue disorders		
Rheumatoid arthritis [A] †	0/48 (0%)	1/48 (2.08%)
Psychiatric disorders		
Depression [A] †	0/48 (0%)	1/48 (2.08%)
Skin and subcutaneous tissue disorders		
Rash [A] †	0/48 (0%)	1/48 (2.08%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (15.1)

Other Adverse Events

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

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
	Affected/At Risk (%)	Affected/At Risk (%)
Total	21/48 (43.75%)	11/48 (22.92%)
Infections and infestations		
Bronchitis [A] †	3/48 (6.25%)	2/48 (4.17%)
Gastroenteritis [A] †	1/48 (2.08%)	3/48 (6.25%)
Nasopharyngitis [A] †	6/48 (12.5%)	1/48 (2.08%)
Upper respiratory tract infection [A] †	6/48 (12.5%)	3/48 (6.25%)
Musculoskeletal and connective tissue disorders		
Rheumatoid arthritis [A] †	2/48 (4.17%)	3/48 (6.25%)
Nervous system disorders		
Headache [A] †	1/48 (2.08%)	3/48 (6.25%)
Respiratory, thoracic and mediastinal disorders		

	Adalimumab + Methotrexate	Tocilizumab + Methotrexate
	Affected/At Risk (%)	Affected/At Risk (%)
Cough [A] †	3/48 (6.25%)	0/48 (0%)
Oropharyngeal pain [A] †	4/48 (8.33%)	0/48 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (15.1)

Limitations and Caveats

Data interpretation was limited by the very small sample size (enrollment 1/7 of planned sample size; not powered for formal statistical analysis) and the open-label observation (study un-blinded following protocol amendment to terminate enrollment).

More Information

Certain Agreements:

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

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

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

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