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A Study of Tocilizumab (RoActemra/Actemra) Versus Adalimumab in Patients With Rheumatoid Arthritis

This study has been completed.

Sponsor:	Hoffmann-La Roche
Collaborators:	
Information provided by (Responsible Party):	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT01119859

Purpose

This randomized, blinded, parallel arm study evaluated the efficacy and safety of tocilizumab (RoActemra/Actemra) versus adalimumab as monotherapy in patients with rheumatoid arthritis who are intolerant of methotrexate or where continued treatment with methotrexate was considered inappropriate. Patients were randomized to receive either tocilizumab 8 mg/kg intravenously (iv) every 4 weeks plus placebo subcutaneously (sc) every 2 weeks, or adalimumab 40 mg sc every 2 weeks plus placebo iv every 4 weeks. Treatment was anticipated to last 24 weeks. With regard to the blind, the study nurse was unblinded due to the nature of the treatment administration, but the investigator and the patient remained blinded.

Condition	Intervention	Phase
Rheumatoid Arthritis	Drug: Tocilizumab Drug: Adalimumab Drug: Placebo to tocilizumab Drug: Placebo to adalimumab	Phase 4

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Investigator), Randomized, Safety/Efficacy Study

Official Title: A Multi-center, Randomized, Blinded, Parallel-group Study of the Reduction of Signs and Symptoms During Monotherapy Treatment With Tocilizumab 8 mg/kg Intravenously Versus Adalimumab 40 mg Subcutaneously in Patients With Rheumatoid Arthritis

Further study details as provided by Hoffmann-La Roche:

Primary Outcome Measure:

- Change From Baseline to Week 24 in the Disease Activity Score 28 (DAS28) [Time Frame: Baseline to Week 24] [Designated as safety issue: No]
  The DAS28 is a combined index for measuring disease activity in rheumatic arthritis (RA) and includes swollen and tender joint counts, erythrocyte sedimentation rate (ESR), and general health (GH) status. The index is calculated with the following formula: DAS28 = (0.56 × √(TJC28)) + (0.28 × √(SJC28)) + (0.7 × log(ESR)) + (0.014 × GH), where TJC28 = tender joint count and SJC28 = swollen joint count, each on 28 joints. GH = a patient's global assessment of disease activity in the previous 24 hours on a 100 mm visual analog scale (left end = no disease activity [symptom-free and no arthritis symptoms], right end = maximum disease activity [maximum arthritis disease activity]). When ESR equaled 0 mm/hr, it was set to 1 mm/hr. The DAS28 scale ranges from 0 to 10, where higher scores represent higher disease activity. A negative change score indicates improvement. The analysis was adjusted for stratification factors of duration of RA (≤ 2 years and > 2 years) and region (US and non-US).

Secondary Outcome Measures:

- Percentage of Patients With a Remission Response (Disease Activity Score 28 [DAS28] < 2.6) at Week 24 [Time Frame: Week 24] [Designated as safety issue: No]
  The percentage of patients who achieved remission of their rheumatic arthritis at Week 24, as measured by a DAS28 score < 2.6, is reported.
- Percentage of Patients With Low Disease Activity (Disease Activity Score 28 [DAS28] ≤ 3.2) at Week 24 [Time Frame: Week 24] [Designated as safety issue: No]
  The percentage of patients who had low rheumatic arthritis disease activity at Week 24, as measured by a DAS28 score of 3.2 or less, is reported.
- Percentage of Patients With an Improvement of at Least 20%, 50%, or 70% in American College of Rheumatology (ACR) Score (ACR20/50/70) From Baseline at Week 24 [Time Frame: Baseline to Week 24] [Designated as safety issue: No]
  Improvement must be seen in tender and swollen joint counts (28 assessed joints) and in at least 3 of the following 5 parameters: Separate patient and physician assessments of patient disease activity in the previous 24 hours on a visual analog scale (VAS, the extreme left end of the line "no disease activity" [symptom-free and no arthritis symptoms] and the extreme right end "maximum disease activity"; patient assessment of pain in previous the 24 hours on a VAS (extreme left end of the line "no pain" and the extreme right end "unbearable pain"); Health Assessment Questionnaire-Disability Index (20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and activities, 0=without difficulty to 3=unable to do); and erythrocyte sedimentation rate.
- Percentage of Patients With a European League Against Rheumatism (EULAR) Good Response at Week 24 [Time Frame: Baseline to Week 24] [Designated as safety issue: No]
  Change of the Disease Activity Score 28 score from baseline was used to determine EULAR responses of good, moderate, or no response. For a post-baseline score ≤ 3.2, a change from baseline of < -1.2 was a good response, < -0.6 to ≥ -1.2 was a moderate response, and ≥ -0.6 was no response. For a post-baseline score > 3.2 to ≤ 5.1, a change from baseline of < -0.6 was a moderate response and ≥ -0.6 was no response. For a post-baseline score > 5.1, a change from baseline < -1.2 was a moderate response and ≥ -1.2 was no response. A good response could not be achieved for post-baseline scores > 3.2.
- Percentage of Patients With a European League Against Rheumatism (EULAR) Good or Moderate Response at Week 24 [Time Frame: Baseline to Week 24] [Designated as safety issue: No]
  Change of the Disease Activity Score 28 score from baseline was used to determine EULAR responses of good, moderate, or no response. For a post-baseline score ≤ 3.2, a change from baseline of < -1.2 was a good response, < -0.6 to ≥ -1.2 was a moderate response, and ≥ -0.6 was no response. For a post-baseline score > 3.2 to ≤ 5.1, a change from baseline of < -0.6 was a moderate response and ≥ -0.6 was no response. For a post-baseline score > 5.1, a change from baseline < -1.2 was a moderate response and ≥ -1.2 was no response. A good response could not be achieved for post-baseline scores > 3.2.

Enrollment: 326

Study Start Date: May 2010
Primary Completion Date: January 2012
Study Completion Date: January 2012

Arms	Assigned Interventions
Experimental: Tocilizumab 8 mg/kg Patients received 6 infusions of tocilizumab 8 mg/kg intravenously every 4 weeks and 12 injections of placebo to adalimumab subcutaneously every 2 weeks.	Drug: Tocilizumab The maximum dose was 800 mg for patients weighing more than 100 kg. Tocilizumab was infused into an arm vein over a 1-hour period. Other Names: RoActemra Actemra Drug: Placebo to adalimumab
Active Comparator: Adalimumab 40 mg Patients received 12 injections of adalimumab 40 mg subcutaneously every 2 weeks and 6 infusions of placebo to tocilizumab intravenously every 4 weeks.	Drug: Adalimumab Drug: Placebo to tocilizumab

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.
- Intolerant of methotrexate or continued treatment with methotrexate is considered inappropriate.
- All disease-modifying anti-rheumatic drugs (DMARD) are to be withdrawn prior to receiving study drug.
- Weight ≤ 150 kg.

Exclusion Criteria:

- Major surgery (including joint surgery) within 12 weeks prior to baseline or planned major surgery within 6 months after baseline.
- History of or current inflammatory joint disease other than rheumatoid arthritis (RA).
- Treatment with a biologic agent at any time prior to baseline.
- Intra-articular or parenteral corticosteroids ≤ 4 weeks prior to baseline.
- Active current infection or history of recurrent bacterial, viral, fungal or mycobacterial infection.

Contacts and Locations

Locations

- United States, Alabama
  - Aniston, Alabama, United States, 36207
  - Birmingham, Alabama, United States, 35294
- United States, Arizona
  - Scottsdale, Arizona, United States, 85258
- United States, Arkansas
  - Hot Springs, Arkansas, United States, 71913
  - Little Rock, Arkansas, United States, 72205
- United States, California
  - San Diego, California, United States, 92108
- United States, Colorado
  - Colorado Springs, Colorado, United States, 80910
- United States, Connecticut
  - Trumbull, Connecticut, United States, 06611
- United States, Florida
  - Boca Raton, Florida, United States, 33486
  - Fort Lauderdale, Florida, United States, 33334
  - Ormond Beach, Florida, United States, 32174
- United States, Idaho
  - Idaho Falls, Idaho, United States, 83404
- United States, Illinois
  - Springfield, Illinois, United States, 62704
- United States, Maryland
  - Cumberland, Maryland, United States, 21502
- United States, Mississippi
  - Flowood, Mississippi, United States, 39232
  - Tupelo, Mississippi, United States, 38802
- United States, Nebraska
  - Lincoln, Nebraska, United States, 68516
- United States, New Hampshire
  - Dover, New Hampshire, United States, 03820
- United States, New Jersey
  - New Brunswick, New Jersey, United States, 08903
- United States, North Carolina
  - Hickory, North Carolina, United States, 28601
- United States, Ohio
  - Dayton, Ohio, United States, 45402
- United States, Pennsylvania
  - Duncansville, Pennsylvania, United States, 16635
  - Willow Grove, Pennsylvania, United States, 19090
  - Wyomissing, Pennsylvania, United States, 19610

United States, South Carolina
- Greenville, South Carolina, United States, 29601

United States, Tennessee
- Hixson, Tennessee, United States, 37343

United States, Texas
- Houston, Texas, United States, 77074
- Lubbock, Texas, United States, 79424
- Mesquite, Texas, United States, 75150
- Nassau Bay, Texas, United States, 77058
- Waco, Texas, United States, 76708

United States, Washington
- Spokane, Washington, United States, 99204
- Tacoma, Washington, United States, 98405

Australia
- Maroochydore, Australia, 4558
- Sydney, Australia, 2050

Belgium
- Bruxelles, Belgium, 1070
- Liege, Belgium, 4000

Brazil
- Curitiba, Brazil, 80060-240
- Goiania, Brazil, 74110010
- Sao Paulo, Brazil, 04266-010

Czech Republic
- Prague, Czech Republic, 12850

Finland
- Helsinki, Finland, 00290
- Jyväskylä, Finland, 40100

Germany
- Baden-baden, Germany, 76530
- Berlin, Germany, 14059
- Essen, Germany, 45239
- Heidelberg, Germany, 69120
- Herne, Germany, 44652
- Hildesheim, Germany, 31134
- Köln, Germany, 50924
- Osnabrück, Germany, 49074
- Ratingen, Germany, 40882
- Würzburg, Germany, 97080

Greece
- Athens, Greece, 11527
- Heraklion, Greece, 71110
- Thessaloniki, Greece, 54642

Mexico
- Mexicali, Mexico, 21100

Mexico, Df, Mexico, 11850
Obregon, Mexico, 85000

Portugal
Almada, Portugal, 2801-951
Lisboa, Portugal, 1649-035
Porto, Portugal, 4200-319

Spain
Barcelona, Spain, 08036
La Coruna, Spain, 15006
Madrid, Spain, 28006
Santiago de Compostela, Spain, 15705
Sevilla, Spain, 41009

Sweden
Stockholm, Sweden, 17176
Uppsala, Sweden, 751 85

Switzerland
Aarau, Switzerland, 5000
Genève, Switzerland, 1211
Lausanne, Switzerland, 1011
St. Gallen, Switzerland, 9007
Zürich, Switzerland, 8091

Turkey
Ankara, Turkey, 06100
Ankara, Turkey, 06100
Antalya, Turkey, 07059
Istanbul, Turkey, 34098

United Kingdom
Cannock, United Kingdom, WS11 5XY
Leeds, United Kingdom, LS7 4SA
London, United Kingdom, E11 1NR
Newcastle Upon Tyne, United Kingdom, NE1 4LP
Poole, United Kingdom, BH15 2JB

Investigators

Study Director:	Clinical Trials	Hoffmann-La Roche

More Information

Responsible Party:	Hoffmann-La Roche
Study ID Numbers:	WA19924
	2009-015845-21
Health Authority:	United States: Food and Drug Administration

Study Results

Participant Flow

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Patients received 6 infusions of tocilizumab 8 mg/kg intravenously every 4 weeks and 12 injections of placebo to adalimumab subcutaneously every 2 weeks.
Adalimumab 40 mg	Patients received 12 injections of adalimumab 40 mg subcutaneously every 2 weeks and 6 infusions of placebo to tocilizumab intravenously every 4 weeks.

Overall Study

	Tocilizumab 8 mg/kg	Adalimumab 40 mg
Started	163	163
Completed	139	133
Not Completed	24	30
Adverse Event	9	10
Death	2	0
Insufficient therapeutic response	7	14
Refused treatment	3	6
Failure to return	3	0

Baseline Characteristics

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Patients received 6 infusions of tocilizumab 8 mg/kg intravenously every 4 weeks and 12 injections of placebo to adalimumab subcutaneously every 2 weeks.
Adalimumab 40 mg	Patients received 12 injections of adalimumab 40 mg subcutaneously every 2 weeks and 6 infusions of placebo to tocilizumab intravenously every 4 weeks.

Baseline Measures

	Tocilizumab 8 mg/kg	Adalimumab 40 mg	Total
Number of Participants	163	162	325
Age, Continuous [1] [units: years] Mean (Standard Deviation)	54.4 (12.95)	53.3 (12.43)	53.9 (12.67)
Gender, Male/Female [1] [units: participants]			
Female	129	133	262
Male	34	29	63

[1] Baseline Characteristics were analyzed for the intent-to-treat (ITT) population which included all randomized patients who received at least 1 dose of tocilizumab or adalimumab and had at least 1 efficacy assessment.

One randomized patient in the adalimumab treatment group did not receive treatment and was not included in any of the data analyses, including demographics.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in the Disease Activity Score 28 (DAS28)
Measure Description	The DAS28 is a combined index for measuring disease activity in rheumatic arthritis (RA) and includes swollen and tender joint counts, erythrocyte sedimentation rate (ESR), and general health (GH) status. The index is calculated with the following formula: DAS28 = (0.56 × √(TJC28)) + (0.28 × √(SJC28)) + (0.7 × log(ESR)) + (0.014 × GH), where TJC28 = tender joint count and SJC28 = swollen joint count, each on 28 joints. GH = a patient's global assessment of disease activity in the previous 24 hours on a 100 mm visual analog scale (left end = no disease activity [symptom-free and no arthritis symptoms], right end = maximum disease activity [maximum arthritis disease activity]). When ESR equaled 0 mm/hr, it was set to 1 mm/hr. The DAS28 scale ranges from 0 to 10, where higher scores represent higher disease activity. A negative change score indicates improvement. The analysis was adjusted for stratification factors of duration of RA (≤ 2 years and > 2 years) and region (US and non-US).
Time Frame	Baseline to Week 24
Safety Issue?	No

Analysis Population Description

Intent-to-treat (ITT) population: All randomized patients who received at least 1 dose of tocilizumab or adalimumab and had at least 1 efficacy assessment.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Patients received 6 infusions of tocilizumab 8 mg/kg intravenously every 4 weeks and 12 injections of placebo to adalimumab subcutaneously every 2 weeks.
Adalimumab 40 mg	Patients received 12 injections of adalimumab 40 mg subcutaneously every 2 weeks and 6 infusions of placebo to tocilizumab intravenously every 4 weeks.

Measured Values

	Tocilizumab 8 mg/kg	Adalimumab 40 mg
Number of Participants Analyzed	163	162
Change From Baseline to Week 24 in the Disease Activity Score 28 (DAS28) [units: Units on a scale] Mean (95% Confidence Interval)	-3.3 (-3.57 to -3.02)	-1.8 (-2.10 to -1.55)

2. Secondary Outcome Measure:

Measure Title	Percentage of Patients With a Remission Response (Disease Activity Score 28 [DAS28] < 2.6) at Week 24
Measure Description	The percentage of patients who achieved remission of their rheumatic arthritis at Week 24, as measured by a DAS28 score < 2.6, is reported.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

Intent-to-treat (ITT) population: All randomized patients who received at least 1 dose of tocilizumab or adalimumab and had at least 1 efficacy assessment.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Patients received 6 infusions of tocilizumab 8 mg/kg intravenously every 4 weeks and 12 injections of placebo to adalimumab subcutaneously every 2 weeks.
Adalimumab 40 mg	Patients received 12 injections of adalimumab 40 mg subcutaneously every 2 weeks and 6 infusions of placebo to tocilizumab intravenously every 4 weeks.

Measured Values

	Tocilizumab 8 mg/kg	Adalimumab 40 mg
Number of Participants Analyzed	163	162
Percentage of Patients With a Remission Response (Disease Activity Score 28 [DAS28] < 2.6) at Week 24 [units: Percentage of patients]	39.9	10.5

3. Secondary Outcome Measure:

Measure Title	Percentage of Patients With Low Disease Activity (Disease Activity Score 28 [DAS28] ≤ 3.2) at Week 24
Measure Description	The percentage of patients who had low rheumatic arthritis disease activity at Week 24, as measured by a DAS28 score of 3.2 or less, is reported.
Time Frame	Week 24
Safety Issue?	No

Analysis Population Description

Intent-to-treat (ITT) population: All randomized patients who received at least 1 dose of tocilizumab or adalimumab and had at least 1 efficacy assessment.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Patients received 6 infusions of tocilizumab 8 mg/kg intravenously every 4 weeks and 12 injections of placebo to adalimumab subcutaneously every 2 weeks.
Adalimumab 40 mg	Patients received 12 injections of adalimumab 40 mg subcutaneously every 2 weeks and 6 infusions of placebo to tocilizumab intravenously every 4 weeks.

Measured Values

	Tocilizumab 8 mg/kg	Adalimumab 40 mg
Number of Participants Analyzed	163	162
Percentage of Patients With Low Disease Activity (Disease Activity Score 28 [DAS28] ≤ 3.2) at Week 24 [units: Percentage of patients]	51.5	19.8

4. Secondary Outcome Measure:

Measure Title	Percentage of Patients With an Improvement of at Least 20%, 50%, or 70% in American College of Rheumatology (ACR) Score (ACR20/50/70) From Baseline at Week 24
Measure Description	Improvement must be seen in tender and swollen joint counts (28 assessed joints) and in at least 3 of the following 5 parameters: Separate patient and physician assessments of patient disease activity in the previous 24 hours on a visual analog scale (VAS, the extreme left end of the line “no disease activity” [symptom-free and no arthritis symptoms] and the extreme right end “maximum disease activity”; patient assessment of pain in previous the 24 hours on a VAS (extreme left end of the line “no pain” and the extreme right end “unbearable pain”); Health Assessment Questionnaire-Disability Index (20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and activities, 0=without difficulty to 3=unable to do); and erythrocyte sedimentation rate.
Time Frame	Baseline to Week 24
Safety Issue?	No

Analysis Population Description

Intent-to-treat (ITT) population: All randomized patients who received at least 1 dose of tocilizumab or adalimumab and had at least 1 efficacy assessment.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Patients received 6 infusions of tocilizumab 8 mg/kg intravenously every 4 weeks and 12 injections of placebo to adalimumab subcutaneously every 2 weeks.
Adalimumab 40 mg	Patients received 12 injections of adalimumab 40 mg subcutaneously every 2 weeks and 6 infusions of placebo to tocilizumab intravenously every 4 weeks.

Measured Values

	Tocilizumab 8 mg/kg	Adalimumab 40 mg
Number of Participants Analyzed	163	162
Percentage of Patients With an Improvement of at Least 20%, 50%, or 70% in American College of Rheumatology (ACR) Score (ACR20/50/70) From Baseline at Week 24 [units: Percentage of patients]		
ACR 20 response	65.0	49.4
ACR 50 response	47.2	27.8
ACR 70 response	32.5	17.9

5. Secondary Outcome Measure:

Measure Title	Percentage of Patients With a European League Against Rheumatism (EULAR) Good Response at Week 24
Measure Description	Change of the Disease Activity Score 28 score from baseline was used to determine EULAR responses of good, moderate, or no response. For a post-baseline score ≤ 3.2, a change from baseline of < -1.2 was a good response, < -0.6 to ≥ -1.2 was a moderate response, and ≥ -0.6 was no response. For a post-baseline score > 3.2 to ≤ 5.1, a change from baseline of < -0.6 was a moderate response and ≥ -0.6 was no response. For a post-baseline score > 5.1, a change from baseline < -1.2 was a moderate response and ≥ -1.2 was no response. A good response could not be achieved for post-baseline scores > 3.2.
Time Frame	Baseline to Week 24
Safety Issue?	No

Analysis Population Description

Intent-to-treat (ITT) population: All randomized patients who received at least 1 dose of tocilizumab or adalimumab and had at least 1 efficacy assessment.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Patients received 6 infusions of tocilizumab 8 mg/kg intravenously every 4 weeks and 12 injections of placebo to adalimumab subcutaneously every 2 weeks.
Adalimumab 40 mg	Patients received 12 injections of adalimumab 40 mg subcutaneously every 2 weeks and 6 infusions of placebo to tocilizumab intravenously every 4 weeks.

Measured Values

	Tocilizumab 8 mg/kg	Adalimumab 40 mg
Number of Participants Analyzed	163	162
Percentage of Patients With a European League Against Rheumatism (EULAR) Good Response at Week 24 [units: Percentage of patients]	51.5	19.8

6. Secondary Outcome Measure:

Measure Title	Percentage of Patients With a European League Against Rheumatism (EULAR) Good or Moderate Response at Week 24

Measure Description	Change of the Disease Activity Score 28 score from baseline was used to determine EULAR responses of good, moderate, or no response. For a post-baseline score ≤ 3.2, a change from baseline of < -1.2 was a good response, < -0.6 to ≥ -1.2 was a moderate response, and ≥ -0.6 was no response. For a post-baseline score > 3.2 to ≤ 5.1, a change from baseline of < -0.6 was a moderate response and ≥ -0.6 was no response. For a post-baseline score > 5.1, a change from baseline < -1.2 was a moderate response and ≥ -1.2 was no response. A good response could not be achieved for post-baseline scores > 3.2.
Time Frame	Baseline to Week 24
Safety Issue?	No

Analysis Population Description

Intent-to-treat (ITT) population: All randomized patients who received at least 1 dose of tocilizumab or adalimumab and had at least 1 efficacy assessment.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Patients received 6 infusions of tocilizumab 8 mg/kg intravenously every 4 weeks and 12 injections of placebo to adalimumab subcutaneously every 2 weeks.
Adalimumab 40 mg	Patients received 12 injections of adalimumab 40 mg subcutaneously every 2 weeks and 6 infusions of placebo to tocilizumab intravenously every 4 weeks.

Measured Values

	Tocilizumab 8 mg/kg	Adalimumab 40 mg
Number of Participants Analyzed	163	162
Percentage of Patients With a European League Against Rheumatism (EULAR) Good or Moderate Response at Week 24 [units: Percentage of patients]	77.9	54.9

Reported Adverse Events

Time Frame	Adverse events were recorded for each patient from Baseline until 12 weeks after the last infusion of a study treatment.
Additional Description	Safety population: All patients who received at least 1 dose of tocilizumab or adalimumab and had at least 1 post-treatment safety assessment.

Reporting Groups

	Description
Tocilizumab 8 mg/kg	Patients received 6 infusions of tocilizumab 8 mg/kg intravenously every 4 weeks and 12 injections of placebo to adalimumab subcutaneously every 2 weeks.
Adalimumab 40 mg	Patients received 12 injections of adalimumab 40 mg subcutaneously every 2 weeks and 6 infusions of placebo to tocilizumab intravenously every 4 weeks.

Serious Adverse Events

	Tocilizumab 8 mg/kg	Adalimumab 40 mg
	Affected/At Risk (%)	Affected/At Risk (%)
Total	19/162 (11.73%)	16/162 (9.88%)
Cardiac disorders		
Acute coronary syndrome [A] †	1/162 (0.62%)	0/162 (0%)
Atrial fibrillation [A] †	1/162 (0.62%)	1/162 (0.62%)
Atrial flutter [A] †	0/162 (0%)	1/162 (0.62%)
Cardiac failure congestive [A] †	0/162 (0%)	1/162 (0.62%)
Myocardial infarction [A] †	1/162 (0.62%)	2/162 (1.23%)
Gastrointestinal disorders		
Enterocolitis [A] †	0/162 (0%)	1/162 (0.62%)
Haemorrhoids [A] †	1/162 (0.62%)	0/162 (0%)
General disorders		
Malaise [A] †	1/162 (0.62%)	0/162 (0%)
Sudden death [A] †	1/162 (0.62%)	0/162 (0%)
Systemic inflammatory response syndrome [A] †	0/162 (0%)	1/162 (0.62%)
Immune system disorders		
Drug hypersensitivity [A] †	0/162 (0%)	1/162 (0.62%)
Infections and infestations		

	Tocilizumab 8 mg/kg	Adalimumab 40 mg
	Affected/At Risk (%)	Affected/At Risk (%)
Appendicitis perforated [A] †	1/162 (0.62%)	0/162 (0%)
Bronchitis [A] †	1/162 (0.62%)	0/162 (0%)
Cellulitis [A] †	0/162 (0%)	2/162 (1.23%)
Haematoma infection [A] †	1/162 (0.62%)	0/162 (0%)
Infective tenosynovitis [A] †	1/162 (0.62%)	0/162 (0%)
Parotitis [A] †	0/162 (0%)	1/162 (0.62%)
Postoperative abscess [A] †	1/162 (0.62%)	0/162 (0%)
Sinusitis [A] †	0/162 (0%)	1/162 (0.62%)
Urinary tract infection [A] †	0/162 (0%)	1/162 (0.62%)
Urosepsis [A] †	0/162 (0%)	1/162 (0.62%)
Vestibular neuronitis [A] †	1/162 (0.62%)	0/162 (0%)
Viral labyrinthitis [A] †	0/162 (0%)	1/162 (0.62%)
Injury, poisoning and procedural complications		
Hip fracture [A] †	0/162 (0%)	1/162 (0.62%)
Overdose [A] †	1/162 (0.62%)	0/162 (0%)
Metabolism and nutrition disorders		
Dehydration [A] †	1/162 (0.62%)	0/162 (0%)
Diabetes mellitus [A] †	0/162 (0%)	1/162 (0.62%)
Musculoskeletal and connective tissue disorders		
Back pain [A] †	1/162 (0.62%)	0/162 (0%)
Fibromyalgia [A] †	1/162 (0.62%)	0/162 (0%)
Intervertebral disc protusion [A] †	1/162 (0.62%)	0/162 (0%)

	Tocilizumab 8 mg/kg	Adalimumab 40 mg
	Affected/At Risk (%)	Affected/At Risk (%)
Rheumatoid arthritis [A] †	3/162 (1.85%)	1/162 (0.62%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Breast cancer [A] †	1/162 (0.62%)	0/162 (0%)
Nervous system disorders		
Cerebrovascular accident [A] †	0/162 (0%)	1/162 (0.62%)
Ischaemic stroke [A] †	1/162 (0.62%)	0/162 (0%)
Transient ischaemic attack [A] †	0/162 (0%)	1/162 (0.62%)
Reproductive system and breast disorders		
Cervical dysplasia [A] †	0/162 (0%)	1/162 (0.62%)
Respiratory, thoracic and mediastinal disorders		
Dyspnoea [A] †	1/162 (0.62%)	0/162 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (14.1)

Other Adverse Events

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

	Tocilizumab 8 mg/kg	Adalimumab 40 mg
	Affected/At Risk (%)	Affected/At Risk (%)
Total	66/162 (40.74%)	65/162 (40.12%)
Gastrointestinal disorders		
Nausea [A] †	6/162 (3.7%)	10/162 (6.17%)
Infections and infestations		
Nasopharyngitis [A] †	17/162 (10.49%)	13/162 (8.02%)
Upper respiratory tract infection [A] †	18/162 (11.11%)	17/162 (10.49%)
Urinary tract infection [A] †	9/162 (5.56%)	11/162 (6.79%)

	Tocilizumab 8 mg/kg	Adalimumab 40 mg
	Affected/At Risk (%)	Affected/At Risk (%)
Musculoskeletal and connective tissue disorders		
Rheumatoid arthritis [A] †	9/162 (5.56%)	15/162 (9.26%)
Nervous system disorders		
Headache [A] †	9/162 (5.56%)	9/162 (5.56%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] †	4/162 (2.47%)	9/162 (5.56%)
Vascular disorders		
Hypertension [A] †	13/162 (8.02%)	7/162 (4.32%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (14.1)

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-La Roche
Phone: 800 821-8590
Email: