Re³ (Re-Cube: Retain Remicade® Response)(Study P04249AM3)

This study has been terminated.

(Study enrollment was stopped due to insufficient subject accrual.)

Sponsor:
Merck Sharp & Dohme Corp.

Collaborator:
Integrated Therapeutics Group

Information provided by (Responsible Party):
Merck Sharp & Dohme Corp.

ClinicalTrials.gov Identifier:
NCT00394589

First received: October 31, 2006
Last updated: April 7, 2015
Last verified: April 2015
History of Changes

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Purpose

This Phase IIIb, randomized, multi-national, multi-center, blinded study of Infliximab (IFX) in subjects aged 18 and older with active RA is being conducted to assess whether increasing either the infusion dose or infusion frequency in patients presenting with a disease flare after an initial response to infliximab results in a significant improvement in disease activity.

Subjects responding to an initial infliximab treatment regimen, who flare during continuation of treatment at 3 mg/kg administered every 8 weeks, will be randomly assigned to one of 3 different dosing regimens of infliximab and will be treated for 4 or 5 consecutive infusions for a total duration of 24 weeks. The infliximab control group and the infliximab increased dose group are evaluator and subject-blinded. The increased frequency group is not blinded. Clinical assessments of disease activity will be based the European League Against Rheumatism (EULAR) criteria for response. Safety parameters will be assessed at every infusion.

A disease flare is defined by an increase in DAS28 with 0.6 or more at screening, when compared to the DAS28 score measured immediately prior to the last Remicade® infusion and depends upon the actual score as well. Since prior to enrollment, the subject received Remicade® as per routine clinical practice, the days on which infusions were administered and assessments are done during the induction period do not have to be exactly at Week 2, 6 and 14.

- Drug: Infliximab Control (double-blinded)
- Drug: Infliximab Increased Dose (double-blinded)
- Drug: Infliximab Increased Frequency (open-label)

Condition	Intervention	Phase
Rheumatoid Arthritis	Drug: Infliximab Increased Frequency Drug: Infliximab Increased Dose Drug: Infliximab Control	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment

Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Primary Purpose: Treatment

Official Title: Randomised Controlled Trial Evaluating Strategies to Optimize Disease Activity Control in RA Patients Treated With Infliximab in Clinical Practice.

Resource links provided by NLM:

Genetics Home Reference related topics: rheumatoid arthritis

Drug Information available for: Infliximab

U.S. FDA Resources

Further study details as provided by Merck Sharp & Dohme Corp.:

Primary Outcome Measures:

- Change in Disease Activity Score Based on 28 Joint Count (DAS28) Score. [Time Frame: Between Screening (Week <=1) and Week 24] [Designated as safety issue: No]

  Descriptive summary of DAS28 (Disease Activity Score Based on 28 Joint Count)change from Baseline to the end of study (Week 24) in the population with available data at both Baseline and Week 24 (increased dose group, n=5; increased frequency group, n=7; and control group, n=5). DAS28 is a unit scale from 2.0 (best value) to 10.0 (worst value).

Enrollment: 43
Study Start Date: March 2006
Study Completion Date: October 2008
Primary Completion Date: October 2008 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Increased Frequency Continuing the same dose of 3 mg/kg infliximab, but at every 6 weeks	Drug: Infliximab Increased Frequency Continuing the same dose of 3 mg/kg infliximab, but at every 6 weeks for 24 weeks Other Name: Increased Frequency
Experimental: Increased Dose 3 mg/kg infliximab + 1 extra vial (100 mg) infliximab, every 8 weeks	Drug: Infliximab Increased Dose 3 mg/kg infliximab + 1 extra vial (100 mg) infliximab every 8 weeks for 24 weeks Other Name: Increased Dose
Active Comparator: Control Continuation of infliximab 3 mg/kg every 8 weeks	Drug: Infliximab Control Continuation of infliximab 3 mg/kg every 8 weeks for 24 weeks Other Name: Control

Eligibility

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

Criteria
Inclusion Criteria:

- aged 18 years or more
- with RA according to ACR criteria
- presented with a disease flare after initial response to infliximab, with both response and flare being defined using the DAS28 score (EULAR criteria)
- received the standard Remicade® dosing schedule per the EU label (3 mg/kg at Weeks 0, 2, 6, [and 14])

- an initial response documented by moderate or good DAS28 improvement (EULAR criteria) from Week 0 to Week 6 or 14.

Exclusion Criteria:

- a female who is, or intends to become, pregnant during or within 6 months of the end of the study, is nursing or not using adequate contraceptive measures
- has not observed the designated periods for concomitant medications
- used any investigational medical product within 30 days prior to Baseline
- any clinically significant deviation from normal in the physical examination or chest X-ray that in the investigator's judgment, may interfere with the study evaluation or affect subject safety
- rheumatic disease other than RA or has any systemic inflammatory condition with signs and symptoms that might confound the evaluations of safety and toxicity
- allergic reaction/sensitivity to the study drug or its excipients that requires corticosteroid pre-infusion medication.

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

No Contacts or Locations Provided

More Information

No publications provided

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT00394589 History of Changes
Other Study ID Numbers:	P04249
Study First Received:	October 31, 2006
Results First Received:	October 28, 2009
Last Updated:	April 7, 2015
Health Authority:	Austria: Federal Ministry for Health and Women Belgium: Ministry of Social Affairs, Public Health and the Environment Denmark: Danish Medicines Agency France: Ministry of Health Germany: Paul-Ehrlich-Institut Greece: Ministry of Health and Welfare Netherlands: Medicines Evaluation Board (MEB) Norway: Norwegian Medicines Agency Portugal: National Pharmacy and Medicines Institute Sweden: Medical Products Agency Turkey: Ministry of Health

Additional relevant MeSH terms:

Arthritis, Rheumatoid	Anti-Inflammatory Agents
Arthritis	Anti-Inflammatory Agents, Non-Steroidal
Autoimmune Diseases	Antirheumatic Agents
Connective Tissue Diseases	Central Nervous System Agents
Immune System Diseases	Dermatologic Agents
Joint Diseases	Gastrointestinal Agents
Musculoskeletal Diseases	Immunologic Factors
Rheumatic Diseases	Peripheral Nervous System Agents
Antibodies, Monoclonal	Pharmacologic Actions
Infliximab	Physiological Effects of Drugs
Analgesics	Sensory System Agents
Analgesics, Non-Narcotic	Therapeutic Uses

ClinicalTrials.gov processed this record on July 07, 2015

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Results First Received: October 28, 2009

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Rheumatoid Arthritis
Interventions:	Drug: Infliximab Increased Frequency Drug: Infliximab Increased Dose Drug: Infliximab Control

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Increased Dose	3 mg/kg infliximab + 1 extra vial (100 mg) infliximab every 8 weeks
Increased Frequency	Continuing the same dose of 3 mg/kg infliximab, but at every 6 weeks
Control	Continuation of infliximab 3 mg/kg every 8 weeks

Participant Flow: Overall Study

	Increased Dose	Increased Frequency	Control
STARTED	**14**	**11**	**18**
COMPLETED	**6**	**8**	**11**
NOT COMPLETED	**8**	**3**	**7**
Adverse Event	**2**	**1**	**2**
Lack of Efficacy	**2**	**2**	**3**
Protocol Violation	**4**	**0**	**2**

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Increased Dose	3 mg/kg infliximab + 1 extra vial (100 mg) infliximab every 8 weeks
Increased Frequency	Continuing the same dose of 3 mg/kg infliximab, but at every 6 weeks
Control	Continuation of infliximab 3 mg/kg every 8 weeks
Total	Total of all reporting groups

Baseline Measures

	Increased Dose	Increased Frequency	Control	Total
Number of Participants [units: participants]	**14**	**11**	**18**	**43**
Age [units: years] Mean (Standard Deviation)	**58.7 (13.0)**	**58.6 (16.1)**	**57.7 (12.3)**	**58.3 (13.3)**
Gender [units: participants]				
Female	**11**	**9**	**14**	**34**
Male	**3**	**2**	**4**	**9**

Outcome Measures

1. Primary: Change in Disease Activity Score Based on 28 Joint Count (DAS28) Score. [Time Frame: Between Screening (Week <=1) and Week 24]

Hide Outcome Measure 1

Measure Type	Primary
Measure Title	Change in Disease Activity Score Based on 28 Joint Count (DAS28) Score.
Measure Description	Descriptive summary of DAS28 (Disease Activity Score Based on 28 Joint Count)change from Baseline to the end of study (Week 24) in the population with available data at both Baseline and Week 24 (increased dose group, n=5; increased frequency group, n=7; and control group, n=5). DAS28 is a unit scale from 2.0 (best value) to 10.0 (worst value).
Time Frame	Between Screening (Week <=1) and Week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-to-treat population; subjects with available data at both Baseline and Week 24

Reporting Groups

	Description
Increased Dose	3 mg/kg infliximab + 1 extra vial (100 mg) infliximab every 8 weeks
Increased Frequency	Continuing the same dose of 3 mg/kg infliximab, but at every 6 weeks
Control	Continuation of infliximab 3 mg/kg every 8 weeks

Measured Values

	Increased Dose	**Increased Frequency**	**Control**
Number of Participants Analyzed [units: participants]	**5**	**7**	**5**
Change in Disease Activity Score Based on 28 Joint Count (DAS28) Score. [units: Score on a Scale] Mean (Standard Deviation)	**-0.4 (1.27)**	**-1.6 (1.23)**	**-1.0 (1.90)**

No statistical analysis provided for Change in Disease Activity Score Based on 28 Joint Count (DAS28) Score.

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Reporting Groups

	Description

Infliximab*3mg/kg+1*Vial Q8W	No text entered.
Infliximab*3mg/kg Q6W	No text entered.
Control*Infliximab*3mg/kg Q8W	No text entered.

Serious Adverse Events

	Infliximab*3mg/kg+1*Vial Q8W	Infliximab*3mg/kg Q6W	Control*Infliximab*3mg/kg Q8W
Total, serious adverse events			
# participants affected / at risk	**2/14 (14.29%)**	**0/11 (0.00%)**	**2/18 (11.11%)**
Ear and labyrinth disorders			
VERTIGO † 1			
# participants affected / at risk	**1/14 (7.14%)**	**0/11 (0.00%)**	**0/18 (0.00%)**
# events	**1**	**0**	**0**
General disorders			
ASTHENIA † 1			
# participants affected / at risk	**0/14 (0.00%)**	**0/11 (0.00%)**	**1/18 (5.56%)**
# events	**0**	**0**	**1**
INFUSION RELATED REACTION † 1			
# participants affected / at risk	**1/14 (7.14%)**	**0/11 (0.00%)**	**0/18 (0.00%)**
# events	**1**	**0**	**0**
PYREXIA † 1			
# participants affected / at risk	**0/14 (0.00%)**	**0/11 (0.00%)**	**1/18 (5.56%)**
# events	**0**	**0**	**1**
Immune system disorders			
ANAPHYLACTIC REACTION † 1			
# participants affected / at risk	**1/14 (7.14%)**	**0/11 (0.00%)**	**0/18 (0.00%)**
# events	**1**	**0**	**0**
Nervous system disorders			
BRAIN STEM SYNDROME † 1			
# participants affected / at risk	**1/14 (7.14%)**	**0/11 (0.00%)**	**0/18 (0.00%)**
# events	**1**	**0**	**0**
DIZZINESS † 1			
# participants affected / at risk	**1/14 (7.14%)**	**0/11 (0.00%)**	**0/18 (0.00%)**
# events	**1**	**0**	**0**
LOSS OF CONSCIOUSNESS † 1			
# participants affected / at risk	**0/14 (0.00%)**	**0/11 (0.00%)**	**1/18 (5.56%)**
# events	**0**	**0**	**1**
SOMNOLENCE † 1			
# participants affected / at risk	**1/14 (7.14%)**	**0/11 (0.00%)**	**0/18 (0.00%)**
# events	**1**	**0**	**0**
Vascular disorders			
DEEP VEIN THROMBOSIS † 1			
# participants affected / at risk	**0/14 (0.00%)**	**0/11 (0.00%)**	**1/18 (5.56%)**
# events	**0**	**0**	**1**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 12.0

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Infliximab*3mg/kg+1*Vial Q8W	No text entered.
Infliximab*3mg/kg Q6W	No text entered.
Control*Infliximab*3mg/kg Q8W	No text entered.

Other Adverse Events

	Infliximab*3mg/kg+1*Vial Q8W	Infliximab*3mg/kg Q6W	Control*Infliximab*3mg/kg Q8W
Total, other (not including serious) adverse events			
# participants affected / at risk	**7/14 (50.00%)**	**5/11 (45.45%)**	**5/18 (27.78%)**
Blood and lymphatic system disorders			
ANAEMIA † 1			
# participants affected / at risk	**2/14 (14.29%)**	**0/11 (0.00%)**	**0/18 (0.00%)**
# events	**2**	**0**	**0**
LEUKOPENIA † 1			
# participants affected / at risk	**1/14 (7.14%)**	**0/11 (0.00%)**	**0/18 (0.00%)**
# events	**1**	**0**	**0**
Cardiac disorders			
CARDIOVASCULAR DISORDER † 1			
# participants affected / at risk	**0/14 (0.00%)**	**0/11 (0.00%)**	**1/18 (5.56%)**
# events	**0**	**0**	**1**
Ear and labyrinth disorders			
TINNITUS † 1			
# participants affected / at risk	**0/14 (0.00%)**	**0/11 (0.00%)**	**1/18 (5.56%)**
# events	**0**	**0**	**1**
Gastrointestinal disorders			
APHTHOUS STOMATITIS † 1			
# participants affected / at risk	**0/14 (0.00%)**	**0/11 (0.00%)**	**1/18 (5.56%)**
# events	**0**	**0**	**1**

GASTROOESOPHAGEAL REFLUX DISEASE † 1			
# participants affected / at risk	**0/14 (0.00%)**	**1/11 (9.09%)**	**0/18 (0.00%)**
# events	**0**	**1**	**0**
General disorders			
OEDEMA PERIPHERAL † 1			
# participants affected / at risk	**1/14 (7.14%)**	**0/11 (0.00%)**	**0/18 (0.00%)**
# events	**1**	**0**	**0**
Infections and infestations			
LARYNGITIS † 1			
# participants affected / at risk	**0/14 (0.00%)**	**1/11 (9.09%)**	**0/18 (0.00%)**
# events	**0**	**1**	**0**
NASOPHARYNGITIS † 1			
# participants affected / at risk	**1/14 (7.14%)**	**0/11 (0.00%)**	**1/18 (5.56%)**
# events	**1**	**0**	**1**
PURULENT DISCHARGE † 1			
# participants affected / at risk	**1/14 (7.14%)**	**0/11 (0.00%)**	**0/18 (0.00%)**
# events	**1**	**0**	**0**
SINUSITIS † 1			
# participants affected / at risk	**1/14 (7.14%)**	**0/11 (0.00%)**	**0/18 (0.00%)**
# events	**1**	**0**	**0**
TINEA MANUUM † 1			
# participants affected / at risk	**0/14 (0.00%)**	**1/11 (9.09%)**	**0/18 (0.00%)**
# events	**0**	**1**	**0**
TOOTH INFECTION † 1			
# participants affected / at risk	**0/14 (0.00%)**	**0/11 (0.00%)**	**1/18 (5.56%)**
# events	**0**	**0**	**1**
UPPER RESPIRATORY TRACT INFECTION † 1			
# participants affected / at risk	**1/14 (7.14%)**	**1/11 (9.09%)**	**0/18 (0.00%)**
# events	**1**	**1**	**0**
Investigations			
ASPARTATE AMINOTRANSFERASE INCREASED † 1			
# participants affected / at risk	**0/14 (0.00%)**	**0/11 (0.00%)**	**1/18 (5.56%)**
# events	**0**	**0**	**1**
HEPATIC ENZYME INCREASED † 1			
# participants affected / at risk	**1/14 (7.14%)**	**0/11 (0.00%)**	**0/18 (0.00%)**
# events	**1**	**0**	**0**
Musculoskeletal and connective tissue disorders			
ARTHRALGIA † 1			
# participants affected / at risk	**1/14 (7.14%)**	**0/11 (0.00%)**	**1/18 (5.56%)**
# events	**1**	**0**	**1**
BURSITIS † 1			
# participants affected / at risk	**0/14 (0.00%)**	**0/11 (0.00%)**	**1/18 (5.56%)**
# events	**0**	**0**	**1**
PAIN IN JAW † 1			

# participants affected / at risk	0/14 (0.00%)	0/11 (0.00%)	1/18 (5.56%)
# events	0	0	1
Nervous system disorders			
HEADACHE † 1			
# participants affected / at risk	0/14 (0.00%)	0/11 (0.00%)	1/18 (5.56%)
# events	0	0	1
SYNCOPE † 1			
# participants affected / at risk	0/14 (0.00%)	1/11 (9.09%)	0/18 (0.00%)
# events	0	1	0
Reproductive system and breast disorders			
VAGINAL HAEMORRHAGE † 1			
# participants affected / at risk	0/14 (0.00%)	0/11 (0.00%)	1/18 (5.56%)
# events	0	0	1
Respiratory, thoracic and mediastinal disorders			
OROPHARYNGEAL PAIN † 1			
# participants affected / at risk	0/14 (0.00%)	0/11 (0.00%)	1/18 (5.56%)
# events	0	0	1
SUFFOCATION FEELING † 1			
# participants affected / at risk	0/14 (0.00%)	1/11 (9.09%)	0/18 (0.00%)
# events	0	1	0
Skin and subcutaneous tissue disorders			
DERMATITIS † 1			
# participants affected / at risk	0/14 (0.00%)	1/11 (9.09%)	0/18 (0.00%)
# events	0	1	0
PRURITUS † 1			
# participants affected / at risk	1/14 (7.14%)	0/11 (0.00%)	0/18 (0.00%)
# events	1	0	0
RASH † 1			
# participants affected / at risk	0/14 (0.00%)	1/11 (9.09%)	1/18 (5.56%)
# events	0	1	1
URTICARIA † 1			
# participants affected / at risk	0/14 (0.00%)	1/11 (9.09%)	0/18 (0.00%)
# events	0	3	0
Vascular disorders			
ANGIODYSPLASIA † 1			
# participants affected / at risk	1/14 (7.14%)	0/11 (0.00%)	0/18 (0.00%)
# events	1	0	0

† Events were collected by systematic assessment

1 Term from vocabulary, MedDRA 12.0

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement

leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.
There is **NOT** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

Results Point of Contact:

Name/Title: Senior Vice President, Global Clinical Development
Organization: Merck, Sharp & Dohme Corp.
e-mail: ClinicalTrialsDisclosure@merck.com

No publications provided

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