Enthesitis With Ultra Sonography Doppler in Spondyloarthropathies Treated With Infliximab (Study P04440) (EUSpA)

This study has been terminated.
(Poor Enrollment)

Sponsor:
Merck Sharp & Dohme Corp.

Collaborator:
Centocor, Inc.

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

ClinicalTrials.gov Identifier:
NCT00686894

First received: May 27, 2008
Last updated: October 19, 2015
Last verified: October 2015
History of Changes

Purpose

Subjects will be given 3 infusions of infliximab according to the label at week 0, 2, and 6. Subjects will be followed for a maximum of 18 weeks or until relapse. This study will assess the ability of the Power Doppler Ultrasonography (PDUS) to be a reliable marker of enthesitis response and relapse in subjects treated with infliximab.

Condition	Intervention	Phase
Spondylitis, Ankylosing (SpA)	Procedure: PDUS Drug: Infliximab	Phase 4

Study Type: Interventional
Study Design: Endpoint Classification: Efficacy Study
Intervention Model: Single Group Assignment
Masking: Open Label
Primary Purpose: Diagnostic

Official Title: Study of Peripheral Enthesitis With Ultra Sonography Doppler in Spondyloarthropathies Treated With Infliximab

Resource links provided by NLM:

MedlinePlus related topics: Ultrasound

Drug Information available for: Infliximab

Genetic and Rare Diseases Information Center resources: Spondylarthropathy

U.S. FDA Resources

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

Primary Outcome Measures:

- The Number of Enthesitis Between Week 4 and Week 12 Evaluated Using Power Doppler Ultrasonography (PDUS) and Proprietary Software. [Time Frame: 8 weeks] [Designated as safety issue: No]

  Two measures were to be used for each enthesis evaluation. 1.) Vascularization: yes/no. 2.) Area of hyper-vascularization: mm^2 (continuous) using proprietary software. This study was terminated early due to slow recruitment. As a result, efficacy analyses were not performed.

Enrollment:	7
Study Start Date:	January 2008
Study Completion Date:	November 2008
Primary Completion Date:	November 2008 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Infliximab 5 mg/kg Infliximab infusions: 5 mg/kg at weeks 0, 2, and 6.	Procedure: PDUS PDUS scored for each enthesitis every 2 weeks for 24 weeks. Drug: Infliximab • 5 mg/kg • IV • Frequency : weeks 0,2,6 Other Names: • SCH 215596 • REMICADE

Eligibility

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

Criteria

Inclusion Criteria:

- Demonstrate willingness to participate in study, adhere to dose and visit schedules, and comply with procedures by signing a written informed consent.
- Negative serum pregnancy test at Week 0.
- Men and women over 18 years of either sex and any race.
- Free of any clinically relevant disease other than SpA that would in the principal investigator's and/or sponsor's opinion, interfere with the conduct of study or its evaluations.
- Eligible for anti-tumor necrosis factor (TNF) treatment according to applicable local guidelines.
- Fulfill the following criteria: European Spondyloarthropathy Study group (ESSG) Classification Criteria, and/or Amor Criteria, and/or New York modified criteria.
- Disease duration of SpA >6 months.
- Incomplete response to non-steriodal anti-inflammatory drug (NSAID).
- Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) >4 including item 2 (axial pain) >=3 on a scale from 0 to 10.
- At least 1 enthesitis assessed by PDUS.
- C-reactive protein (CRP) twice upper normal laboratory value or inflammatory signal on magnetic resonance imaging (MRI) of spine or sacroiliac joint within the last 3 months.
- Practicing adequate contraception during the study and for 6 months after last infusion.
- Week 0 laboratory tests must meet protocol criteria.

Exclusion Criteria:

- Is a female who is pregnant, or intends to become pregnant during the study (or within 6 months after receiving the last infusion);
- Is a female who is nursing, or intends to be nursing during the study or within 6 month after having received the last infusion;
- Has childbearing potential without contraception throughout the study and for 6 months after receiving the last infusion.
- Has not observed the designated washout periods for any of the prohibited medications outlined in the protocol;
- Has any clinically significant deviation from the appropriate reference range in the physical examination, Chest X-ray, that, in the investigator's judgment, may interfere with the study evaluation or affect subject safety;
- Is in a situation or condition that, in the opinion of the investigator, may interfere with optimal participation in the study.
- Is on the staff, affiliated with, or a family member of the staff personnel directly involved with this study;
- Is allergic to or has sensitivity to the study drug or its excipients;
- Has intolerance to or contraindication for infliximab.
- Has an history of allergy to murine products.
- Is uncooperative or has not signed the consent form.
- Cannot understand the protocol.
- Has participated in a study within 3 months prior to inclusion.
- Had treatment with unstable doses of analgesic drugs (paracetamol, phenylbutazone, morphine) steroid, NSAID, or immunosuppressive agent, including methotrexate, within 4 weeks prior to inclusion.
- Had Intra articular steroid within 4 weeks prior to inclusion.
- Had Previous treatment with infliximab
- Had previous treatment with etanercept, adalimumab or any other TNF agent within 2 last months.
- Had an history of, ongoing or recurrent medical condition as follows :
  - Infectious disease, including but not limited to chronic renal infection, chronic chest infection (e.g. bronchectasis), sinusitis, recurrent urinary tract infection (recurrent pyelonephritis or chronic nonremeting cystitis) open, draining or infected skin wound, or ulcer. Serious infection(s) (such as hepatitis, pneumonia or pyelonephritis) within 3 months prior to inclusion.
  - Malignancy within the previous 5 years with the exception of basal cell carcinoma of the skin that has been treated with no evidence of recurrence.
  - Active tuberculosis or previous history of non treated or insufficiently treated tuberculosis.
- Patients with a positive intradermal tuberculosis test according to the local recommendation
- For the patients who could have been in contact with a person having tuberculosis, the inclusion will be possible under specific conditions depending of local recommendations issued in France, Denmark, Hungary, Italy, Spain.
  - Herpes zoster (shingles) infection within 2 months prior to the first infusion
  - Opportunistic infections, e.g. cytomegalovirus, Pneumocystis carinii pneumonia, aspergillosis, histoplasmosis or atypical mycobacterium infection.
- Has any of the following clinical conditions:
  - Severe, progressive or uncontrolled renal, hepatic, hematologic, gastrointestinal, endocrine, pulmonary, cardiac, neurologic, psychiatric or cerebral diseases
  - Known to be infected with human immunodeficiency virus (HIV), hepatitis B or hepatitis C
  - Known lymphoproliferative disease, including lymphoma, or signs suggestive of lymphoproliferative disease, such as lymphadenoma of unusual size and localization or splenomegaly.
  - Have received live (attenuated) vaccination during the last 30 days
  - Have been treated with a monoclonal antibody or a fusion protein except etanercept, adalimumab or any other anti TNF agent
- Leukopenia < 3,500/mm^3, Hemoglobin < 9g/dl, thrombopenia < 100,000/mm^3.
- Congestive heart failure (CHF) including medically controlled, asymptomatic CHF or unstable hemodynamic cardiac conditions.
- Scheduled surgical intervention at any time during the study.
- Multiple sclerosis or symptomatic demyelination of central nervous system.
- Subjects who have an history of drug abuse or alcoholism

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:	NCT00686894 History of Changes
Other Study ID Numbers:	P04440 2006-001579-40
Study First Received:	May 27, 2008
Results First Received:	November 24, 2009
Last Updated:	October 19, 2015
Health Authority:	France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)

Additional relevant MeSH terms:

Spondylarthropathies	Analgesics
Spondylitis	Analgesics, Non-Narcotic
Spondylitis, Ankylosing	Anti-Inflammatory Agents
Ankylosis	Anti-Inflammatory Agents, Non-Steroidal
Arthritis	Antirheumatic Agents
Bone Diseases	Central Nervous System Agents
Bone Diseases, Infectious	Dermatologic Agents
Infection	Gastrointestinal Agents
Joint Diseases	Peripheral Nervous System Agents
Musculoskeletal Diseases	Pharmacologic Actions
Spinal Diseases	Physiological Effects of Drugs
Spondylarthritis	Sensory System Agents
Infliximab	Therapeutic Uses

ClinicalTrials.gov processed this record on April 10, 2016

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Results First Received: November 24, 2009

Study Type:	Interventional
Study Design:	Endpoint Classification: Efficacy Study; Intervention Model: Single Group Assignment; Masking: Open Label; Primary Purpose: Diagnostic
Conditions:	Spondylitis, Ankylosing (SpA)
Interventions:	Procedure: PDUS Drug: Infliximab

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
Infliximab 5 mg/kg	Infliximab infusions: 5 mg/kg at weeks 0, 2, and 6.

Participant Flow: Overall Study

	Infliximab 5 mg/kg
STARTED	**7**
COMPLETED	**1**
NOT COMPLETED	**6**
Relapse	**2**
Protocol Violation	**4**

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
Infliximab 5 mg/kg	Infliximab infusions: 5 mg/kg at weeks 0, 2, and 6.

Baseline Measures

	Infliximab 5 mg/kg
Number of Participants [units: participants]	**7**
Age [units: participants]	
<=18 years	**0**
Between 18 and 65 years	**7**
>=65 years	**0**
Gender [units: participants]	
Female	**1**
Male	**6**

Outcome Measures

1. Primary: The Number of Enthesitis Between Week 4 and Week 12 Evaluated Using Power Doppler Ultrasonography (PDUS) and Proprietary Software. [Time Frame: 8 weeks]

Hide Outcome Measure 1

Measure Type	Primary
Measure Title	The Number of Enthesitis Between Week 4 and Week 12 Evaluated Using Power Doppler Ultrasonography (PDUS) and Proprietary Software.
Measure Description	Two measures were to be used for each enthesis evaluation. 1.) Vascularization: yes/no. 2.) Area of hyper-vascularization: mm^2 (continuous) using proprietary software. This study was terminated early due to slow recruitment. As a result, efficacy analyses were not performed.
Time Frame	8 weeks
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.
No text entered.

Reporting Groups

	Description
Infliximab 5 mg/kg	Infliximab infusions: 5 mg/kg at weeks 0, 2, and 6.

Measured Values

	Infliximab 5 mg/kg
Number of Participants Analyzed [units: participants]	**7**
The Number of Enthesitis Between Week 4 and Week 12 Evaluated Using Power Doppler Ultrasonography (PDUS) and Proprietary Software. [units: Number of Enthesitis]	**0**

No statistical analysis provided for The Number of Enthesitis Between Week 4 and Week 12 Evaluated Using Power Doppler Ultrasonography (PDUS) and Proprietary Software.

Serious Adverse Events

Hide Serious Adverse Events

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

Reporting Groups

	Description
Infliximab 5 mg/kg	Infliximab infusions: 5 mg/kg at weeks 0, 2, and 6.

Serious Adverse Events

	Infliximab 5 mg/kg
Total, serious adverse events	
# participants affected / at risk	**0/7 (0.00%)**

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 5 mg/kg	Infliximab infusions: 5 mg/kg at weeks 0, 2, and 6.

Other Adverse Events

	Infliximab 5 mg/kg
Total, other (not including serious) adverse events	
# participants affected / at risk	**2/7 (28.57%)**
Ear and labyrinth disorders	
Vertigo † 1	
# participants affected / at risk	**1/7 (14.29%)**
# events	**1**
Gastrointestinal disorders	
Constipation † 1	
# participants affected / at risk	**1/7 (14.29%)**
# events	**1**
Nausea † 1	

# participants affected / at risk	**1/7 (14.29%)**
# events	**1**
Infections and infestations	
Oral Herpes † 1	
# participants affected / at risk	**1/7 (14.29%)**
# events	**1**
Skin and subcutaneous tissue disorders	
Pruritis † 1	
# participants affected / at risk	**1/7 (14.29%)**
# events	**1**
Pruritis Generalised † 1	
# participants affected / at risk	**1/7 (14.29%)**
# events	**1**
Rash † 1	
# participants affected / at risk	**1/7 (14.29%)**
# events	**2**
Skin Plaque † 1	
# participants affected / at risk	**1/7 (14.29%)**
# events	**1**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 11.1

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** 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.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

Restriction Description: The PI agrees not to publish or publicly present any interim results of the study without prior written consent of

the sponsor. The PI further agrees to provide 45 days written notice to the sponsor prior to submission for publication or presentation to permit the sponsor to review copies of abstracts or manuscripts for publication which report any results of the study. The sponsor shall have the right to review and comment on any presentation.

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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