ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 04/04/2016

ClinicalTrials.gov ID: NCT00424502

Study Identification

Unique Protocol ID:	ML20538
Brief Title:	A Study of MabThera (Rituximab) in Patients With Rheumatoid Arthritis Who Have Had an Inadequate Response to a TNF-Blocker.
Official Title:	An Open-label Study to Evaluate the Effect of MabThera on Treatment Response in Patients With Rheumatoid Arthritis Who Have Had an Inadequate Response to Previous TNF Inhibition.
Secondary IDs:	

Study Status

Record Verification:	April 2016
Overall Status:	Completed
Study Start:	January 2007
Primary Completion:	October 2009 [Actual]
Study Completion:	October 2009 [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: 27613/40/2006 Board Name: National Institut of Pharmacy Board Affiliation: Dept. of Clinical Trials Phone: +36 1 117 1488 Email: klinvizsg@ogyi.hu
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Hungary: Ministry of Health

Study Description

Brief Summary:	This single arm study will evaluate the efficacy and safety of MabThera in patients with active rheumatoid arthritis whose current treatment with one or more TNF blocker had produced an inadequate response. Patients will receive MabThera (1g infusion) on day 1 and day 15, and will continue on their basic methotrexate therapy (10-25mg/week). The anticipated time on study treatment is 3-12 months, and the target sample size is <100 individuals.
Detailed Description:	

Conditions

Conditions:	Rheumatoid Arthritis
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 4
Intervention Model:	Single Group Assignment
Number of Arms:	1
Masking:	Open Label
Allocation:	N/A
Endpoint Classification:	Safety/Efficacy Study

Enrollment: 20 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1	Drug: rituximab [MabThera/Rituxan] 1g iv on days 1 and 15 Other Names: • MabThera/Rituxan Drug: Methotrexate 10-25mg po/week

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;
- diagnosed RA for >=3 months prior to first administration of study medication;
- inadequate response or intolerance to >=1 anti-TNF therapies, alone or in combination with methotrexate;
- if using NSAIDS, analgesics or oral corticosteroids, must be on a stable dose for >=2 weeks prior to start of study.

Exclusion Criteria:

- other chronic inflammatory diseases;
- use of parental corticosteroids within 4 weeks prior to screening;
- severe heart failure, or severe, uncontrolled cardiac disease.

Contacts/Locations

Study Officials: Clinical Trials
Study Director

Hoffmann-La Roche

Locations: Hungary
Budapest, Hungary, 1027

Budapest, Hungary, 1023

Debrecen, Hungary, 4032

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Rituximab 1000 Milligrams (mg)	Participants received rituximab 1000 mg intravenously (IV) and methylprednisolone 100 mg IV on Days 0 and 14.

Overall Study

	Rituximab 1000 Milligrams (mg)
Started	20
Completed	20
Not Completed	0

Baseline Characteristics

Analysis Population Description
All enrolled participants

Reporting Groups

	Description
Rituximab 1000 mg	Participants received rituximab 1000 mg IV and methylprednisolone 100 mg IV on Days 0 and 14.

Baseline Measures

	Rituximab 1000 mg
Number of Participants	20
Age, Continuous [units: years] Mean (Standard Deviation)	48.70 (12.88)
Gender, Male/Female [units: participants]	
Female	16
Male	4

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Disease Activity Score Based on 28-Joint Count (DAS28)
Measure Description	DAS28 consists of swollen joint count (SJC) and tender joint count (TJC) measurements, erythrocyte sedimentation rate (ESR) (millimeters per hour [mm/hr]), and Patient Global Assessment of Disease Activity (participant-rated assessment of arthritis) with transformed scores ranging from 0 to 10. Higher scores indicated greater affectation due to disease activity. DAS28 equal to or less than (≤)3.2 equals (=) low disease activity, greater than (>)3.2 to 5.1 = moderate to high disease activity.
Time Frame	Day 0 and Week 24
Safety Issue?	No

Analysis Population Description

All enrolled participants who received at least one dose of study treatment.

Reporting Groups

	Description
Rituximab 1000 mg	Participants received rituximab 1000 mg IV and methylprednisolone 100 mg IV on Days 0 and 14.

Measured Values

	Rituximab 1000 mg
Number of Participants Analyzed	20
Disease Activity Score Based on 28-Joint Count (DAS28) [units: units on a scale] Mean (Standard Deviation)	
Day 0	6.03 (0.96)
Week 24	4.01 (1.49)

Statistical Analysis 1 for Disease Activity Score Based on 28-Joint Count (DAS28)

Statistical Analysis Overview	Comparison Groups	Rituximab 1000 mg
	Comments	Change from Baseline to Week 24
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	t-test, 2 sided
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	2.017
	Confidence Interval	(2-Sided) 95% 1.39 to 2.64
	Parameter Dispersion	Type: Standard Deviation Value: 1.34
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Health Assessment Questionnaire - Disability Index (HAQ-DI) Scores

Measure Description	The HAQ-DI score consists of questions referring to 8 categories: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and common daily activities. For each of the categories, participants reported the amount of difficulty they had in performing 2 or 3 specific subcategory items. The standard disability score was calculated from the 8 categories by dividing the sum of the individual categories by the number of categories answered, yielding a score from 0 (without any difficulty) to 3 (unable to do).
Time Frame	Day 0 and Week 24
Safety Issue?	No

Analysis Population Description

All enrolled participants. n (number) = number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
Rituximab 1000 mg	Participants received rituximab 1000 mg IV and methylprednisolone 100 mg IV on Days 0 and 14.

Measured Values

	Rituximab 1000 mg
Number of Participants Analyzed	20
Health Assessment Questionnaire - Disability Index (HAQ-DI) Scores [units: units on a scale] Mean (Standard Deviation)	
Day 0 (n=20)	1.14 (0.31)
Week 24 (n=19)	0.87 (0.36)

Statistical Analysis 1 for Health Assessment Questionnaire - Disability Index (HAQ-DI) Scores

Statistical Analysis Overview	Comparison Groups	Rituximab 1000 mg
	Comments	Change from baseline to Week 24
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]

	Method	t-test, 2 sided
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.276
	Confidence Interval	(2-Sided) 95% 0.151 to 0.401
	Parameter Dispersion	Type: Standard Deviation Value: 0.259
	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Anti-cyclic Citrullinated Peptide (Anti-CCP)
Measure Description	Anti-CCP measured as absorbance units per milliliter (AU/mL).
Time Frame	Day 0 and Week 24
Safety Issue?	No

Analysis Population Description

All participants who received at least 1 dose of study drug; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
Rituximab 1000 mg	Participants received rituximab 1000 mg IV and methylprednisolone 100 mg IV on Days 0 and 14.

Measured Values

	Rituximab 1000 mg
Number of Participants Analyzed	20
Anti-cyclic Citrullinated Peptide (Anti-CCP) [units: AU/mL] Mean (Standard Deviation)	
Day 0 (n=20)	731.07 (569.83)
Week 24 (n=19)	846.41 (988.18)

4. Secondary Outcome Measure:

Measure Title	Vascular Endothelial Growth Factor (VEGF)
Measure Description	VEGF was measured as picograms per milliliter (pg/mL).
Time Frame	Day 0 and Week 24
Safety Issue?	No

Analysis Population Description

All participants who received at least 1 dose of study drug.

Reporting Groups

	Description
Rituximab 1000 mg	Participants received rituximab 1000 mg IV and methylprednisolone 100 mg IV on Days 0 and 14.

Measured Values

	Rituximab 1000 mg
Number of Participants Analyzed	20
Vascular Endothelial Growth Factor (VEGF) [units: pg/mL] Mean (Standard Deviation)	
Day 0	516.68 (523.89)
Week 24	520.15 (451.10)

5. Secondary Outcome Measure:

Measure Title	Erythrocyte Sedimentation Rate (ESR)
Measure Description	ESR was measured in mm/hr.
Time Frame	Day 0 and Week 24
Safety Issue?	No

Analysis Population Description

All participants who received at least 1 dose of study drug.

Reporting Groups

	Description
Rituximab 1000 mg	Participants received rituximab 1000 mg IV and methylprednisolone 100 mg IV on Days 0 and 14.

Measured Values

	Rituximab 1000 mg
Number of Participants Analyzed	20
Erythrocyte Sedimentation Rate (ESR) [units: mm/hr] Mean (Standard Deviation)	
Day 0	45.25 (22.40)
Week 24	30.85 (4.58)

Statistical Analysis 1 for Erythrocyte Sedimentation Rate (ESR)

Statistical Analysis Overview	Comparison Groups	Rituximab 1000 mg
	Comments	Change from baseline to Week 24
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.012
	Comments	[Not specified]
	Method	t-test, 2 sided
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	14.40
	Confidence Interval	(2-Sided) 95% 3.52 to 25.28
	Parameter Dispersion	Type: Standard Deviation Value: 23.24
	Estimation Comments	[Not specified]

6. Secondary Outcome Measure:

Measure Title	C-Reactive Protein (CRP)
Measure Description	CRP was measured in milligrams per liter (mg/L).
Time Frame	Day 0 and Week 24
Safety Issue?	No

Analysis Population Description

All participants who received at least 1 dose of study drug.

Reporting Groups

	Description
Rituximab 1000 mg	Participants received rituximab 1000 mg IV and methylprednisolone 100 mg IV on Days 0 and 14.

Measured Values

	Rituximab 1000 mg
Number of Participants Analyzed	20
C-Reactive Protein (CRP) [units: mg/L] Mean (Standard Deviation)	
Day 0	6.13 (9.77)
Week 24	4.32 (6.51)

Statistical Analysis 1 for C-Reactive Protein (CRP)

Statistical Analysis Overview	Comparison Groups	Rituximab 1000 mg
	Comments	Change from baseline to Week 24
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.337
	Comments	[Not specified]
	Method	t-test, 2 sided

	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	1.81
	Confidence Interval	(2-Sided) 95% -2.03 to 5.65
	Parameter Dispersion	Type: Standard Deviation Value: 8.21
	Estimation Comments	[Not specified]

Reported Adverse Events

Time Frame	Adverse events (AEs) and serious AEs (SAEs) were reported up to Week 48.
Additional Description	[Not specified]

Reporting Groups

	Description
Rituximab 1000 mg	Participants received rituximab 1000 mg IV and methylprednisolone 100 mg IV on Days 0 and 14.

Serious Adverse Events

	Rituximab 1000 mg
	Affected/At Risk (%)
Total	0/20 (0%)

Other Adverse Events

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

	Rituximab 1000 mg
	Affected/At Risk (%)
Total	9/20 (45%)
Blood and lymphatic system disorders	
Haemorrhagic suffusion [A] *	1/20 (5%)

	Rituximab 1000 mg
	Affected/At Risk (%)
Leucopenia [A] *	1/20 (5%)
Eye disorders	
Acute conjunctivitis [A] *	1/20 (5%)
Blurred vision [A] *	1/20 (5%)
Dry eye sensation [A] *	1/20 (5%)
Gastrointestinal disorders	
Blood in stool [A] *	1/20 (5%)
Throat pain [A] *	2/20 (10%)
General disorders	
Feeling of weakness [A] *	1/20 (5%)
Fever [A] *	2/20 (10%)
Infections and infestations	
Upper respiratory tract infection [A] *	2/20 (10%)
Injury, poisoning and procedural complications	
Infusion site pruritus [A] *	1/20 (5%)
Infusion site swelling [A] *	1/20 (5%)
Musculoskeletal and connective tissue disorders	
Progression of rheumatoid arthritis [A] *	1/20 (5%)
Psychiatric disorders	
Mood change [A] *	1/20 (5%)
Sleep disturbance [A] *	1/20 (5%)
Respiratory, thoracic and mediastinal disorders	
Cough [A] *	1/20 (5%)

	Rituximab 1000 mg
	Affected/At Risk (%)
Skin and subcutaneous tissue disorders	
Skin lesion [A] *	1/20 (5%)

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

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

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

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

The Study being conducted under this Agreement is part of the Overall Study. Investigator is free to publish in reputable journals or to present at professional conferences the results of the Study, but 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:

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