A Multi-Center, Open-Label Study of the Fully Human Anti-TNF Monoclonal Antibody Adalimumab for the Induction and Maintenance of Clinical Remission in Subjects with Moderate to Severe Crohn's Disease.

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Investigating the safety of adalimumab when administered in subjects with Crohn*s Disease as well as evaulating the efficacy of adalimumab for the induction and maintenance of clinical remission and fistula closure in subjects with moderate to...

Ethical review	Not approved
Status	Will not start
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON29989

Source
ToetsingOnline

Brief title
Safety and efficacy of adalimumab 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: industrie

Intervention

Keyword: Adalimumab, Crohn's Disease, Fistula, Harvey-Bradshaw

Outcome measures

Primary outcome

The study variables for safety are Adverse Events, laboratory data and the physical exams. For the efficacy they are the Harvey-Bradshaw score, fistula closure, SIBDQ, WPAI, external disease manifestations and unscheduled inpatient*s and hospital visits and admissions.

Secondary outcome

Not applicable.

Study description

Background summary

Despite existing treatment methods for Crohn*s Disease a lot of patients still suffer from the symptoms of Crohn*s Disease. Anti-tumor necrosis factor therapy has proven it*s value in the treatment of Crohn*s Disease. A lot of patients are becoming intolerant, allergic or insensitive to this therapy due to the forming of antibodies. Adalimumab is fully human and is not expected to have this adverse event. Also, adalimumab can be given at home contrary to the anti-TNF therapy used now. By means of this study the safety and efficacy of adalimumab for the induction and maintenance of clinical remission in subjects with moderate to severe Crohn*s Disease will be researched. The results are important to compare the efficacy of adalimumab with the existing anti-TNF therapy, with the expectation that adalimumab is as effective without the

occurance of intolerance, allergy or insensitivity.

Study objective

Investigating the safety of adalimumab when administered in subjects with Crohn*s Disease as well as evaulating the efficacy of adalimumab for the induction and maintenance of clinical remission and fistula closure in subjects with moderate to severe Crohn*s Disease and evaluating the impact of adalimumab on external disease manifestations and patient reported outcomes.

Study design

A multi-center study.

Intervention

Patients receive at randomisation: 160 mg adalimumab, at week 2 80 mg adalimumab and as of week 4 40 mg adalimumab every other week. Adalimumab will be administered as 40 mg (0,8 ml) adalimumab per subcutaenous injection with an injectionpen.

Study burden and risks

The subjects will participate in the study for a period of 20 weeks at the most, followed by a Compassionate Use Program until adalimumab has been approved and reimbursed. During the first 20 Weeks study, the subject will come to the hospital 7 times in connection with the study. If desired, the patient will remain in the study and he/she will come to the hospital only once every 12 weeks until the moment that adalimumab will be reimbursed by the insurance. If the investigator deems it necessary, extra visits can be scheduled. Seventy days after any last injection with adalumimab, the subject will be contacted by telephone.
During the screening visit an ECG and x-rays of the chest will be made of the subject. During the x-rays of the chest the subject will be exposed to a small amount of radiation. This radiation is not considered a significant risk.
During the screening visit a PPD (or Mantoux) and a C Difficile test will be done also. At all visits the subject will undergo a physical exam and blood and urine will be collected. The drawing of blood can lead to fainting, infections of the artery, pain, bruising and infection. Also, a bleeding can occur at the injection site.
The subject will be asked to keep a dosing form, a form for adverse events and a medication diary during the study. The subject will also be asked to fill out two questionaires six times.
The subject may experience adverse events when the study drug is used. The most common adverse events of adalimumab were reactions at the injection site. Subjects suffered from redness, itching, bruising, pain and/or swelling of the

injection site. Most injection site reactions were described as mild, and most of them dissapeared without having to stop using the medication. In this study a pre-filled pen will be used instead of a pre-filled syringe. It is expected that previously mentioned adverse events will occur less.
In the rheumatoid artritis studies, in which the subjects with adalimumab were compared to subjects with placebo (injection with a non-active substance), the following adverse events occurred more frequently in the adalimumab group, with a percentage of less than 5%: upper respiratory infection, headache, rash, sinusitis, accidental injuries, nausea, abdominal pain, back pain, urinary tract infection, high blood pressure and flu syndrome.
Women of childbearing potential should use a reliable contraceptive method as described in the protocol.
The use of certain medications (combinations) is not permitted if the subject is participating in the study. 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 moderate to severe Crohn's Disease confirmed by endoscopy or radiologic evaluation for greater than 4 months (16 weeks).
2. Inadequate response to conventional therapy for Crohn's Disease in the opinion of and as documented by the treating physician.
3. Harvey Bradshaw Index score >= 7.
4. Males and females >=18 and <=75 years of age at the Baseline visit.
5. Negative pregnancy test.
6. Use of reliable contraception.
7. Subjects must be able and willing to give written informed consent and to comply with the requirements of this study protocol.
8. Adequate cardiac, renal and hepatic function as determined by the principal investigator and demonstrated by Screening laboratory evaluations, questionnaires, and physical examination results that are within normal limits.
9. Subjects must be able to self-inject study medication or have a designee or healthcare professional who can inject the study medication.

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), chronic or active Hepatitis B, an immunodeficiency syndrome, central nervous system (CNS), demyelinating disease or active tuberculosis (TB).
3. Subjects with abscess or suspicion of abscess.
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. Females who are pregnant or will not discontinue breast-feeding.
6. Subject who has an active infection or has had systemic antibiotic, antiviral, or antifungal treatment within 3 weeks prior to Baseline for infection. Subjects are allowed to be on ciprofloxacin or metronidazole for their non-infectious Crohn's symptoms.
7. Subject with a history of clinically significant drug or alcohol abuse in the last year.
8. Subjects with a poorly controlled medical condition.
9. Subjects with positive C. difficile stool assay.
10. Previous treatment with adalimumab or previous participation in an adalimumab clinical study.
11. Abnormal, clinically significant screening laboratory and other analyses (including ECG).
12. Subjects with any prior exposure to Tysabri® (natalizumab).
13. Subjects on prednisone >40 mg/day (or equivalent), subjects on budesonide >9 mg/day, or subjects who are taking prednisone and budesonide concurrently at Baseline.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	45
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:	17-08-2006
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	10-10-2006
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Not approved Date:	12-10-2006
Application type:	First submission

Review commission: METC Isala Klinieken (Zwolle)

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	EUCTR2006-002078-23-NL
CCMO	NL13963.075.06