A Multi-Center, Randomized, Double-Blind, Placebo ??? Controlled Study of the Human Anti-TNF Monoclonal Antibody Adalimumab Endoscopy Trial to Evaluate the Effects on Mucosal Healing in Subjects with Crohn's Disease Involving the Colon.

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To demonstrate the efficacy of adalimumab on mucosal healing in subjects with moderate to severe ileocolonic Crohn's disease and to delineate the safety of adalimumab when administered to subjects with Crohn's disease.

Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON29817

Source
ToetsingOnline

Brief title
Effects of Adalimumab on mucosal healing in Crohn*s disease

Condition

- Gastrointestinal inflammatory conditions
- Autoimmune disorders

Synonym

Crohn's Disease, Inflammatory disorder affecting the lining of the gastrointestinal tract

Research involving
Human

Sponsors and support

Primary sponsor: Abbott
Source(s) of monetary or material Support: Abbott,industrie

Intervention

Keyword: Adalimumab, Colon, Crohn's Disease, Mucosal

Outcome measures

Primary outcome

The primary efficacy variable is the presence or absence of mucosal ulceration

by endoscopy. The primary outcome analysis will be a comparison of the

proportions of subjects without mucosal ulceration on endoscopy in the

adalimumab and placebo groups at Week 12.

Secondary outcome

Secondary efficacy variables will be:

- Crohn's Disease Endoscopic Index of Severity (CDEIS) scores,

- the Simple Endoscopic Score for Crohn's Disease (SES-CD) and ulcer counts

- CDAI score

- number of subjects discontinued from steroids

- total IBDQ scores

- WPAI scores

- SF * 36

- dimension scores

- Unscheduled Outpatient Visits

- Emergency Room Visits

- Hospitalizations Questionnaire

Study description

Background summary

Despite the current treatment options for Crohn*s disease a lot of patients still do experience Crohn*s disease symptoms. There is evidence for the efficacy of TNF antagonists in treating patients with Crohn*s disease. After a while a large number of the patients do no longer tolerate the treatment, become allergic or don*t respond because antibodies are formed. Adalimumab is an almost fully human and this adverse reaction is not expected. Adalimumab can be administered at home unlike TNF therapies currently used. In this trial will the efficacy of Adalimumab on mucosal healing in subjects with moderate to server ileocolonic Crohn*s be compared to a placebo. The results will be of importance to compare the efficacy of Adalimumab to existing anti-TNF therapies. It is expected that Adalimumab works just as good but without intolerance, allergy or non-responce.

Study objective

To demonstrate the efficacy of adalimumab on mucosal healing in subjects with moderate to severe ileocolonic Crohn's disease and to delineate the safety of adalimumab when administered to subjects with Crohn's disease.

Study design

A Multi-Center, Randomized, Double-Blind, Placebo-Controlled Study

Intervention

Study medication will be administered by sc injection. At Baseline (Week 0), all subjects will receive an open-label dose of 160 mg adalimumab. At Week 2, all subjects will receive an open-label dose of 80 mg adalimumab. At Week 4, all subjects will be randomized to receive injections of adalimumab 40 mg eow or placebo eow. At page 17 of the study protocol is a schematic overview of the study medication dosing.

Study burden and risks

The subject will participate in the trial for a maximum period of 52 weeks.

During this period will the subject the visit hospital 13 times. At the discretion of the investigator can additional visits be planned. 70 days after the last visit will the subject contacted by telephone.
A full physical examination will be performed during the screening visit. The subject may experience some bruising and/or slight soreness, and possible infection or bleeding at the blood collection site. The patient may also develop fainting or dizziness after the blood sample is taken.
The subject will be asked to keep a dosing sheet and an adverse event log. The subject will be asked 5 times to complete 3 questionnaires.
The subject will undergo an endoscopy for a maximum of 4 times. During this endoscopy will a biopt be taken. Depending on the instructions preparation for the endoscopy may involve a limitation on the kinds of food the subject may eat for 1-2 days prior to the test. Preparation for the endoscopy may also involve the use of laxatives that may produce loose stools. Possible risks during the endoscopy are getting a puncture (or hole) in the colon wall, which may require surgery to correct, and bleeding that requires getting blood from donors. The risk of the sedation medication, usually given during an endoscopy to help you relax, may cause allergic reactions such as nausea, skin rash, dizziness with a drop in blood pressure, a slowing down of your breathing so much that in very rare cases a breathing machine will be used, and death from sedation-related heart problems. These risks are small, fewer than 1 in 100 subjects.
During x-rays of the chest the subject will be exposed to a small amount of radiation. The amount of radiation is not considered a significant risk.
While using the study medication the subject may experience adverse reactions. The adverse reactions most often reported when comparing subjects on Adalimumab to placebo (injection with no active drug) the following side effects were more frequent in Adalimumab group and occurred at a rate of >= 5%: upper respiratory infection, headache, rash, sinusitis, accidental injury, nausea, abdominal pain, back pain, urinary tract infection, hypertension and flu syndrome.
Women of childbearing potential have to use an effective method of birth control as described in the study protocol.
The use of some medication is not allowed for subjects participating in the trial. This medication is described in the protocol.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Diagnosis of Crohn's Disease for greater than 4 months.
2. A diagnosis of ileocolonic Crohn's Disease confirmed by endoscopy or radiologic evaluation within 3 years of Baseline.
3. For subjects that have had operations in the ileocolonic region of the intestine after documented diagnosis of ileocolonic disease, postoperative recurrence of the disease must be documented.
4. Endoscopic documentation of ulceration at Screening corresponding to a score of 2 or 3 on the Ulcerated Surface subscore of the SES-CD.
5. Crohn's Disease Activity Index (CDAI) score of ><= 220 and <<= 450.
6. Males and females ><= 18 and ><= 75 years of age at the Baseline visit.
7. Subjects must be able to self-inject study medication or have a designee or healthcare professional who can inject the study medication.
8. Subjects must agree to undergo up to 4 endoscopies.

Exclusion criteria

1. History of cancer or lymphoproliferative disease other than a successfully and completely treated cutaneous squamous cell or basal cell carcinoma or carcinoma in-situ of the cervix.
2. History of listeria, human immunodeficiency virus (HIV), Hepatitis B, an immunodeficiency syndrome, central nervous system (CNS) demyelinating disease or untreated TB.
3. Subject with a current diagnosis of ulcerative colitis or indeterminate colitis as determined

by the investigator and Abbott Medical Monitor.
4. Subject who has had surgical bowel resections within the past 6 months or is planning any resection at any time point while enrolled in the study.
5. Subject with an ostomy or ileoanal pouch. (Subjects with a previous ileo-rectal anastomosis are not excluded).
6. Subject who has previously used infliximab or any anti-TNF agent and has not clinically responded.
7. Previous treatment with adalimumab or previous participation in an adalimumab clinical study.
8. Subjects on prednisone >40 mg/day (or equivalent).
9. Subjects on budesonide >9 mg/day.
10. Subjects with any prior exposure to Tysabri® (natalizumab).

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2006
Enrollment:	7
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Humira
Generic name:	adalimumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	13-07-2006
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-10-2006
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-12-2007
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-06-2008
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-08-2008
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2005-005291-32-NL
CCMO	NL12174.018.06