ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 07/22/2014

ClinicalTrials.gov ID: NCT00951275

Study Identification

Unique Protocol ID:	ML22462
Brief Title:	A Study of Tocilizumab + DMARDs in Patients With Moderate to Severe Active Rheumatoid Arthritis
Official Title:	A Single Arm, Open-label Study of Early Improvement of Anemia and Fatigue During Treatment With Tocilizumab (TCZ) in Combination With DMARDs, in Adult Patients With Moderate to Severe Active Rheumatoid Arthritis.
Secondary IDs:	2009-011105-17

Study Status

Record Verification:	July 2014
Overall Status:	Completed
Study Start:	October 2009
Primary Completion:	July 2011 [Actual]
Study Completion:	July 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: unknown Board Name: Azienda Ospedaliera Universitaria Vittorio Emanuele, Catania Board Affiliation: unknown Phone: 00390957431111 Email:
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Italy: The Italian Medicines Agency

Study Description

Brief Summary:	This single arm study will assess the effect of tocilizumab + DMARDs (Disease Modifying Anti-Rheumatic Drugs)on improvement of anemia and fatigue in patients with moderate to severe active rheumatoid arthritis. Eligible patients who have had an inadequate response to DMARDs will receive tocilizumab 8mg/kg iv every 4 weeks in combination with standard DMARDs, for 6 months. The anticipated time on study treatment is 3-12 months, and the target sample size is 100-500 individuals.
Detailed Description:	

Conditions

Conditions:	Rheumatoid Arthritis
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Single Group Assignment
Number of Arms:	1
Masking:	Open Label
Allocation:	Non-Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	105 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1	Drug: tocilizumab [RoActemra/Actemra] 8mg/kg iv every 4 weeks for 6 months Drug: Standard DMARDs (Disease Modifying Anti Rheumatic Drugs) As prescribed

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;
- rheumatoid arthritis >=6 months duration;
- DAS28>=3.2;
- inadequate response to prior treatment with a stable dose (>=8 weeks) of DMARD therapy.

Exclusion Criteria:

- rheumatic autoimmune disease other than rheumatoid arthritis;
- history of or current inflammatory joint disease other than rheumatoid arthritis;
- unsuccessful treatment with an anti-TNF agent;
- previous/concurrent treatment with any cell-depleting therapies.

Contacts/Locations

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: Italy
Catania, Sicilia, Italy, 95124

Parma, Emilia-Romagna, Italy, 43100

Palermo, Sicilia, Italy, 90127

Viterbo, Lazio, Italy, 01100

Scafati, Campania, Italy, 84018

Napoli, Campania, Italy, 80131

Martina Franca, Puglia, Italy, 74015

Palermo, Sicilia, Italy, 90146

Rozzano, Lombardia, Italy, 20089

Monza, Lombardia, Italy, 20052

Bergamo, Lombardia, Italy, 24127

Savona, Liguria, Italy, 17100

Venezia, Veneto, Italy, 30127

Piacenza, Emilia-Romagna, Italy, 29100

Massa, Toscana, Italy, 54100

San Cesario Di Lecce, Puglia, Italy, 73016

Roma, Lazio, Italy, 00153

Brindisi, Puglia, Italy, 72100

Torino, Piemonte, Italy, 10154

Gazzi, Sicilia, Italy, 98125

Benevento, Campania, Italy, 82100

Roma, Lazio, Italy, 00133

Napoli, Campania, Italy, 80131

Bologna, Emilia-Romagna, Italy, 40138

Roma, Lazio, Italy, 00189

Telese Terme, Campania, Italy, 82037

Palermo, Sicilia, Italy, 90146

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Participants received tocilizumab 8 milligrams per kilogram (mg/kg) (maximum dose 800 mg) intravenously (IV) once every 4 weeks for a total of 6 infusions.

Overall Study

	Tocilizumab 8 mg/kg
Started	105
Completed	92
Not Completed	13
Administrative Reason	1
Adverse Event	7
Withdrawal by Subject	4
Protocol Violation	1

Baseline Characteristics

Analysis Population Description

Intent-to-Treat (ITT) population: all enrolled participants who recieved at least 1 dose of study medication.

Reporting Groups

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

Baseline Measures

	Tocilizumab 8 mg/kg
Number of Participants	105
Age, Continuous [units: years] Mean (Standard Deviation)	55.0 (12.8)
Gender, Male/Female [units: participants]	
Female	89
Male	16

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Improvement of Anemia at Week 4 Assessed as Change From Baseline in Hemoglobin
Measure Description	Hemoglobin levels were measured as grams/deciliter (g/dL).
Time Frame	Week 4
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

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

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	101

	Tocilizumab 8 mg/kg
Improvement of Anemia at Week 4 Assessed as Change From Baseline in Hemoglobin [units: g/dL] Mean (Standard Deviation)	0.40 (0.78)

2. Primary Outcome Measure:

Measure Title	Improvement in Fatigue at Week 4 Assessed as Change From Baseline 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 greater than or equal to (≥)5-point change from Baseline.
Time Frame	Week 4
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

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

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	101
Improvement in Fatigue at Week 4 Assessed as Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Scores [units: units on a scale] Mean (Standard Deviation)	8.76 (8.83)

3. Secondary Outcome Measure:

Measure Title	Mean Hemoglobin Levels During the Study
Measure Description	
Time Frame	Baseline, Weeks 2, 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

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

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	105
Mean Hemoglobin Levels During the Study [units: g/dL] Mean (Standard Deviation)	
Baseline (n=105)	12.41 (1.51)
Week 2 (n=99)	12.84 (1.47)
Week 4 (n=101)	12.79 (1.44)
Week 8 (n=100)	12.95 (1.45)
Week 12 (n=94)	13.06 (1.49)
Week 16 (n=95)	13.10 (1.42)
Week 20 (n=90)	13.13 (1.40)
Week 24/End of Study (n=100)	13.12 (1.39)

4. Secondary Outcome Measure:

Measure Title	Improvement of Anemia Assessed as Change From Baseline in Hemoglobin
Measure Description	Improvement of anemia was evaluated as change in hemoglobin levels from baseline.
Time Frame	Weeks 2, 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

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

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	105
Improvement of Anemia Assessed as Change From Baseline in Hemoglobin [units: g/dL] Mean (Standard Deviation)	
Week 2 (n=99)	0.47 (0.69)
Week 4 (n=101)	0.40 (0.78)
Week 8 (n=100)	0.56 (0.95)
Week 12 (n=94)	0.64 (1.04)
Week 16 (n=95)	0.62 (1.08)
Week 20 (n=90)	0.67 (1.10)
Week 24/End of Study (n=100)	0.64 (1.20)

5. Secondary Outcome Measure:

Measure Title	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, Weeks 2, 4, 8,12, 16, 20 and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

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

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	105
FACIT-F Scores [units: units on a scale] Mean (Standard Deviation)	
Baseline (n=105)	28.60 (9.77)
Week 2 (n=102)	35.54 (8.53)
Week 4 (n=101)	37.24 (8.46)
Week 8 (n=102)	39.16 (7.35)
Week 12 n=94	39.02 (8.01)
Week 16 (n=97)	40.21 (7.87)
Week 20 (n=91)	40.05 (7.77)
Week 24/End of Study (n=102)	39.69 (8.39)

6. Secondary Outcome Measure:

Measure Title	Improvement of Fatigue Assessed as Change From Baseline in 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	Weeks 2, 4, 8, 12, 16, 20 and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

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

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	102
Improvement of Fatigue Assessed as Change From Baseline in FACIT-F Scores [units: units on a scale] Mean (Standard Deviation)	
Week 2 (n=102)	7.11 (8.40)
Week 4 (n=101)	8.76 (8.83)
Week 8 (n=102)	10.74 (9.49)
Week 12 (n=94)	10.60 (10.13)
Week 16 (n=97)	11.47 (10.24)
Week 20 (n=91)	11.63 (10.22)
Week 24/End of Study (n=102)	10.84 (11.00)

7. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving American College of Rheumatology (ACR) 20 Percent (%), 50% or 70% Improvement
Measure Description	The ACR response rates ACR20, ACR50, and ACR70 were defined as ≥20%, ≥50% and ≥ 70% improvement, respectively, in: swollen joint count (SJC) (66 joints) and tender joint count (TJC) (68 joints) and 3 of the 5 remaining ACR parameters: Patient assessment of pain; Patient Global Assessment of Disease Activity; Investigator Global Assessment of Disease Activity; participant self-rated assessment of disability measured by the Health Assessment Questionnaire Disability Index (HAQ-DI); and acute phase response (erythrocyte sedimentation rate [ESR] or C-reactive protein [CRP]).
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 (maximum dose 800 mg) IV once every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	105
Percentage of Participants Achieving American College of Rheumatology (ACR) 20 Percent (%), 50% or 70% Improvement [units: percentage of participants] Number (95% Confidence Interval)	
ACR20	81.0 (73.44 to 88.46)
ACR50	59.0 (49.64 to 68.45)
ACR70	42.9 (33.39 to 52.32)

8. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 24 in TJC
Measure Description	Sixty-eight (68) joints were assessed at each visit for tenderness; joints were assessed and classified as tender/ not tender. Tender joint count 68 (TJC-68) was calculated as the number of tender joints from 68 joints; the number of tender joints was summed (maximum score 68). Calculated values were used for the analysis. A negative score 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 (maximum dose 800 mg) IV once every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	102
Percent Change From Baseline to Week 24 in TJC [units: percent change in tender joints] Mean (Standard Deviation)	-70.65 (47.71)

9. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 24 in SJC
Measure Description	Sixty-six (66) joints were assessed at each visit for swelling; joints were assessed and classified as swollen/not swollen. Swollen joint count 66 (SJC-66) was calculated as the number of swollen joints from 66 joints; the number of swollen joints was summed (maximum score 66). Calculated values were used for the analysis. A negative score 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 (maximum dose 800 mg) IV once every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	100
Percent Change From Baseline to Week 24 in SJC [units: percent change in swollen joints] Mean (Standard Deviation)	-77.59 (31.22)

10. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 24 in Patient Global Assessment of Pain
Measure Description	The participant's assessment of their current level of pain was displayed on a 100-millimeter (mm) horizontal visual analog scale (VAS). The left-hand extreme of the line was described as "no pain" and the right-hand as "unbearable pain". The participant was asked to mark the line that corresponded to their current level of pain; 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 (maximum dose 800 mg) IV once every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	100
Percent Change From Baseline to Week 24 in Patient Global Assessment of Pain	-52.25 (56.88)

	Tocilizumab 8 mg/kg
[units: percent change in mm] Mean (Standard Deviation)	

11. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 24 in Patient's Global Assessment of Disease Activity
Measure Description	The participant's overall assessment of their current disease activity was displayed on a 100-mm horizontal VAS. The left-hand extreme of the line was described as “no disease activity” (symptom free and no arthritis symptoms) and the right-hand extreme as “maximum disease activity” (maximum arthritis disease activity). Participants were asked to assess their current level of disease activity and mark the line; 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 (maximum dose 800 mg) IV once every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	103
Percent Change From Baseline to Week 24 in Patient's Global Assessment of Disease Activity [units: percent change in mm] Mean (Standard Deviation)	-55.43 (56.12)

12. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 24 in Investigator's Global Assessment of Disease Activity

Measure Description	The physician’s assessment of the participant's current disease activity was displayed on a 100-mm horizontal VAS. The left-hand extreme of the line was described as “no disease activity” (symptom-free and no arthritis symptoms) and the right-hand extreme was considered “maximum disease activity”. The physician’s global assessment of disease activity was completed by the Efficacy Assessor who could or could not be a physician. The assessor was asked to mark the line corresponding to their assessment of the participant's present level of disease activity; 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 (maximum dose 800 mg) IV once every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	103
Percent Change From Baseline to Week 24 in Investigator's Global Assessment of Disease Activity [units: percent change in mm] Mean (Standard Deviation)	-65.89 (36.72)

13. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 24 in HAQ-DI
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 (equals)=without difficulties; 1= with some difficulties; 2=with great difficulties; and 3=unable to perform these actions at all.
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 (maximum dose 800 mg) IV once every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	101
Percent Change From Baseline to Week 24 in HAQ-DI [units: percent change from baseline] Mean (Standard Deviation)	-45.94 (54.17)

14. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 24 in High-Sensitivity CRP (Hs-CRP)
Measure Description	hs-CRP is an acute phase reactant protein that is a clinical marker for Rheumatoid Arthritis (RA). hsCRP is measured in milligrams per liter (mg/L).
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 (maximum dose 800 mg) IV once every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	98

	Tocilizumab 8 mg/kg
Percent Change From Baseline to Week 24 in High-Sensitivity CRP (Hs-CRP) [units: percent change in mg/L] Mean (Standard Deviation)	-53.33 (149.9)

15. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 24 in ESR
Measure Description	ESR is a blood test used to monitor therapy in inflammatory diseases such as RA and reflects acute phase reactant levels. ESR is measured in mm per hour (mm/hr); active disease in RA is defined by an ESR greater than 30 mm/hr.
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 (maximum dose 800 mg) IV once every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	98
Percent Change From Baseline to Week 24 in ESR [units: percent change in mm/hr] Mean (Standard Deviation)	-66.00 (47.73)

16. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a Response at Week 24 by European League Against Rheumatism (EULAR) Category

Measure Description	Disease response was assessed using EULAR Disease Activity Score Based on 28-Joint Count (DAS28) categories of Good, Moderate, or No Response. Good response was defined as a DAS28 score of less than (<)3.2 and improvement from baseline of >1.2; Moderate response was defined as a DAS28 score of 3.2-5.1 and improvement from baseline of 1.2-0.6 or a DAS28 score of >5.1 and improvement from baseline of >1.2; No response was defined as a DAS28 score of >5.1 and improvement from baseline of <1.2. Participants who discontinued prematurely were identified as non-responders.
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 (maximum dose 800 mg) IV once every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	105
Percentage of Participants With a Response at Week 24 by European League Against Rheumatism (EULAR) Category [units: percentage of participants] Number (95% Confidence Interval)	
No Response	12.4 (6.08 to 18.68)
Moderate Response	23.8 (15.66 to 31.96)
Good Response	63.8 (54.62 to 73.00)

17. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a Response at Week 24 by DAS28 Category
Measure Description	DAS28 calculated from the number of swollen joints (SJC) and tender joints (TJC) using the 28 joints count, the ESR (mm/hr) and patient's global assessment of disease activity (participant rated arthritis activity assessment) with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity). DAS28 ≤3.2=low disease activity, DAS28 >5.1=high disease activity and DAS <2.6=remission.

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 (maximum dose 800 mg) IV once every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	105
Percentage of Participants With a Response at Week 24 by DAS28 Category [units: percentage of participants] Number (95% Confidence Interval)	
DAS28 <2.6	49.5 (39.96 to 59.09)
DAS28 ≥2.6	50.5 (40.91 to 60.04)

18. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Week 24 in DAS28 Score
Measure Description	DAS28 calculated from the number of swollen joints (SJC) and tender joints (TJC) using the 28 joints count, the ESR (mm/hr) and patient's global assessment of disease activity (participant rated arthritis activity assessment) with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity). DAS28 ≤3.2=low disease activity, DAS28 >5.1=high disease activity and DAS <2.6=remission.
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 (maximum dose 800 mg) IV once every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	97
Percent Change From Baseline to Week 24 in DAS28 Score [units: percent change from baseline] Mean (Standard Deviation)	-55.78 (23.49)

19. Secondary Outcome Measure:

Measure Title	Percentage of Participants With an Improvement of ≥1 g/dL in Hemoglobin
Measure Description	
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 (maximum dose 800 mg) IV once every 4 weeks for a total of 6 infusions.

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	105
Percentage of Participants With an Improvement of ≥1 g/dL in Hemoglobin [units: percentage of participants] Number (95% Confidence Interval)	31.4 (22.55 to 40.31)

20. Secondary Outcome Measure:

Measure Title	Number of Days as Assessed by Short Form-Health and Labour Questionnaire (SF-HLQ)
Measure Description	The SF-HLQ assessed productivity losses related to health problems in individuals with paid or unpaid work and consists of three modules (absenteeism from paid work, production losses without absenteeism from paid work and hindrance in the performance of paid and unpaid work). Any missed working days or number of worked days with reduced efficiency during the last month were reported.
Time Frame	Baseline
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter.

Reporting Groups

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

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	25
Number of Days as Assessed by Short Form-Health and Labour Questionnaire (SF-HLQ) [units: days] Mean (Standard Deviation)	
Missed working days (n=25)	3.6 (5.0)
Days with reduced capacity (n=19)	11.8 (8.8)

21. Secondary Outcome Measure:

Measure Title	Change From Baseline to Weeks 12 and 24 in Number of Days as Assessed by SF-HLQ

Measure Description	The SF-HLQ assessed productivity losses related to health problems in individuals with paid or unpaid work and consists of three modules (absenteeism from paid work, production losses without absenteeism from paid work and hindrance in the performance of paid and unpaid work). Any missed working days or number of worked days with reduced efficiency during the last month were reported.
Time Frame	Weeks 12 and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter.

Reporting Groups

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

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	25
Change From Baseline to Weeks 12 and 24 in Number of Days as Assessed by SF-HLQ [units: days] Mean (Standard Deviation)	
Missed working days, Week 12 (n=25)	-3.5 (5.1)
Days with reduced capacity, Week 12 (n=19)	-4.2 (10.9)
Missed working days, Week 24 (n=25)	-3.3 (5.1)
Days with reduced capacity, Week 24 (n=19)	-6.1 (10.7)

22. Secondary Outcome Measure:

Measure Title	Number of Hours as Assessed by SF-HLQ
Measure Description	Number of working hours lost, and number of hours of support in in taking over and performing usual household tasks in the last month: chores done by family members, chores done by other persons receiving no pay, home care, other paid care, total number of unpaid hours, and total number of hours during the last month were reported.
Time Frame	Baseline

Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter.

Reporting Groups

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

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	77
Number of Hours as Assessed by SF-HLQ [units: hours] Mean (Standard Deviation)	
Work lost (n=17)	13.6 (19.8)
Chores by family (n=77)	10.3 (26.5)
Chores by other unpaid person (n=77)	0.2 (0.8)
Home care (n=77)	0.0 (0.0)
Other paid care (n=77)	1.1 (4.2)
Total unpaid (n=77)	10.4 (26.5)
Total (n=77)	11.5 (26.4)

23. Secondary Outcome Measure:

Measure Title	Change From Baseline to Weeks 12 and 24 in Number of Hours as Assessed by SF-HLQ
Measure Description	Number of working hours lost, and number of hours of support in in taking over and performing usual household tasks in the last month: chores done by family members, chores done by other persons receiving no pay, home care, other paid care, total number of unpaid hours, and total number of hours during the last month were reported. Changes from baseline were only calculated in participants who completed the questionnaire at all times (baseline, Week 12, and Week 24). Negative number indicates improvement.
Time Frame	Baseline
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter.

Reporting Groups

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

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	77
Change From Baseline to Weeks 12 and 24 in Number of Hours as Assessed by SF-HLQ [units: hours] Mean (Standard Deviation)	
Work lost, Week 12 (n=17)	-8.9 (15.2)
Work lost, Week 24 (n=17)	-12.1 (20.3)
Chores by family, Week 12 (n=77)	-4.4 (27.4)
Chores by family, Week 24 (n=77)	-3.2 (32.0)
Chores by other unpaid person, Week 12 (n=77)	-0.1 (0.8)
Chores by other unpaid person, Week 24 (n=77)	-0.2 (0.8)
Other paid care, Week 12 (n=77)	1.8 (15.5)
Other paid care, Week 24 (n=77)	-0.1 (5.1)
Total unpaid, Week 12 (n=77)	-4.5 (27.3)
Total unpaid, Week 24 (n=77)	-3.6 (32.0)
Total, Week 12 (n=77)	-2.7 (31.7)
Total, Week 24 (n=77)	-3.7 (32.4)

24. Secondary Outcome Measure:

Measure Title	SF-HLQ Hindrance Score

Measure Description	Participants were asked if their health problems hindered their paid work on a scale of 1 to 3 (1=no, 2=yes, slightly, 3=yes, very much) and their unpaid work including household work, going shopping, odd jobs, specific activities sharing the household on a scale of 0 to 3 (0=performed without being bothered by healthy problems; 1=performed although bothered by health problems; 2=not performed because of health problems; 3=not performed for reasons other than health problems). The total hindrance score for unpaid work was derived by adding up the item scores. This hindrance score is a measure of the hindrance experienced as a result of health problems during the performance of unpaid work. The minimum score per item for hindrance score was 0, maximum score was 2 (Score of 3 was not considered since the reasons were "other than health problems"). Total score was calculated by adding all 4 items together and ranged from 0 (best possible score) to 8 (worst possible score).
Time Frame	Baseline
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter.

Reporting Groups

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

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	85
SF-HLQ Hindrance Score [units: units on a scale] Mean (Standard Deviation)	
Paid work (n=23)	0.9 (0.5)
Household work (n=84)	1.1 (0.5)
Going shopping (n=84)	1.0 (0.6)
Odd jobs (n=84)	1.1 (0.7)
Activities for/with children (n=85)	0.6 (0.6)
Total score (n=84)	3.7 (1.7)

25. Secondary Outcome Measure:

Measure Title	Change From Baseline to Weeks 12 and 24 SF-HLQ Hindrance Score
Measure Description	Participants were asked if health problems hindered their paid work on a scale of 1 to 3 (1=no, 2=yes, slightly, 3=yes, very much) and their unpaid work including household work, going shopping, odd jobs, specific activities sharing the household on a scale of 0 to 3 (0=performed without being bothered by healthy problems; 1=performed although bothered by health problems; 2=not performed because of health problems; 3=not performed for reasons other than health problems). Hindrance score is a measure of the hindrance experienced as a result of health problems during the performance of unpaid work. The minimum score per item for hindrance score was 0, maximum score was 2 (Score of 3 was not considered since the reasons were "other than health problems"). Total score was calculated by adding all 4 items together and ranged from 0 (best possible score) to 8 (worst possible score). A negative change from baseline indicates improvement.
Time Frame	Baseline
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter.

Reporting Groups

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

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	85
Change From Baseline to Weeks 12 and 24 SF-HLQ Hindrance Score [units: units on a scale] Mean (Standard Deviation)	
Paid work, Week 12 (n=23)	-0.30 (0.70)
Paid work, Week 24 (n=23)	-0.39 (0.58)
Household work, Week 12 (n=84)	-0.40 (0.70)
Household work, Week 24 (n=84)	-0.40 (0.68)
Going shopping, Week 12 (n=84)	-0.40 (0.64)
Going shopping, Week 24 (n=84)	-0.40 (0.62)
Odd jobs, Week 12 (n=84)	-0.38 (0.79)

	Tocilizumab 8 mg/kg
Odd jobs, Week 24 (n=84)	-0.36 (0.83)
Activities for/with children, Week 12 (n=85)	-0.16 (0.69)
Activities for/with children, Week 24 (n=85)	-0.24 (0.70)
Total score, Week 12 (n=84)	-1.33 (2.19)
Total score, Week 24 (n=84)	-1.38 (2.18)

26. Secondary Outcome Measure:

Measure Title	Efficiency as Assessed by SF-HLQ
Measure Description	Participants were ask to rate their efficiency in working on a scale of of 0 to 10 (0=very worse, 10=as usual). Overall efficiency score was based on the first 6 items of Question 6, which is a descriptive instrument comprised of 7 items designed to evaluate the specific problems affecting production. These 7 items relate to the effect of health problems on concentration, work pace, the need to be alone, making decisions, postponing and transferring work to others. The participant can choose from 4 possible answers: (almost) never, sometimes, often and (nearly) always. Efficiency score range=6 to 24; higher scores indicate higher impairment.
Time Frame	Baseline
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter.

Reporting Groups

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

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	24
Efficiency as Assessed by SF-HLQ [units: units on a scale] Mean (Standard Deviation)	
Efficiency in working (n=21)	6.3 (2.4)

	Tocilizumab 8 mg/kg
Efficiency score (n=24)	10.1 (3.2)

27. Secondary Outcome Measure:

Measure Title	Change From Baseline to Weeks 12 and 24 in Efficiency as Assessed by SF-HLQ
Measure Description	Participants were ask to rate their efficiency in working on a scale of of 0 to 10 (0=very worse, 10=as usual). Overall efficiency score was based on the first 6 items of Question 6, which is a descriptive instrument comprised of 7 items designed to evaluate the specific problems affecting production. These 7 items relate to the effect of health problems on concentration, work pace, the need to be alone, making decisions, postponing and transferring work to others. The participant can choose from 4 possible answers: (almost) never, sometimes, often and (nearly) always. Efficiency score range=6 to 24; higher scores indicate higher impairment. Change from baseline was only calculated for participants who completed the questionnaire at all times (baseline, Week 12 and Week 24). A negative change from baseline indicates improvement.
Time Frame	Baseline
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter.

Reporting Groups

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

Measured Values

	Tocilizumab 8 mg/kg
Number of Participants Analyzed	24
Change From Baseline to Weeks 12 and 24 in Efficiency as Assessed by SF-HLQ [units: units on a scale] Mean (Standard Deviation)	
Efficiency in working, Week 12 (n=21)	2.0 (2.3)
Efficiency in working, Week 24 (n=21)	2.2 (2.4)
Efficiency score, Week 12 (n=24)	-2.3 (3.0)

	Tocilizumab 8 mg/kg
Efficiency score, Week 24 (n=24)	-2.7 (3.0)

Reported Adverse Events

Time Frame	Adverse events (AEs) were collected through the entire study period.
Additional Description	Nonserious AEs presented in this record include all AEs reported during the study, not just nonserious events.

Reporting Groups

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

Serious Adverse Events

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Total	4/105 (3.81%)
General disorders	
Chest pain [A] *	1/105 (0.95%)
Infections and infestations	
Pneumonia [A] *	1/105 (0.95%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Diffuse large B-cell lymphoma [A] *	1/105 (0.95%)
Vascular disorders	
Deep Vein Thrombosis [A] *	1/105 (0.95%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA (12.0)

Other Adverse Events

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

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Total	64/105 (60.95%)
Blood and lymphatic system disorders	
Iron deficiency anaemia [A] *	3/105 (2.86%)
Leukopenia [A] *	2/105 (1.9%)
Lymphadenopathy [A] *	1/105 (0.95%)
Neutropenia [A] *	1/105 (0.95%)
Thrombocytopenia [A] *	2/105 (1.9%)
Cardiac disorders	
Palpitations [A] *	1/105 (0.95%)
Ear and labyrinth disorders	
Vertigo [A] *	1/105 (0.95%)
Gastrointestinal disorders	
Abdominal pain [A] *	3/105 (2.86%)
Abdominal pain upper [A] *	3/105 (2.86%)
Diarrhoea [A] *	2/105 (1.9%)
Dyspepsia [A] *	2/105 (1.9%)
Frequent bowel movements [A] *	1/105 (0.95%)
Haematochezia [A] *	1/105 (0.95%)
Nausea [A] *	5/105 (4.76%)
Stomatitis [A] *	1/105 (0.95%)
Vomiting [A] *	2/105 (1.9%)
General disorders	

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Asthenia [A] *	1/105 (0.95%)
Discomfort [A] *	1/105 (0.95%)
Fatigue [A] *	1/105 (0.95%)
Oedema peripheral [A] *	1/105 (0.95%)
Pyrexia [A] *	3/105 (2.86%)
Hepatobiliary disorders	
Cholelithiasis [A] *	1/105 (0.95%)
Hyperbilirubinaemia [A] *	1/105 (0.95%)
Hypertransaminasaemia [A] *	2/105 (1.9%)
Immune system disorders	
Anaphylactic reaction [A] *	1/105 (0.95%)
Hypersensitivity [A] *	1/105 (0.95%)
Infections and infestations	
Abscess [A] *	1/105 (0.95%)
Bronchitis [A] *	4/105 (3.81%)
Candidiasis [A] *	1/105 (0.95%)
Folliculitis [A] *	1/105 (0.95%)
Gastroenteritis [A] *	1/105 (0.95%)
Gastrointestinal infection [A] *	1/105 (0.95%)
Herpes simplex [A] *	1/105 (0.95%)
Herpes zoster [A] *	2/105 (1.9%)
Influenza [A] *	1/105 (0.95%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Laryngitis [A] *	1/105 (0.95%)
Mastitis [A] *	1/105 (0.95%)
Nasopharyngitis [A] *	1/105 (0.95%)
Pharyngitis [A] *	1/105 (0.95%)
Respiratory tract infection [A] *	1/105 (0.95%)
Sinusitis [A] *	1/105 (0.95%)
Skin infection [A] *	1/105 (0.95%)
Injury, poisoning and procedural complications	
Fractured coccyx [A] *	1/105 (0.95%)
Investigations	
Alanine aminotransferase increased [A] *	1/105 (0.95%)
Aspartate aminotransferase increased [A] *	1/105 (0.95%)
Blood cholesterol increased [A] *	1/105 (0.95%)
Blood triglycerides increased [A] *	1/105 (0.95%)
Gamma-glutamyltransferase increased [A] *	1/105 (0.95%)
Heart rate increased [A] *	1/105 (0.95%)
Lipids increased [A] *	1/105 (0.95%)
Neutrophil count decreased [A] *	1/105 (0.95%)
Platelet count decreased [A] *	1/105 (0.95%)
Transaminases abnormal [A] *	1/105 (0.95%)
Transaminases increased [A] *	5/105 (4.76%)
Metabolism and nutrition disorders	

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Glucose tolerance impaired [A] *	1/105 (0.95%)
Hypercholesterolaemia [A] *	6/105 (5.71%)
Hypertriglyceridaemia [A] *	2/105 (1.9%)
Hypokalaemia [A] *	1/105 (0.95%)
Musculoskeletal and connective tissue disorders	
Arthralgia [A] *	1/105 (0.95%)
Back pain [A] *	1/105 (0.95%)
Muscle spasms [A] *	1/105 (0.95%)
Neck pain [A] *	1/105 (0.95%)
Osteoporosis [A] *	1/105 (0.95%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Angiolipoma [A] *	1/105 (0.95%)
Gammopathy [A] *	1/105 (0.95%)
Hepatic haemangioma rupture [A] *	1/105 (0.95%)
Nervous system disorders	
Dizziness [A] *	2/105 (1.9%)
Epilepsy [A] *	1/105 (0.95%)
Headache [A] *	2/105 (1.9%)
Reproductive system and breast disorders	
Metrorrhagia [A] *	1/105 (0.95%)
Respiratory, thoracic and mediastinal disorders	
Cough [A] *	3/105 (2.86%)
Epistaxis [A] *	1/105 (0.95%)

	Tocilizumab 8 mg/kg
	Affected/At Risk (%)
Oropharyngeal pain [A] *	2/105 (1.9%)
Skin and subcutaneous tissue disorders	
Erythema [A] *	1/105 (0.95%)
Pigmentation disorder [A] *	1/105 (0.95%)
Pruritus [A] *	3/105 (2.86%)
Skin ulcer [A] *	1/105 (0.95%)
Urticaria [A] *	1/105 (0.95%)
Surgical and medical procedures	
Bunion operation [A] *	1/105 (0.95%)
Vascular disorders	
Hypertension [A] *	2/105 (1.9%)
Hypertensive crisis [A] *	1/105 (0.95%)
Phlebitis [A] *	1/105 (0.95%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (12.0)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

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

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

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

Results Point of Contact:

Name/Official Title: Medical Communications
Organization: Hoffmann- LaRoche
Phone: 800-821-8590
Email: genentech@druginfo.com