A Multicenter, Double-Blind Study to Evaluate the Safety, Efficacy and Pharmacokinetics of the Human Anti-TNF Monoclonal Antibody Adalimumab in Pediatric Subjects with Moderate to Severe Crohn*s Disease

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

Summary

ID

NL-OMON31545

Source
ToetsingOnline

Brief title
M06-806

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn's Disease

Research involving

Human

Sponsors and support

Primary sponsor: Abbott
Source(s) of monetary or material Support: Pharmaceutisch bedrijf: Abbott GmbH & Ko KG

Intervention

Keyword: Adalimumab, Anti-TNF, Crohn Disease, Pediatric Subjects

Outcome measures

Primary outcome

The primary efficacy variable is the proportion of subjects who are in clinical

remission at Week 26. Clinical remission is defined as PCDAI score > 10.

Secondary outcome

Major secondary efficacy endpoints are:

- proportion of subjects in PCDAI clinical remission at Week 52

- proportion of subjects in PCDAI clinical response at Week 26 and in week 52

- proportion of subjects receiving corticosteroid at Baseline who have

discontinued corticosteroid for at least 90 consecutive days prior to Week 26

and are in PCDAI clinical remission at Week 26

- change from Baseline in *z*- scores (for height velocity) at Week 26

- change from Baseline in total IMPACT III scores at Week 26.

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Study description

Background summary

While adalimumab was approved for the treatment of adult Crohn*s disease in the United States on 27 Feb 2007, in the European Union on 04 Jun 2007, and in Canada on 05 Jul 2007, it is still being tested in subjects with moderate to severe Crohn*s disease.

Adalimumab is made in the laboratory and is identical to a natural human antibody. Adalimumab is believed to work by blocking the inflammatory process, thus helping to relieve the signs and symptoms of Crohn*s disease.

Your child has Crohn*s disease and is currently being treated. Despite this treatment, your child is still experiencing signs and symptoms of Crohn*s disease (for example: stomach pain, diarrhea, and fatigue). It is believed that adalimumab may help patients with Crohn*s disease who have not had complete relief of their symptoms with currently available medications.

This study is sponsored by Abbott Laboratories and is being conducted at approximately 55 treatment centers in the United States, Canada and Europe. Approximately 184 children with Crohn*s disease will participate in this study for up to 55 weeks.

Study objective

The purpose of this study is to evaluate the safety and effectiveness of adalimumab for the treatment of moderate to severe Crohn*s disease in children between 6-17 years of age. In addition, information will be collected to select the most effective dose of adalimumab.

Study design

At the start of the study, all subjects will receive an open-label induction dose of adalimumab. If the child weighs greater than or equal to 40 kg at the Baseline study visit, he/she will receive an initial dose of 160 mg adalimumab (4 shots of 40 mg) at baseline and 80 mg adalimumab (2 shots of 40 mg) at Week 2. If the child weighs less than 40 kg at the Baseline study visit, he/she will receive an initial dose of 80 mg adalimumab (2 shots of 40 mg) at baseline (week 0) and 40 mg adalimumab (1 shot of 40 mg) at Week 2.

These induction doses will be followed by blinded treatment of adalimumab every other week from Week 4 through Week 52. There are two dosing groups of adalimumab that are being tested in this study, a high dose and a low dose depending on the child*s weight at the Week 4 study visit. The child will be selected by chance.

If the child weighs less than 40 kg, he/she will either receive 20 mg adalimumab every other week or 10 mg adalimumab every other week beginning from Week 4. If the child weighs greater than or equal to 40 kg, he/she will

either receive 40 mg every other week or 20 mg every other week beginning from Week 4.

If at or after Week 12 the child*s Crohn*s disease becomes more active or he/she does not respond to treament, the study medication can be changed to weekly injections of the same adalimumab dose. Following 8 weeks of every week blinded dosing, if the child*s Crohn*s disease becomes more active or does not respond to treatment, the study medication may be changed to open-label adalimumab.
If the child*s body weight has increased from below 40 kg to above 40 kg at Week 26, then the dose of study medication will be increased.
If the child does complete the study he/she can participate in the open-label extension study.

see protocol p21

Intervention

The patients will have a subcutaneous injection every other week. In case of non-response or flare this can be changed in weekly injections from week 12 on.

Study burden and risks

Before treatment is started, the child would undergo some tests and examinations during a screening period to be sure that he/she meets the study entry requirements and that it is safe for him/her to enter the study. During this screening period, the child*s medical history will be reviewed and several medical examinations performed.

During the study, the child will visit the study doctor at screening, baseline, Week 2; 4; 8; 12; 16; 20; 26; 32; 40; 48 and 52.
At all visits your child will undergo vital sign measurements, a physical exam, clinical assessment, and have a urine test and blood test performed. Approximately 9 mls-17 mls of blood will be drawn at each of these visits. At some visits, up to 35 mls of blood will be collected.

If the child is 13 years of age or older at the baseline visit, he/she will be required to take a card home and record the number of bowel movements he/she has in a day, how much pain he/she are experiencing, and rate his/her general well being. The child will also be asked to complete a card to record information about any new medications or any changes in medication your child takes on an ongoing basis throughout the study.
At every study visit the child will be asked about any side effects he/she is experiencing, problems he/she are having.

Subjects > 10 years old at Baseline will complete an IMPACT III questionnaire

about his/her health at Baseline, Week 12, Week 26, and Week 52/ Early Termination visits. At every visit the parent/guardian, will be asked to complete one questionnaire on the impact of the child*s Crohn*s disease on his/her day to day activities.

Eventual risks: zie section E9.

Contacts

Public
Abbott

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Scientific
Abbott

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67061 Ludwigshafen
Duitsland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

Main Inclusion:
1. Subjects between the ages of 6 and 17, inclusive prior to baseline dosing.
2. Subjects with a diagnosis of Crohn*s disease for greater than 12 weeks prior to screening

confirmed by endoscopy or radiologic evaluation.
3. Subjects with a PCDAI score of >30.
4. Parent or guardian has voluntarily signed and dated an informed consent form, approved by an Institutional Review Board (IRB)/Independent Ethics Committee (IEC), after the nature of the study has been explained and the subject*s parent or legal guardian has had the opportunity to ask questions. The informed consent must be signed before any study-specific procedures are performed or before any medication is discontinued for the purpose of this study. Pediatric subjects will be included in all discussions in order to obtain verbal or written assent.
5. Parent or legal guardian must be willing to actively supervise storage and administration of study drug and to ensure that the time of each dose is accurately recorded in the subject*s diary.
6. Adequate cardiac, renal and hepatic function as determined by principal investigator and demonstrated by Screening laboratory evaluations, questionnaires, and physical examination results that are within normal limits.
7. Subjects may have previously received infliximab providing the subject had an initial response and then discontinued use due to a loss of response or discontinued use due to intolerance.

Exclusion criteria

Main Exclusion:
a. 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.
b. History of listeria, histoplasmosis, chronic or active hepatitis B infection, human immunodeficiency virus (HIV), an immunodeficiency syndrome, central nervous system (CNS) demyelinating disease, or active TB (receiving treatment or not receiving treatment), severe infections such as sepsis and opportunistic infections.
c. Subject with infectious colitis, ulcerative colitis or indeterminate colitis as determined by the investigator and Abbott Medical Monitor.
d. Subject who has had surgical bowel resections within the past 24 weeks or is planning any resection at any time point while enrolled in the study.
e. Subject with an ostomy or ileoanal pouch. (Subjects with a previous ileo-rectal anastomosis are not excluded).
f. Females who are pregnant or are currently breast-feeding.
g. Subject with a history of clinically significant drug or alcohol abuse in the last year.
h. Subjects with a poorly controlled medical condition such as: uncontrolled diabetes mellitus, moderate to severe heart failure, recent cerebrovascular accidents and any other condition which, in the opinion of the investigator or the sponsor, would put the subject at risk by participation in the protocol.
i. Subjects on azathioprine, 6-MP, or MTX who have not been on these medications for at least eight weeks prior to Baseline and on stable doses of these medications for at least four weeks prior to Baseline. Subjects who have been on azathioprine, 6-MP, or MTX who have discontinued these medications within 8 weeks of Baseline.
j. Subjects on aminosalicylates, or Crohn's-related antibiotics (fluoroquinolones such as

ciprofloxacin or nitroimidazole derivatives such as metronidazole) who have not been on stable doses of these medications for at least four weeks prior to Baseline. In addition, subjects on aminosalicylates or Crohn's-related antibiotic treatments who have discontinued these medications within four weeks of Baseline.
k. Subjects on Growth Hormone who have not been on a stable dose for at least 12 weeks prior to Baseline. Subjects must consent to remain on a stable dose through the duration of the study.
l. Subjects on prednisone > 40 mg/day (or equivalent) or subjects on < 10 mg/day prednisone or budesonide > 9 mg/day and subjects who were not on stable doses for at least 2 weeks prior to Baseline. In addition, subjects who discontinued either corticosteroid within 2 weeks of Baseline. Subjects taking both budesonide and prednisone (or equivalent) are excluded.
m. Subject who has previously used infliximab within 8 weeks of Baseline.
n. Previous treatment with adalimumab or previous participation in an adalimumab clinical study.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-10-2008
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	adalimumab
Generic name:	Humira

Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	08-02-2008
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-03-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-04-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-04-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-06-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-07-2008
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-11-2008
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-01-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-02-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-11-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-12-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-02-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-06-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-08-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2006-004814-41-NL
CCMO	NL21165.078.08