ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 07/14/2014

A Pharmacokinetic and Pharmacodynamic Study of MabThera (Rituximab) Plus Methotrexate in Patients With Rheumatoid Arthritis (RA)

This study has been terminated.
(Study was terminated after enrollment of 3 participants due to recruitment difficulties.)

Sponsor:	Hoffmann-La Roche
Collaborators:	
Information provided by (Responsible Party):	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT00422942

Purpose

This single arm study will investigate the pattern of B cell depletion in synovial tissue and peripheral blood of patients with active RA, after MabThera (1000mg iv x 2 on days 1 and 15) + methotrexate (10-25mg/week po) treatment. The clinical efficacy and pharmacokinetic profile of MabThera after treatment and retreatment will also be investigated. The anticipated time on study treatment is 2+ years, and the target sample size is <100 individuals.

Condition	Intervention	Phase
Rheumatoid Arthritis	Drug: rituximab [MabThera/Rituxan] Drug: Methotrexate	Phase 2

Study Type: Interventional
Study Design: Treatment, Single Group Assignment, Open Label, Non-Randomized, Pharmacokinetics/Dynamics Study
Official Title: An Open-label, Exploratory Study of the Pharmacokinetic and Pharmacodynamic Activity of MabThera in Combination With Methotrexate in Synovial Tissue and in Peripheral Blood of Patients With Active Rheumatoid Arthritis.

Further study details as provided by Hoffmann-La Roche:

Primary Outcome Measure:

- Change From Baseline in Absolute B Cell Cluster Differential 19 Positive (CD19+) Counts in Synovial Tissues [Time Frame: Weeks 12, 24, and 36] [Designated as safety issue: No]
  The change from baseline in absolute B cell (CD19+) counts at each visit calculated as (B cell count at visit minus B cell count at baseline) for synovial tissues.
- Change From Baseline in Absolute B Cell CD19+ Counts in Peripheral Blood [Time Frame: Weeks 4, 12, 24, 36, and 48] [Designated as safety issue: No]
  The change from baseline in absolute B cell (CD19+) count at each visit calculated as (B cell count at visit minus B cell count at baseline) for peripheral blood.

Secondary Outcome Measures:

- Change From Baseline in Absolute Counts of Cells Expressing CD20+ and CD22+ in Absolute B Cell (CD19+) Counts in Synovial Tissues [Time Frame: Weeks 12, 24, and 36] [Designated as safety issue: No]
  The change in absolute counts of cells expressing the key B cell markers (CD20+ and CD22+) in absolute B cell (CD19+) counts in synovial tissues at Weeks 12, 24, and 36, relative to baseline.
- Change From Baseline in Absolute Counts of Cells Expressing CD20+ and CD22+ in Absolute B Cell (CD19+) Counts in Peripheral Blood [Time Frame: Weeks 4,12, 24, 36, and 48] [Designated as safety issue: No]
  The change in absolute counts of cells expressing the key B cell markers (CD20+ and CD22+) in absolute B cell (CD19+) counts in peripheral blood at Weeks 4,12, 24, 36, and 48, relative to baseline.
- Change From Baseline in Levels of Key Cytokines (Interleukin [IL]-1beta [β], Tumor Necrosis Factor [TNF]-Alpha [α], IL-4, IL-6, IL-10, and IL-13) in Blood (Serum) [Time Frame: Days 15 and 183 and Weeks 4, 12, 24, 36, and 48] [Designated as safety issue: No]
  The change in levels of key cytokines (IL-1β, TNF-α, IL-4, IL-6, IL-10, and IL-13) in blood (serum) on Days 15 and 183 and at Weeks 4, 12, 24, 36, and 48, relative to baseline.
- Change From Baseline in Levels of Key Cytokines in (IL-1β, TNF-α, IL-6, and IL-10) in Synovial Tissues [Time Frame: Weeks 12, 24, and 36] [Designated as safety issue: No]
  The change in levels of key cytokines in (IL-1β, TNF-α, IL-6, and IL-10) in synovial tissues at Weeks 12, 24, and 36, relative to baseline.
- Change From Baseline in Myelocytomatosis Oncogene (C-myc) and BCL2-associated X Protein (BAX) in Peripheral Blood [Time Frame: Days 15 and 183] [Designated as safety issue: No]
  The change in ribonucleic acid (RNA) expression of markers of apoptosis (C-myc and BAX) in peripheral blood at Days 15 and 183, relative to baseline.
- Percentage of Participants Achieving American College of Rheumatology 20 Percent (20%) 50%, and 70% (ACR20/50/70) Response [Time Frame: Week 48] [Designated as safety issue: No]
  ACR20/50/70 response is greater than or equal to (≥) 20%, 50%, or 70% improvement, respectively, in tender joint count (TJC) and swollen joint count (SJC); and improvement in at least 3 of 5 remaining ACR core measures: patient assessment of pain; patient global assessment of disease activity; physician global assessment of disease activity; self-assessed disability (disability index of the Health Assessment Questionnaire [HAQ]); and C-Reactive Protein (CRP).
- Change From Baseline in Disease Activity Score Based on 28 Joint Count (DAS28) Erythrocyte Sedimentation Rate (ESR) Score [Time Frame: Weeks 12, 24, 36, and 48] [Designated as safety issue: No]
  The change in DAS28-ESR at Weeks 12, 24, 36, and 48, relative to baseline. DAS28-ESR was calculated from SJC and TJC using 28-joint count, ESR (millimeters per hour [mm/hour]) and patient global assessment of disease activity (participant-rated arthritis activity assessment). Total score range: 0-9.4, higher score equals (=) more disease activity. DAS28-ESR less than or equal to (≤) 3.2 implied low disease activity and greater than (>)3.2 to 5.1 implied moderate to high disease activity, and DAS28-ESR <2.6 = remission.
- Percentage of Participants Achieving Response by European League Against Rheumatism (EULAR) Category [Time Frame: Weeks 24, 36, and 48] [Designated as safety issue: No]
  The DAS28-based EULAR response criteria were used to measure individual response as none, good, and moderate, depending on the extent of change from baseline and the level of disease activity reached. Good responders: change from baseline >1.2 with DAS28 ≤ 3.2; moderate responders:

change from baseline >1.2 with DAS28 >3.2 to ≤ 5.1 or change from baseline >0.6 to ≤ 1.2 with DAS28 ≤ 5.1; non-responders: change from baseline ≤ 0.6 or change from baseline >0.6 and ≤ 1.2 with DAS28 >5.1.

- Change From Baseline in ACR Core Set [Time Frame: Week 48] [Designated as safety issue: No]
  The changes from baseline in the ACR core set parameters at Week 48. Change from baseline to Week 48 over time in ACR core set: SJC, TJC, physician's global assessment of disease activity, patient's global assessment of disease activity, patient's assessment of pain, HAQ, ESR, and CRP. ACR20/50/70 response: ≥20%/50%/70% improvement in SJC; ≥20%/50%/70% improvement in TJC; and ≥20%/50%/70% improvement in at least 3 of 5 remaining ACR core measures: participant assessment of pain; physician's global assessment of disease activity, participant's assessment of disease activity, participant assessment of functional disability via a HAQ, and CRP at each visit.
- Change From Baseline in Modified Total Sharp Score (mTSS) [Time Frame: Weeks 24 and 48] [Designated as safety issue: No]
  mTSS = sum of erosion and Joint Space Narrowing (JSN) scores for 44 joints (16 per hand and 6 per foot). mTSS scores ranged from 0 (normal) to 448 (worst possible total score). Change: scores at observation minus score at baseline. An increase in mTSS from baseline. An increase in mTSS from baseline represented disease progression and/or joint worsening, no change represented halting of disease progression, and a decrease represented improvement.
- Change From Baseline in Erosion Score [Time Frame: Weeks 24 and 48] [Designated as safety issue: No]
  Changes from baseline in modified Sharp radiographic erosion score from baseline to Weeks 24 and 48. The change in score at week X (where X=Week 24 or Week 48, as appropriate) calculated as: Change = week X score minus screening score.
- Change From Baseline in Joint Space Narrowing (JSN) Score [Time Frame: Weeks 24 and 48] [Designated as safety issue: No]
  Changes from baseline in modified Sharp radiographic JSN score from baseline to Weeks 24 and 48. The change in score at week X (where X=Week 24 or Week 48, as appropriate) calculated as: Change = week X score minus screening score.

Enrollment: 3
Study Start Date: January 2006
Primary Completion Date: June 2010
Study Completion Date: June 2010

Arms	Assigned Interventions
Experimental: 1	Drug: rituximab [MabThera/Rituxan] 1000mg iv on days 1 and 15 Drug: Methotrexate 10-25mg po weekly

Eligibility

Ages Eligible for Study: 18 Years to 80 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- adult patients 18-80 years of age;
- RA for >=3 months;
- receiving outpatient treatment;

- failed treatment with >=1 DMARD (but not anti TNF or other biologic therapy);
- inadequate response to methotrexate, having taken and tolerated it for >=12 weeks, with a stable dose for >=4 weeks.

Exclusion Criteria:

- rheumatic autoimmune disease other than RA, or significant systemic involvement secondary to RA;
- history of, or current, inflammatory joint disease other than RA, or other systemic autoimmune disorder;
- diagnosis of RA before the age of 16;
- bone/joint surgery within 12 weeks of study;
- prior use of anti-TNF or other biologic therapy, an anti-alpha 4 integrin, or any cell-depleting therapies.

Contacts and Locations

Locations

Netherlands

Amsterdam, Netherlands, 1105 AZ

Investigators

Study Director:	Clinical Trials	Hoffmann-La Roche

More Information

Responsible Party:	Hoffmann-La Roche
Study ID Numbers:	WA19078
Health Authority:	Netherlands: Central Committee on Research inv. Human Subjects (CCMO)

Study Results

Participant Flow

Reporting Groups

	Description
Rituximab + Methotrexate (MTX)	Participants received rituximab 1000 milligrams (mg) via intravenous (IV) infusion on Days 1 and 15 and also on Days 169 and 183 (for those meeting retreatment criteria) or as needed (PRN) if retreatment criteria were not met; premedication with methylprednisolone (MP) 100 mg IV was administered at least 30 minutes prior to each rituximab infusion. Participants also received MTX 10-25 mg per week (mg/week; oral or parenteral) for up to 48 weeks and folate (greater than or equal to [≥]5 mg/week) given as either a single weekly dose or as divided dose for up to 48 weeks.

Overall Study

	Rituximab + Methotrexate (MTX)
Started	3
Completed	0
Not Completed	3
Study terminated by Sponsor	3

Baseline Characteristics

Reporting Groups

	Description
Rituximab + MTX	Participants received rituximab 1000 mg via IV infusion on Days 1 and 15 and also on Days 169 and 183 (for those meeting retreatment criteria) or PRN if retreatment criteria were not met; premedication with MP 100 mg IV was administered at least 30 minutes prior to each rituximab infusion. Participants also received MTX 10-25 mg/week (oral or parenteral) for up to 48 weeks and folate (≥5 mg/week) given as either a single weekly dose or as divided dose for up to 48 weeks.

Baseline Measures

	Rituximab + MTX
Number of Participants	0
Age, Continuous [units: years] Mean (Standard Deviation)	
Gender, Male/Female [units: participants]	
Female	
Male	
Region of Enrollment Netherlands [units: participants]	

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change From Baseline in Absolute B Cell Cluster Differential 19 Positive (CD19+) Counts in Synovial Tissues

Measure Description	The change from baseline in absolute B cell (CD19+) counts at each visit calculated as (B cell count at visit minus B cell count at baseline) for synovial tissues.
Time Frame	Weeks 12, 24, and 36
Safety Issue?	No

Analysis Population Description

No participant data were analyzed. Study was terminated after enrollment of 3 participants as it was decided that it would not be appropriate to expose further participants to study drug since the objectives and data sought from this study had been published from other, independent sources and given the recruitment difficulties encountered.

Reporting Groups

	Description
Rituximab + MTX	Participants received rituximab 1000 mg via IV infusion on Days 1 and 15 and also on Days 169 and 183 (for those meeting retreatment criteria) or PRN if retreatment criteria were not met; premedication with MP 100 mg IV was administered at least 30 minutes prior to each rituximab infusion. Participants also received MTX 10-25 mg/week (oral or parenteral) for up to 48 weeks and folate (≥5 mg/week) given as either a single weekly dose or as divided dose for up to 48 weeks.

Measured Values

	Rituximab + MTX
Number of Participants Analyzed	0

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

2. Primary Outcome Measure:

Measure Title	Change From Baseline in Absolute B Cell CD19+ Counts in Peripheral Blood
Measure Description	The change from baseline in absolute B cell (CD19+) count at each visit calculated as (B cell count at visit minus B cell count at baseline) for peripheral blood.
Time Frame	Weeks 4, 12, 24, 36, and 48
Safety Issue?	No

Analysis Population Description

No participant data were analyzed. Study was terminated after enrollment of 3 participants as it was decided that it would not be appropriate to expose further participants to study drug since the objectives and data sought from this study had been published from other, independent sources and given the recruitment difficulties encountered.

Reporting Groups

	Description
Rituximab + MTX	Participants received rituximab 1000 mg via IV infusion on Days 1 and 15 and also on Days 169 and 183 (for those meeting retreatment criteria) or PRN if retreatment criteria were not met; premedication with MP 100 mg IV was administered at least 30 minutes prior to each rituximab infusion. Participants also received MTX 10-25 mg/week (oral or parenteral) for up to 48 weeks and folate (≥5 mg/week) given as either a single weekly dose or as divided dose for up to 48 weeks.

Measured Values

	Rituximab + MTX
Number of Participants Analyzed	0

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

3. Secondary Outcome Measure:

Measure Title	Change From Baseline in Absolute Counts of Cells Expressing CD20+ and CD22+ in Absolute B Cell (CD19+) Counts in Synovial Tissues
Measure Description	The change in absolute counts of cells expressing the key B cell markers (CD20+ and CD22+) in absolute B cell (CD19+) counts in synovial tissues at Weeks 12, 24, and 36, relative to baseline.
Time Frame	Weeks 12, 24, and 36
Safety Issue?	No

Analysis Population Description

No participant data were analyzed. Study was terminated after enrollment of 3 participants as it was decided that it would not be appropriate to expose further participants to study drug since the objectives and data sought from this study had been published from other, independent sources and given the recruitment difficulties encountered.

Reporting Groups

	Description
Rituximab + MTX	Participants received rituximab 1000 mg via IV infusion on Days 1 and 15 and also on Days 169 and 183 (for those meeting retreatment criteria) or PRN if retreatment criteria were not met; premedication with MP 100 mg IV was administered at least 30 minutes prior to each rituximab infusion. Participants also received MTX 10-25 mg/week (oral or parenteral) for up to 48 weeks and folate (≥5 mg/week) given as either a single weekly dose or as divided dose for up to 48 weeks.

Measured Values

	Rituximab + MTX
Number of Participants Analyzed	0

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

4. Secondary Outcome Measure:

Measure Title	Change From Baseline in Absolute Counts of Cells Expressing CD20+ and CD22+ in Absolute B Cell (CD19+) Counts in Peripheral Blood
Measure Description	The change in absolute counts of cells expressing the key B cell markers (CD20+ and CD22+) in absolute B cell (CD19+) counts in peripheral blood at Weeks 4,12, 24, 36, and 48, relative to baseline.
Time Frame	Weeks 4,12, 24, 36, and 48
Safety Issue?	No

Analysis Population Description

No participant data were analyzed. Study was terminated after enrollment of 3 participants as it was decided that it would not be appropriate to expose further participants to study drug since the objectives and data sought from this study had been published from other, independent sources and given the recruitment difficulties encountered.

Reporting Groups

	Description
Rituximab + MTX	Participants received rituximab 1000 mg via IV infusion on Days 1 and 15 and also on Days 169 and 183 (for those meeting retreatment criteria) or PRN if retreatment criteria were not met; premedication with MP 100 mg IV was administered at least 30 minutes prior to each rituximab infusion. Participants also received MTX 10-25 mg/week (oral or parenteral) for up to 48 weeks and folate (≥5 mg/week) given as either a single weekly dose or as divided dose for up to 48 weeks.

Measured Values

	Rituximab + MTX
Number of Participants Analyzed	0

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

5. Secondary Outcome Measure:

Measure Title	Change From Baseline in Levels of Key Cytokines (Interleukin [IL]-1beta [β], Tumor Necrosis Factor [TNF]-Alpha [α], IL-4, IL-6, IL-10, and IL-13) in Blood (Serum)

Measure Description	The change in levels of key cytokines (IL-1β, TNF-α, IL-4, IL-6, IL-10, and IL-13) in blood (serum) on Days 15 and 183 and at Weeks 4, 12, 24, 36, and 48, relative to baseline.
Time Frame	Days 15 and 183 and Weeks 4, 12, 24, 36, and 48
Safety Issue?	No

Analysis Population Description

No participant data were analyzed. Study was terminated after enrollment of 3 participants as it was decided that it would not be appropriate to expose further participants to study drug since the objectives and data sought from this study had been published from other, independent sources and given the recruitment difficulties encountered.

Reporting Groups

	Description
Rituximab + MTX	Participants received rituximab 1000 mg via IV infusion on Days 1 and 15 and also on Days 169 and 183 (for those meeting retreatment criteria) or PRN if retreatment criteria were not met; premedication with MP 100 mg IV was administered at least 30 minutes prior to each rituximab infusion. Participants also received MTX 10-25 mg/week (oral or parenteral) for up to 48 weeks and folate (≥5 mg/week) given as either a single weekly dose or as divided dose for up to 48 weeks.

Measured Values

	Rituximab + MTX
Number of Participants Analyzed	0

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

6. Secondary Outcome Measure:

Measure Title	Change From Baseline in Levels of Key Cytokines in (IL-1β, TNF-α, IL-6, and IL-10) in Synovial Tissues
Measure Description	The change in levels of key cytokines in (IL-1β, TNF-α, IL-6, and IL-10) in synovial tissues at Weeks 12, 24, and 36, relative to baseline.
Time Frame	Weeks 12, 24, and 36
Safety Issue?	No

Analysis Population Description

No participant data were analyzed. Study was terminated after enrollment of 3 participants as it was decided that it would not be appropriate to expose further participants to study drug since the objectives and data sought from this study had been published from other, independent sources and given the recruitment difficulties encountered.

Reporting Groups

	Description
Rituximab + MTX	Participants received rituximab 1000 mg via IV infusion on Days 1 and 15 and also on Days 169 and 183 (for those meeting retreatment criteria) or PRN if retreatment criteria were not met; premedication with MP 100 mg IV was administered at least 30 minutes prior to each rituximab infusion. Participants also received MTX 10-25 mg/week (oral or parenteral) for up to 48 weeks and folate (≥5 mg/week) given as either a single weekly dose or as divided dose for up to 48 weeks.

Measured Values

	Rituximab + MTX
Number of Participants Analyzed	0

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

7. Secondary Outcome Measure:

Measure Title	Change From Baseline in Myelocytomatosis Oncogene (C-myc) and BCL2-associated X Protein (BAX) in Peripheral Blood
Measure Description	The change in ribonucleic acid (RNA) expression of markers of apoptosis (C-myc and BAX) in peripheral blood at Days 15 and 183, relative to baseline.
Time Frame	Days 15 and 183
Safety Issue?	No

Analysis Population Description

No participant data were analyzed. Study was terminated after enrollment of 3 participants as it was decided that it would not be appropriate to expose further participants to study drug since the objectives and data sought from this study had been published from other, independent sources and given the recruitment difficulties encountered.

Reporting Groups

	Description
Rituximab + MTX	Participants received rituximab 1000 mg via IV infusion on Days 1 and 15 and also on Days 169 and 183 (for those meeting retreatment criteria) or PRN if retreatment criteria were not met; premedication with MP 100 mg IV was administered at least 30 minutes prior to each rituximab infusion. Participants also received MTX 10-25 mg/week (oral or parenteral) for up to 48 weeks and folate (≥5 mg/week) given as either a single weekly dose or as divided dose for up to 48 weeks.

Measured Values

	Rituximab + MTX
Number of Participants Analyzed	0

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

8. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving American College of Rheumatology 20 Percent (20%) 50%, and 70% (ACR20/50/70) Response
Measure Description	ACR20/50/70 response is greater than or equal to (≥) 20%, 50%, or 70% improvement, respectively, in tender joint count (TJC) and swollen joint count (SJC); and improvement in at least 3 of 5 remaining ACR core measures: patient assessment of pain; patient global assessment of disease activity; physician global assessment of disease activity; self-assessed disability (disability index of the Health Assessment Questionnaire [HAQ]); and C-Reactive Protein (CRP).
Time Frame	Week 48
Safety Issue?	No

Analysis Population Description

No participant data were analyzed. Study was terminated after enrollment of 3 participants as it was decided that it would not be appropriate to expose further participants to study drug since the objectives and data sought from this study had been published from other, independent sources and given the recruitment difficulties encountered.

Reporting Groups

	Description
Rituximab + MTX	Participants received rituximab 1000 mg via IV infusion on Days 1 and 15 and also on Days 169 and 183 (for those meeting retreatment criteria) or PRN if retreatment criteria were not met; premedication with MP 100 mg IV was administered at least 30 minutes prior to each rituximab infusion. Participants also received MTX 10-25 mg/week (oral or parenteral) for up to 48 weeks and folate (≥5 mg/week) given as either a single weekly dose or as divided dose for up to 48 weeks.

Measured Values

	Rituximab + MTX
Number of Participants Analyzed	0

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

9. Secondary Outcome Measure:

Measure Title	Change From Baseline in Disease Activity Score Based on 28 Joint Count (DAS28) Erythrocyte Sedimentation Rate (ESR) Score
Measure Description	The change in DAS28-ESR at Weeks 12, 24, 36, and 48, relative to baseline. DAS28-ESR was calculated from SJC and TJC using 28-joint count, ESR (millimeters per hour [mm/hour]) and patient global assessment of disease activity (participant-rated arthritis activity assessment). Total score range: 0-9.4, higher score equals (=) more disease activity. DAS28-ESR less than or equal to (≤) 3.2 implied low disease activity and greater than (>)3.2 to 5.1 implied moderate to high disease activity, and DAS28-ESR <2.6 = remission.
Time Frame	Weeks 12, 24, 36, and 48
Safety Issue?	No

Analysis Population Description

No participant data were analyzed. Study was terminated after enrollment of 3 participants as it was decided that it would not be appropriate to expose further participants to study drug since the objectives and data sought from this study had been published from other, independent sources and given the recruitment difficulties encountered.

Reporting Groups

	Description
Rituximab + MTX	Participants received rituximab 1000 mg via IV infusion on Days 1 and 15 and also on Days 169 and 183 (for those meeting retreatment criteria) or PRN if retreatment criteria were not met; premedication with MP 100 mg IV was administered at least 30 minutes prior to each rituximab infusion. Participants also received MTX 10-25 mg/week (oral or parenteral) for up to 48 weeks and folate (≥5 mg/week) given as either a single weekly dose or as divided dose for up to 48 weeks.

Measured Values

	Rituximab + MTX
Number of Participants Analyzed	0

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

10. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving Response by European League Against Rheumatism (EULAR) Category
Measure Description	The DAS28-based EULAR response criteria were used to measure individual response as none, good, and moderate, depending on the extent of change from baseline and the level of disease activity reached. Good responders: change from baseline >1.2 with DAS28 ≤ 3.2; moderate responders: change from baseline >1.2 with DAS28 >3.2 to ≤ 5.1 or change from baseline >0.6 to ≤ 1.2 with DAS28 ≤ 5.1; non-responders: change from baseline ≤ 0.6 or change from baseline >0.6 and ≤ 1.2 with DAS28 >5.1.
Time Frame	Weeks 24, 36, and 48

Safety Issue?	No

Analysis Population Description

No participant data were analyzed. Study was terminated after enrollment of 3 participants as it was decided that it would not be appropriate to expose further participants to study drug since the objectives and data sought from this study had been published from other, independent sources and given the recruitment difficulties encountered.

Reporting Groups

	Description
Rituximab + MTX	Participants received rituximab 1000 mg via IV infusion on Days 1 and 15 and also on Days 169 and 183 (for those meeting retreatment criteria) or PRN if retreatment criteria were not met; premedication with MP 100 mg IV was administered at least 30 minutes prior to each rituximab infusion. Participants also received MTX 10-25 mg/week (oral or parenteral) for up to 48 weeks and folate (≥5 mg/week) given as either a single weekly dose or as divided dose for up to 48 weeks.

Measured Values

	Rituximab + MTX
Number of Participants Analyzed	0

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

11. Secondary Outcome Measure:

Measure Title	Change From Baseline in ACR Core Set
Measure Description	The changes from baseline in the ACR core set parameters at Week 48. Change from baseline to Week 48 over time in ACR core set: SJC, TJC, physician's global assessment of disease activity, patient's global assessment of disease activity, patient's assessment of pain, HAQ, ESR, and CRP. ACR20/50/70 response: ≥20%/50%/70% improvement in SJC; ≥20%/50%/70% improvement in TJC; and ≥20%/50%/70% improvement in at least 3 of 5 remaining ACR core measures: participant assessment of pain; physician's global assessment of disease activity, participant's assessment of disease activity, participant assessment of functional disability via a HAQ, and CRP at each visit.
Time Frame	Week 48
Safety Issue?	No

Analysis Population Description

No participant data were analyzed. Study was terminated after enrollment of 3 participants as it was decided that it would not be appropriate to expose further participants to study drug since the objectives and data sought from this study had been published from other, independent sources and given the recruitment difficulties encountered.

Reporting Groups

	Description
Rituximab + MTX	Participants received rituximab 1000 mg via IV infusion on Days 1 and 15 and also on Days 169 and 183 (for those meeting retreatment criteria) or PRN if retreatment criteria were not met; premedication with MP 100 mg IV was administered at least 30 minutes prior to each rituximab infusion. Participants also received MTX 10-25 mg/week (oral or parenteral) for up to 48 weeks and folate (≥5 mg/week) given as either a single weekly dose or as divided dose for up to 48 weeks.

Measured Values

	Rituximab + MTX
Number of Participants Analyzed	0

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

12. Secondary Outcome Measure:

Measure Title	Change From Baseline in Modified Total Sharp Score (mTSS)
Measure Description	mTSS = sum of erosion and Joint Space Narrowing (JSN) scores for 44 joints (16 per hand and 6 per foot). mTSS scores ranged from 0 (normal) to 448 (worst possible total score). Change: scores at observation minus score at baseline. An increase in mTSS from baseline. An increase in mTSS from baseline represented disease progression and/or joint worsening, no change represented halting of disease progression, and a decrease represented improvement.
Time Frame	Weeks 24 and 48
Safety Issue?	No

Analysis Population Description

No participant data were analyzed. Study was terminated after enrollment of 3 participants as it was decided that it would not be appropriate to expose further participants to study drug since the objectives and data sought from this study had been published from other, independent sources and given the recruitment difficulties encountered.

Reporting Groups

	Description
Rituximab + MTX	Participants received rituximab 1000 mg via IV infusion on Days 1 and 15 and also on Days 169 and 183 (for those meeting retreatment criteria) or PRN if retreatment criteria were not met; premedication with MP 100 mg IV was administered at least 30 minutes prior to each rituximab infusion. Participants also received MTX 10-25 mg/week (oral or parenteral) for up to 48 weeks and folate (≥5 mg/week) given as either a single weekly dose or as divided dose for up to 48 weeks.

Measured Values

	Rituximab + MTX
Number of Participants Analyzed	0

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

13. Secondary Outcome Measure:

Measure Title	Change From Baseline in Erosion Score
Measure Description	Changes from baseline in modified Sharp radiographic erosion score from baseline to Weeks 24 and 48. The change in score at week X (where X=Week 24 or Week 48, as appropriate) calculated as: Change = week X score minus screening score.
Time Frame	Weeks 24 and 48
Safety Issue?	No

Analysis Population Description

No participant data were analyzed. Study was terminated after enrollment of 3 participants as it was decided that it would not be appropriate to expose further participants to study drug since the objectives and data sought from this study had been published from other, independent sources and given the recruitment difficulties encountered.

Reporting Groups

	Description
Rituximab + MTX	Participants received rituximab 1000 mg via IV infusion on Days 1 and 15 and also on Days 169 and 183 (for those meeting retreatment criteria) or PRN if retreatment criteria were not met; premedication with MP 100 mg IV was administered at least 30 minutes prior to each rituximab infusion. Participants also received MTX 10-25 mg/week (oral or parenteral) for up to 48 weeks and folate (≥5 mg/week) given as either a single weekly dose or as divided dose for up to 48 weeks.

Measured Values

	Rituximab + MTX
Number of Participants Analyzed	0

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

14. Secondary Outcome Measure:

Measure Title	Change From Baseline in Joint Space Narrowing (JSN) Score

Measure Description	Changes from baseline in modified Sharp radiographic JSN score from baseline to Weeks 24 and 48. The change in score at week X (where X=Week 24 or Week 48, as appropriate) calculated as: Change = week X score minus screening score.
Time Frame	Weeks 24 and 48
Safety Issue?	No

Analysis Population Description

No participant data were analyzed. Study was terminated after enrollment of 3 participants as it was decided that it would not be appropriate to expose further participants to study drug since the objectives and data sought from this study had been published from other, independent sources and given the recruitment difficulties encountered.

Reporting Groups

	Description
Rituximab + MTX	Participants received rituximab 1000 mg via IV infusion on Days 1 and 15 and also on Days 169 and 183 (for those meeting retreatment criteria) or PRN if retreatment criteria were not met; premedication with MP 100 mg IV was administered at least 30 minutes prior to each rituximab infusion. Participants also received MTX 10-25 mg/week (oral or parenteral) for up to 48 weeks and folate (≥5 mg/week) given as either a single weekly dose or as divided dose for up to 48 weeks.

Measured Values

	Rituximab + MTX
Number of Participants Analyzed	0

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

Reported Adverse Events

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

Reporting Groups

	Description
Rituximab + MTX	Participants received rituximab 1000 mg via IV infusion on Days 1 and 15 and also on Days 169 and 183 (for those meeting retreatment criteria) or PRN if retreatment criteria were not met; premedication with MP 100 mg IV was administered at least 30 minutes prior to each rituximab infusion. Participants also received MTX 10-25 mg/week (oral or parenteral) for up to 48 weeks and folate (≥5 mg/week) given as either a single weekly dose or as divided dose for up to 48 weeks.

Serious Adverse Events

	Rituximab + MTX
	Affected/At Risk (%)
Total	0/0

Other Adverse Events

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

	Rituximab + MTX
	Affected/At Risk (%)
Total	0/0

Limitations and Caveats

Study terminated after enrollment of 3 participants due to recruitment difficulties and since the objectives and data under study had been published from other, independent sources it was not appropriate to expose further participants to study drug.

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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