Adalimumab for the treatment of perianal fistulas in Crohnâ¤*s disease more effective alone or combined to ciprofloxacin (ADAFI study)

Published: 27-12-2007
Last updated: 11-05-2024

To assess whether a combination of ciprofloxacin and adalimumab is more effective than adalimumab alone.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal signs and symptoms
Study type	Interventional

Summary

ID

NL-OMON35435

Source
ToetsingOnline

Brief title
ADAFI

Condition

- Gastrointestinal signs and symptoms

Synonym
Perianal Fistulizing Crohns disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: anti-TNF, ciprofloxacine, fistulizing Crohns disease

Outcome measures

Primary outcome

Primary outcome (response):

· Reduction of 50% or more from baseline to week 12 in the number of draining

fistulas. Closure is defined as no drainage despite firm finger compression.

Secondary outcome

Secondary outcomes:

· Proportion of patients in remission

· Safety and tolerability of adalimumab combined with ciprofloxacin

· Quality of life and psychopathology by psychological assessment using the

IBDQ questionnaire

· Change of PDAI score

Study description

Background summary

Perianal fistulas in Crohn*s disease rarely heal spontaneously; medical or surgical treatment is often required. The main medical therapies include antibiotics, azathioprine or 6-mercaptopurine, and infliximab. The efficacy of antibiotics for the treatment of Crohn*s fistulas has only been tested in uncontrolled studies, which have suggested a short-term benefit of both ciprofloxacin and metronidazole either alone or in combination. However, drug discontinuation or dose reduction often led to disease relapse. Ciprofloxacin is often preferred to metronidazole because it is associated with fewer side effects (1-6).
Clinical trials have shown that chimeric monoclonal antibody to TNF, infliximab is effective for the induction and maintenance therapy of patients with perianal fistulas in Crohn*s disease (7,8). However, the use of infliximab is

associated with the formation of antibodies to infliximab, which can lead to allergic reactions and a reduced response. A combination of ciprofloxacin and infliximab seems to be more effective than infliximab alone (9).
Adalimumab (D2E7, Humira; Abbott laboratories, Chicago, IL) is a recombinant human immunoglobulin G1 (IgG1) monoclonal antibody that binds with high affinity and specificity to human soluble TNF. A recent randomised trial showed that adalimumab was superior to a placebo for induction of remission in patients with moderate to severe Crohn*s disease naive to anti-TNF therapy (10). Open-label studies have found adalimumab to be well tolerated and beneficial in patients who have previously lost there response to, or cannot tolerate infliximab (11-13). There is only one small open label study available focusing on the use of adalimumab in the treatment of perianal fistulas in Crohn*s disease. In this study 64% of patients showed a partial or complete closure of all fistulas (14).

Study objective

To assess whether a combination of ciprofloxacin and adalimumab is more effective than adalimumab alone.

Study design

3. DESIGN OF THE STUDY

3.1 Setting
Principal centers:
· Department of Gastroenterology & Hepatology, Erasmus MC Rotterdam, The Netherlands
Others:
· Multiple centers in The Netherlands will participate in this study.

3.2 Number of patients
146 patients will be included, with 73 patients in each treatment group.

3.3 Design (type of trial)
Multicenter, randomized, double-blind study with two arms.

Intervention

Medication, dosage and duration
- Group A receive Adalimumab 160 mg at day 0, 80 mg at week 2, 40 mg at week 4

and every 14 days thereafter by subcutaneous injection combined with oral Ciprofloxacin 2 X 500 mg.
- Group B receive Adalimumab 160 mg at day 0, 80 mg at week 2, 40 mg at week 4 and every 14 days thereafter by subcutaneous injection combined with oral Placebo 2 x 500 mg.
Combination therapy will be given for a total treatment period of 12 weeks.
After 12 weeks treatment will be continued with subcutaneously Adalimumab only.

Study burden and risks

Patients need to come 3 times extra to the hosptial compared to patients not in this study.

Contacts

Public
Stichting Leveronderzoek

s Gravendijkwal 320, Hs212
3015 CE Rotterdam
NL
Scientific
Stichting Leveronderzoek

s Gravendijkwal 320, Hs212
3015 CE Rotterdam
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Endoscopically or histologically proven Crohn*s disease before 3 months prior to randomization
Single or multiple draining perianal fistulas
Age 18-70 years
Written informed consent
Adequate contraception for males and females during treatment and follow up

Exclusion criteria

Abscesses perianal
lactation, pregnancy
TBC or other infectious diseaseses
expected surgery in 6 months

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:	Recruitment stopped
Start date (anticipated):	16-09-2008
Enrollment:	146
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	27-12-2007
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-07-2008
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-11-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-12-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-08-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	24-08-2009
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:	26-11-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-07-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-08-2010
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	EUCTR2007-005832-10-NL
ClinicalTrials.gov	NCT00736983
CCMO	NL21136.078.07