ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 11/06/2014

A Study of RoActemra/Actemra (Tocilizumab) in Combination With DMARDs Versus Current Best Practice DMARD Therapy in Patients With Rheumatoid Arthritis

This study has been terminated.
(The study was stopped prematurely due to lack of enrollment.)

Sponsor:	Hoffmann-La Roche
Collaborators:	
Information provided by (Responsible Party):	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT01251120

Purpose

This randomized, open-label, parallel-group study will assess the effect on disease remission of RoActemra/Actemra (tocilizumab) in combination with disease-modifying antirheumatic drugs (DMARDs) versus current best practice non-biologic DMARD therapy in patients with moderate-to-severe active rheumatoid arthritis. Patients who are randomly assigned to the RoActemra/Actemra treatment group will receive 8 mg/kg RoActemra/Actemra intravenously every 4 weeks. The anticipated time on study treatment is 12 months.

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

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Open Label, Randomized, Safety/Efficacy Study
Official Title: A Pragmatic, Randomized, Parallel Group Study of the Effect on Disease Remission, Work Productivity and Tolerability of Tocilizumab in Combination With DMARDs and Individually Designed Best Practice DMARD Therapy in Patients With Early, Moderate to Severe Rheumatoid Arthritis

Further study details as provided by Hoffmann-La Roche:
Primary Outcome Measure:

- Percentage of Participants Achieving Disease Remission at Month 12 Assessed Using the Disease Activity Score Based on 28-Joint Count (DAS28) [Time Frame: Month 12] [Designated as safety issue: No]

  The DAS28 is a combined index for measuring disease activity in Rheumatoid Arthritis (RA). The index includes swollen and tender joint counts (SJC and TJC), acute phase response, and general health status. For this study Erythrocyte sedimentation Rate (ESR) was to be used to calculate DAS28 score. The DAS28, which uses a 28 joint count, is derived from the original DAS which includes a 44 swollen joint count. The DAS28 has been validated in RA. The index is calculated using the following formula: DAS28 equals (=) 0.56 times (×) square root of √(TJC) plus (+) 0.28 × √(SJC) + 0.70 × ln(ESR) + 0.014 × GH Where, TJC28 = tender joint count on 28 joints, SJC28 = swollen joint count on 28 joints, ln = natural log, ESR measured as millimeters per hour (mm/hr), and GH = general health, which is participant's global assessment of disease activity (100-mm Visual Analog Scale [VAS]). DAS28 less than/equal to (≤) 2.6 defined remission.

Secondary Outcome Measures:

- Number of Hours Absent From Work [Time Frame: Baseline and 6 and 12 months] [Designated as safety issue: No]

  Work productivity measures include absence from work (participant reported and registries), permanent work disability (pension, participant reported and registries), presenteeism (Quantity and Quality instrument, QQ).
- Percentage of Participants Achieving Disease Remission at Month 6 Assessed Using DAS28 [Time Frame: Month 6] [Designated as safety issue: No]

  The DAS28 is a combined index for measuring disease activity in RA. The index includes SJC and TJC, acute phase response, and general health status. For this study ESR was to be used to calculate DAS28 score. The DAS28, which uses a 28 joint count, is derived from the original DAS which includes a 44 swollen joint count. The DAS28 has been validated in RA. The index is calculated using the following formula: DAS28 = 0.56 × √(TJC) + 0.28 × √(SJC) + 0.70 × ln(ESR) + 0.014 × GH Where, TJC28 = tender joint count on 28 joints, SJC28 = swollen joint count on 28 joints, ln = natural log, ESR measured as millimeters per hour (mm/hr), and GH = general health, which is participant's global assessment of disease activity (100-mm VAS). DAS28 ≤ 2.6 defined remission.
- Percentage of Participants Achieving Responses According to American College of Rheumatology (ACR) Criteria [Time Frame: Months 6 and 12] [Designated as safety issue: No]

  The ACR definition of response includes tender and swollen joint counts, VAS scales for pain, participant and investigator global assessment of disease activity, participant-assessed disability using Health Assessment Questionnaire (HAQ) and acute phase response.
- Percentage of Participants Achieving Remission at Months 6 and 12 Assessed Using Clinical Activity Disease Index (CDAI) [Time Frame: Months 6 and 12] [Designated as safety issue: No]

  The CDAI is a purely clinical index to measure disease activity. The index includes swollen and tender joint counts, participant global assessment of disease activity, and evaluator global assessment of disease activity (EGA).
- Change From Baseline to Months 6 and 12 in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT F) Scores [Time Frame: Baseline and Months 6 and 12] [Designated as safety issue: No]

  The FACIT-Fatigue score was calculated according to a 13-item questionnaire that assesses self-reported fatigue and its impact upon daily activities and function. FACIT-F is a 13-item questionnaire. Participants scored each item on a 5-point scale: 0 (Not at all) to 4 (Very much). The larger the participant's response to the questions (with the exception of 2 negatively stated), the greater the participants fatigue. For all questions, except for the 2 negatively stated ones, the code was reversed and a new score was calculated as (4 minus the participant's response). The sum of all responses resulted in the FACIT-Fatigue score for a total possible score of 0 (worse score) to 52 (better score). Clinically relevant improvement is defined as a ≥5-point change from Baseline.
- Change From Baseline to Months 6 and 12 in European Quality of Life-5D (EQ-5D) Score [Time Frame: Baseline and Months 6 and 12] [Designated as safety issue: No]

  EQ-5D is a participant rated questionnaire to assess health-related quality of life in terms of a single utility score. Health State Profile component assesses level of current health for 5 domains: mobility, self-care, usual activities, pain and discomfort, and anxiety and depression; 1 indicates better health state (no problems); 3 indicates worst health state (confined to bed). Scoring formula developed by EuroQoL Group assigns a utility value for each domain in the profile. Score is transformed and results in a total score range -0.594 to 1.000; higher score indicates a better health state.
- Change From Baseline to Months 6 and 12 in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score [Time Frame: Baseline and Months 6 and 12] [Designated as safety issue: No]

HAQ-DI includes 20 questions concerning participant's activities of daily life, grouped in 8 scales of 2 to 3 questions for each activity. To respond to each question, a four-level response (score of 0 to 3 points), with higher scores showing larger functional limitations, was chosen. Overall score was computed as the sum of the domain scores and divided by the number of domains answered. Total possible score range was 0-3 where 0=without difficulties; 1= with some difficulties; 2=with great difficulties; and 3=unable to perform these actions at all.

Enrollment: 2
Study Start Date: November 2011
Primary Completion Date: January 2013
Study Completion Date: January 2013

Arms	Assigned Interventions
Experimental: 1	Drug: tocilizumab [RoActemra/Actemra] 8 mg/kg intravenously every 4 weeks plus background DMARDs (including methotrexate)
Active Comparator: 2	Drug: DMARD Non-biologic DMARDs (including methotrexate) according to current best practice

Eligibility

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

Criteria

Inclusion Criteria:

- Adult patients, over the age of 18 years
- Diagnosis of moderate-to-severe active early rheumatoid arthritis (RA) of less than 2 years duration
- DAS28 >3.2
- Swollen joint count (SJC) >/=6 (66 joint count), and tender joint count (TJC) >/=6 (68 joint count)
- Patients who have received DMARDs (including methotrexate) for 3-7 months

Exclusion Criteria:

- Major surgery (including joint surgery) within 8 weeks prior to screening or planned major surgery within 6 months after baseline
- Rheumatic autoimmune disease other than rheumatoid arthritis (secondary Sjögrens syndrome or nodulosis with RA is permitted)
- Functional class III or IV as defined by ACR Classification of Functional Status in Rheumatoid Arthritis
- Prior history of or current inflammatory joint disease other than RA

Contacts and Locations

Locations

Finland
Helsinki, Finland, 00029
Hämeenlinna, Finland, 13530
Jyväskylä, Finland, 40620
Kuopio, Finland, 70101
Riihimäki, Finland, 11101
Rovaniemi, Finland, 96101

Investigators

Study Director:	Clinical Trials	Hoffmann-La Roche

More Information

Responsible Party:	Hoffmann-La Roche
Study ID Numbers:	ML25346
Health Authority:	Finland: Finnish Medicines Agency

Study Results

Participant Flow

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 milligrams per kilogram (mg/kg) intravenously every 4 weeks along with background disease-modifying antirheumatic drugs (DMARDs) including methotrexate. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.
Non-biologic DMARDs	Participants received non-biologic DMARDs (including methotrexate) according to current best practice. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.

Overall Study

	Tocilizumab	Non-biologic DMARDs
Started	1	1
Completed	1	0
Not Completed	0	1
Lack of Efficacy	0	1

Baseline Characteristics

Analysis Population Description

Due to limited number of participants (n=2) the study was prematurely terminated.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg intravenously every 4 weeks plus background DMARDs (including methotrexate)
Placebo	Participants received Non-biologic DMARDs (including methotrexate) according to current best practice

Baseline Measures

	Tocilizumab	Placebo	Total
Number of Participants	1	1	2
Age, Continuous [units: years] Mean (Standard Deviation)	63.2 (0.0)	48.2 (0.0)	55.7 (7.5)
Gender, Male/Female [units: participants]			
Female	1	1	2
Male	0	0	0

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants Achieving Disease Remission at Month 12 Assessed Using the Disease Activity Score Based on 28-Joint Count (DAS28)
Measure Description	The DAS28 is a combined index for measuring disease activity in Rheumatoid Arthritis (RA). The index includes swollen and tender joint counts (SJC and TJC), acute phase response, and general health status. For this study Erythrocyte sedimentation Rate (ESR) was to be used to calculate DAS28 score. The DAS28, which uses a 28 joint count, is derived from the original DAS which includes a 44 swollen joint count. The DAS28 has been validated in RA. The index is calculated using the following formula: DAS28 equals (=) 0.56 times (×) square root of √(TJC) plus (+) 0.28 × √(SJC) + 0.70 × ln(ESR) + 0.014 × GH Where, TJC28 = tender joint count on 28 joints, SJC28 = swollen joint count on 28 joints, ln = natural log, ESR measured as millimeters per hour (mm/hr), and GH = general health, which is participant's global assessment of disease activity (100-mm Visual Analog Scale [VAS]). DAS28 less than/equal to (≤) 2.6 defined remission.
Time Frame	Month 12

Safety Issue?	No

Analysis Population Description

Because of the limited number (n) of participants (n=2), the study was terminated prematurely. No statistical analysis could be performed.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg intravenously every 4 weeks along with background DMARDs including methotrexate. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.
Non-biologic DMARDs	Participants received non-biologic DMARDs (including methotrexate) according to current best practice. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.

Measured Values

	Tocilizumab	Non-biologic DMARDs
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

2. Secondary Outcome Measure:

Measure Title	Number of Hours Absent From Work
Measure Description	Work productivity measures include absence from work (participant reported and registries), permanent work disability (pension, participant reported and registries), presenteeism (Quantity and Quality instrument, QQ).
Time Frame	Baseline and 6 and 12 months
Safety Issue?	No

Analysis Population Description

Because of the limited number of participants (n=2), the study was terminated prematurely. No statistical analysis could be performed.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg intravenously every 4 weeks along with background DMARDs including methotrexate. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.
Non-biologic DMARDs	Participants received non-biologic DMARDs (including methotrexate) according to current best practice. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.

Measured Values

	Tocilizumab	Non-biologic DMARDs
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving Disease Remission at Month 6 Assessed Using DAS28
Measure Description	The DAS28 is a combined index for measuring disease activity in RA. The index includes SJC and TJC, acute phase response, and general health status. For this study ESR was to be used to calculate DAS28 score. The DAS28, which uses a 28 joint count, is derived from the original DAS which includes a 44 swollen joint count. The DAS28 has been validated in RA. The index is calculated using the following formula: DAS28 = 0.56 × √(TJC) + 0.28 × √(SJC) + 0.70 × ln(ESR) + 0.014 × GH Where, TJC28 = tender joint count on 28 joints, SJC28 = swollen joint count on 28 joints, ln = natural log, ESR measured as millimeters per hour (mm/hr), and GH = general health, which is participant's global assessment of disease activity (100-mm VAS). DAS28 ≤ 2.6 defined remission.
Time Frame	Month 6
Safety Issue?	No

Analysis Population Description

Because of the limited number of participants (n=2), the study was terminated prematurely. No statistical analysis could be performed.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg intravenously every 4 weeks along with background DMARDs including methotrexate. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.
Non-biologic DMARDs	Participants received non-biologic DMARDs (including methotrexate) according to current best practice. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.

Measured Values

	Tocilizumab	Non-biologic DMARDs
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving Responses According to American College of Rheumatology (ACR) Criteria
Measure Description	The ACR definition of response includes tender and swollen joint counts, VAS scales for pain, participant and investigator global assessment of disease activity, participant-assessed disability using Health Assessment Questionnaire (HAQ) and acute phase response.
Time Frame	Months 6 and 12
Safety Issue?	No

Analysis Population Description

Because of the limited number of participants (n=2), the study was terminated prematurely. No statistical analysis could be performed.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg intravenously every 4 weeks along with background DMARDs including methotrexate. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.
Non-biologic DMARDs	Participants received non-biologic DMARDs (including methotrexate) according to current best practice. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.

Measured Values

	Tocilizumab	Non-biologic DMARDs
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving Remission at Months 6 and 12 Assessed Using Clinical Activity Disease Index (CDAI)
Measure Description	The CDAI is a purely clinical index to measure disease activity. The index includes swollen and tender joint counts, participant global assessment of disease activity, and evaluator global assessment of disease activity (EGA).
Time Frame	Months 6 and 12
Safety Issue?	No

Analysis Population Description

Because of the limited number of participants (n=2), the study was terminated prematurely. No statistical analysis could be performed.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg intravenously every 4 weeks along with background DMARDs including methotrexate. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.
Non-biologic DMARDs	Participants received non-biologic DMARDs (including methotrexate) according to current best practice. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.

Measured Values

	Tocilizumab	Non-biologic DMARDs
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

6. Secondary Outcome Measure:

Measure Title	Change From Baseline to Months 6 and 12 in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT F) Scores
Measure Description	The FACIT-Fatigue score was calculated according to a 13-item questionnaire that assesses self-reported fatigue and its impact upon daily activities and function. FACIT-F is a 13-item questionnaire. Participants scored each item on a 5-point scale: 0 (Not at all) to 4 (Very much). The larger the participant's response to the questions (with the exception of 2 negatively stated), the greater the participants fatigue. For all questions, except for the 2 negatively stated ones, the code was reversed and a new score was calculated as (4 minus the participant's response). The sum of all responses resulted in the FACIT-Fatigue score for a total possible score of 0 (worse score) to 52 (better score). Clinically relevant improvement is defined as a ≥5-point change from Baseline.
Time Frame	Baseline and Months 6 and 12
Safety Issue?	No

Analysis Population Description

Because of the limited number of participants (n=2), the study was terminated prematurely. No statistical analysis could be performed.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg intravenously every 4 weeks along with background DMARDs including methotrexate. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.
Non-biologic DMARDs	Participants received non-biologic DMARDs (including methotrexate) according to current best practice. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.

Measured Values

	Tocilizumab	Non-biologic DMARDs
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

7. Secondary Outcome Measure:

Measure Title	Change From Baseline to Months 6 and 12 in European Quality of Life-5D (EQ-5D) Score
Measure Description	EQ-5D is a participant rated questionnaire to assess health-related quality of life in terms of a single utility score. Health State Profile component assesses level of current health for 5 domains: mobility, self-care, usual activities, pain and discomfort, and anxiety and depression; 1 indicates better health state (no problems); 3 indicates worst health state (confined to bed). Scoring formula developed by EuroQoL Group assigns a utility value for each domain in the profile. Score is transformed and results in a total score range -0.594 to 1.000; higher score indicates a better health state.
Time Frame	Baseline and Months 6 and 12
Safety Issue?	No

Analysis Population Description

Because of the limited number of participants (n=2), the study was terminated prematurely. No statistical analysis could be performed.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg intravenously every 4 weeks along with background DMARDs including methotrexate. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.
Non-biologic DMARDs	Participants received non-biologic DMARDs (including methotrexate) according to current best practice. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.

Measured Values

	Tocilizumab	Non-biologic DMARDs
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

8. Secondary Outcome Measure:

Measure Title	Change From Baseline to Months 6 and 12 in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score

Measure Description	HAQ-DI includes 20 questions concerning participant's activities of daily life, grouped in 8 scales of 2 to 3 questions for each activity. To respond to each question, a four-level response (score of 0 to 3 points), with higher scores showing larger functional limitations, was chosen. Overall score was computed as the sum of the domain scores and divided by the number of domains answered. Total possible score range was 0-3 where 0=without difficulties; 1= with some difficulties; 2=with great difficulties; and 3=unable to perform these actions at all.
Time Frame	Baseline and Months 6 and 12
Safety Issue?	No

Analysis Population Description

Because of the limited number of participants (n=2), the study was terminated prematurely. No statistical analysis could be performed.

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg intravenously every 4 weeks along with background DMARDs including methotrexate. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.
Non-biologic DMARDs	Participants received non-biologic DMARDs (including methotrexate) according to current best practice. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.

Measured Values

	Tocilizumab	Non-biologic DMARDs
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

Reported Adverse Events

Time Frame	The study was terminated prematurely due to lack of enrollment. Adverse events were recorded from the date of screening until study termination.
Additional Description	[Not specified]

Reporting Groups

	Description
Tocilizumab	Participants received tocilizumab 8 mg/kg intravenously every 4 weeks along with background DMARDs including methotrexate. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.

	Description
Non-biologic DMARDs	Participants received non-biologic DMARDs (including methotrexate) according to current best practice. All participants who received methotrexate also received at least 5 mg oral folic acid weekly.

Serious Adverse Events

	Tocilizumab		Non-biologic DMARDs	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	0/1 (0%)		0/1 (0%)	

Other Adverse Events

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

	Tocilizumab		Non-biologic DMARDs	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	1/1 (100%)		0/1 (0%)	
Gastrointestinal disorders				
Gastointestinal Disorder *	1/1 (100%)		0/1 (0%)	0

* Indicates events were collected by non-systematic methods.

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.

Results Point of Contact:

Name/Official Title: Medical Communications

Organization: Hoffmann- LaRoche

Phone: 1-800-821-8590
Email: genentech@druginfo.com

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