Multimodal treatment of perianal fistulas in Crohn's disease: seton vs anti-TNF vs advancement plasty

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Anal and rectal conditions NEC
Study type	Interventional

Summary

ID

NL-OMON45001

Source
ToetsingOnline

Brief title
PISA-trial

Condition

- Anal and rectal conditions NEC

Synonym
perianal fistula

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: advancementy plasty, anti-TNF, Crohn's disease, LIFT, perianal fistula, seton

Outcome measures

Primary outcome

The primary outcome parameter is the number patients needing fistula-related re-intervention(s).

Secondary outcome

Secondary outcomes are the number of patients with closed fistulas and the percentage of closed fistulas (based on MRI) after 18 months, and the number of antibiotic courses that was required during treatment. Furthermore we evaluate the Perianal Disease Activity Index, quality of life, and costs.

Study description

Background summary

Crohn*s disease is a chronic disease that typically affects young adults. In The Netherlands only, there are 20,000 patients of whom approximately 20% have perianal fistulas. Perianal fistulising disease is associated with local pain, discharge, and considerable morbidity rates (including recurrent abcessess and sphincter destruction). This results in a negative impact on quality of life with sick-leave and an enormous impact on health care resources.
There are several treatment options for complex high fistulas with one internal opening. Until last decade, the most frequently used treatment approach has been surgical seton placement for chronic drainage of the fistula which maintains patency of the tract and eliminates the accumulation of pus which prevents the recurrent formation of tracts and abscesses, One disadvantage of this technique is that the fistula will not close with the seton in situ and that the patient has a chronic trans-anal drainage. Another option is surgical closure of the internal fistula opening by creating an advancement plasty or performing a LIFT. Unfortunately re-interventions were required in almost 50% of patients. Nowadays most patients receive treatment with anti-TNF agents. A randomized controleld trial demonstrated a significant increase in fistula closure with infliximab when compared to placebo treatment. However only 60% of

patients were responsive to medical treatment and after cessation of medication there was re-opening of the fistulas in 50%. Thereby treatment with anti-TNF is expensive (>25,000 Euros pp/year) and its efficiency has been never compared to surgical strategies.

Study objective

Currently, there is no guideline for the treatment of perianal Crohn's fistulas. the aim of this study, in which surgical strategies (seton drainage and surgical closure with advancement plasty/LIFT) will be compared to medical treatment. We hope to provide treatment consensus for daily practice. Thereby we will also assess the quality of life and cost-effectivenes.

Study design

Multicenter randomised controlled trial

Intervention

Group I: chronic seton (seton drainage for 1 year) and 6MP
Group II: anti-TNF (seton for 6 weeks under anti-TNF, followed by seton removal with continuation of medication for 1 year) and 6MP
Group III: advancement plasty or LIFT (in patients with a transsfincteric fistula) (seton drainage under anti-TNF. After 8-10 weeks, surgical closure with advancement plasty under anti-TNF for 4 months) and 6MP

Study burden and risks

The study compares three accepted management strategies. So there is no experimental treatment group.

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

- * 18 years;- Written informed consent;- High tract (intersphincteric, transsphincteric, suprasphincteric) perianal fistula located in the upper ;two-thirds of the external sphincter ;- Fistula with one internal opening (based on MRI imaging). The number of external fistulas does not ;have to be taken into account;- Both new fistulas or recurrent active fistula (defined as any producing fistula)

Exclusion criteria

- Proctitis (defined as any active mucosal inflammation or ulcer > 5mm in the rectum);- Anorectal stenosis (defined as the impossibility to introduce a proctoscope);- Submucosal fistulas & low intersphincteric fistulas (lower one-third of external sphincter);- Rectovaginal fistula;- Multiple internal openings;- Seton in situ for more than 3 months;- Use of Anti-TNF medication during last 3 months;- Previous Anti-TNF medication without any effect on perianal fistulas;- Previously demonstrated allergy for anti-TNF medication. If this allergy only concerns the chimeric ;monoclonal mouse-antibody infliximab, the patient could be randomised for adalumimab;- Patients with a stoma;- Immunocompromised patients (i.e. haematological malignancies, HIV/AIDS, bone marrow ;transplantation, splenectomy, genetic disorders such as severe combined immunodeficiency, ;chemotherapy, dialysis, solid organ transplant and long term immunosuppressant use such as ;corticosteroids in patients with rheumatoid arthritis);- Life expectancy < 2 years;- The inability of reading/understanding and filling in the questionnaires;- Dementia or altered mental status that would prohibit the understanding and giving of informed ;consent

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-11-2013
Enrollment:	111
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:	Remicade
Generic name:	Infliximab
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	24-07-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	21-08-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-02-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-03-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-03-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-04-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-05-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-06-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-07-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-09-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	12-09-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-01-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-06-2016
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	EUCTR2013-002932-25-NL
CCMO	NL44901.018.13

Study results

Date completed:	10-04-2018
Results posted:	04-09-2018
Actual enrolment:	42

Summary results
Trial is onging in other countries

First publication
04-09-2018