De-escalation of anti-TNF therapy in adolescents and young adults with IBD with tight faecal calprotectin and trough level monitoring

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To evaluate whether a faecal calprotectin guided strategy of anti-TNF dosing interval lengthening is non-inferior in maintaining remission in patients with IBD compared with an unchanged dosing interval.

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

Summary

ID

NL-OMON52654

Source
ToetsingOnline

Brief title
FREE-study

Condition

- Gastrointestinal inflammatory conditions
- Autoimmune disorders

Synonym
Crohn's disease, ulcerative colitis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,BÜHLMANN Laboratories AG

Intervention

Keyword: Adalimumab, Crohn's Disease, Inflammatory Bowel Diseases, Infliximab

Outcome measures

Primary outcome

The cumulative incidence of out-of-range FC results at 48 weeks follow-up.

Secondary outcome

(1) time to get out-of-range FC results

(2) cumulative incidence of anti-TNF-associated respiratory infections and

dermatological adverse effects at 48 weeks follow-up

(3) evolution of FC and anti-TNF trough levels in the first 16 weeks after

reverting to previous dosing interval

(4) proportion of patients developing loss-of-response in the first 16 weeks

after reverting to the previous dosing interval

(5) identification of predictors of successful de-escalation.

Study description

Background summary

Treatment outcomes of patients with inflammatory bowel disease (IBD) have improved enormously during the past decade due to the use of anti-tumour necrosis factor (anti-TNF) therapy. As a result, 67 to 91% of paediatric patients and 66% of adult patients is still in sustained remission two years after the initiation of anti-TNF therapy. Prolonged use of anti-TNFs comes with disadvantages such as dose dependent susceptibility to infections and

dermatological adverse effects. Preliminary, mostly uncontrolled studies suggest that dose reduction by dosing interval lengthening is a realistic option in a relevant proportion of patients with IBD, provided that intensive follow-up is applied.

Study objective

To evaluate whether a faecal calprotectin guided strategy of anti-TNF dosing interval lengthening is non-inferior in maintaining remission in patients with IBD compared with an unchanged dosing interval.

Study design

International, multi-centre, prospective, partially randomised patient-preference trial.

Intervention

In patients treated with adalimumab, the dosing interval will be lengthened from 2 to 3 weeks. In patients treated with infliximab, the dosing interval will be lengthened from 8 to 12 weeks. FC rapid tests will be performed every 4 weeks and rapid tests for anti-TNF trough levels will be performed every 12 weeks.

Study burden and risks

Patients with reduced anti-TNF exposure may have a higher risk of out-of-range FC results and, on the other hand, may benefit from fewer hospital visits or injections and possibly a decrease in adverse effects of anti-TNF therapy. Tight monitoring of FC levels (i.e. 4 weekly) will allow institution of re-escalation before the patient manifests clinical signs of relapse. This study could not be conducted without the participation of minors, who typically have a short disease duration and therefore have a window of opportunity to de-escalate anti-TNF therapy.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)

Inclusion criteria

- Aged 12-25 years
- Diagnosed with luminal Crohn*s disease or ulcerative colitis
- Treated with either 8-weekly infliximab or 2-weekly adalimumab
- Current anti-TNF agent as first ever anti-TNF agent or prior anti-TNF agent discontinued for reason other than primary non-response or secondary loss-of-response
- No previous attempts to lengthen the dosing interval
- Three consecutive faecal calprotectin (FC) results in the target range (i.e. <250 µg/g for CD patients; <150 µg/g for UC patients) in the previous 6 months
or
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confirmed endoscopic remission within 2 months before study entry (i.e. simple endoscopic score for Crohn*s disease (SES-CD) <3 points; ulcerative colitis endoscopic index of severity (UCEIS) <=1 point or Mayo endoscopic subscore <=1 point)
- Absence of symptoms associated with active IBD (judged by the local IBD-team)
- Written informed consent granted

Exclusion criteria

- Perianal fistula
- Presence of ileostomy or ileoanal pouch
- Any inflammatory comorbidity, such as rheumatoid arthritis
- Current treatment with corticosteroids (prednisone or budesonide)
- Current pregnancy

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-03-2021
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	flixabi
Generic name:	infliximab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	inflectra
Generic name:	infliximab

Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	remicade
Generic name:	infliximab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	remsima
Generic name:	infliximab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	zessly
Generic name:	infliximab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	08-07-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-09-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-07-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-12-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-12-2022
Application type:	Amendment

Review commission: METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2020-001811-26-NL
CCMO	NL73966.042.20