Control Crohn Safe with episodic adalimumab monotherapy as first line treatment study.

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This study has been transitioned to CTIS with ID 2024-516002-33-01 check the CTIS register for the current data. The aim of this study is to compare the long-term efficacy and safety of periodic adalimumab as initial treatment in newly diagnosed CD...

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

Summary

ID

NL-OMON52419

Source
ToetsingOnline

Brief title
CoCroS trial

Condition

- Gastrointestinal inflammatory conditions

Synonym
Chronic inflammatory bowel disease, Crohn's disease

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: ZonMW Goed Gebruik Geneesmiddelen

Intervention

Keyword: Early Crohn's disease, Periodic treatment with adalimumab, Randomised controlled open label trial, Treatment strategy

Outcome measures

Primary outcome

The primary endpoint is the difference in number of yearly-quarters of

corticosteroid free clinical and biochemical remission at week 96.

Safety outcomes are disease progression at week 96, drug related adverse events

and disease related serious adverse events (hospitalisations, surgery).

Secondary outcome

The secondary outcomes are total health care costs, cumulative corticosteroid

dose, proportion of patient with endoscopic remission w24, drug-related side

effects and patient reported outcome measures on quality of life, (work)

disability and treatment-tolerability

Study description

Background summary

Crohn*s disease (CD) is a chronic disease with a heterogeneous clinical presentation, relapse rate and treatment response. Insufficient control of mucosal inflammation results in irreversible bowel damage and complications and at present no markers are available to predict such a complicated disease course at diagnosis. Therefore, to prevent overtreatment of low risk patients, step-up treatment with subsequent introduction of corticosteroids, thiopurines maintenance and TNF-blockers if a previous category fails is standard care. Combination treatment with thiopurines and a TNF-blocker is more effective than monotherapy but associated with a higher risk for infectious complications. Landmark studies convincingly showed an improved long-term outcome if the TNF-blocker infliximab is introduced early after diagnosis. The standard step-care approach thus prolongs steroid exposure and delays start of disease modifying biologicals in high risks patients. Given the higher efficacy of

combination therapy with a thiopurine of infliximab and potential allergic reactions and lower response rates after re-initiation of this chimeric biological, temporary monotherapy with this TNF-blocker has not been studied as first line treatment before. Adalimumab is a humanised monoclonal antibody and subsequently, combination therapy of adalimumab + thiopurines has only a marginal effect on anti-drug anti-body formation. Furthermore, combination therapy with adalimumab does not enhance the clinical response. Therefore, periodic treatment with adalimumab in combination with close monitoring after drug-discontinuation, in newly diagnosed CD might improve outcome, reduce drug-related side effects while still preventing overtreatment.

Study objective

This study has been transitioned to CTIS with ID 2024-516002-33-01 check the CTIS register for the current data.

The aim of this study is to compare the long-term efficacy and safety of periodic adalimumab as initial treatment in newly diagnosed CD patients compared to standard step-care with corticosteroid/budesonide as the initial treatment

Study design

Pragmatic randomised open label multicentre trial

Intervention

24 weeks adalimumab treatment compared to standard step-care starting with corticosteroids/budesonide. Both study groups are strictly monitored with the validated telemedicine tool myIBDcoach and a calprotectin point of care test during the study period.

Study burden and risks

This study compares standard care with corticosteroids as first line drug with adalimumab as first line treatment in maintenance treatment naïve CD patients. Outpatient clinic visits and diagnostics during the study are mainly standard care. Strict monitoring with a colonoscopy, the telemedicine tool myIBDcoach and calprotectin test is routine care in the participating hospitals. The first line drug in the intervention arm of this trial is subcutaneous administered in contrast with oral treatment with corticosteroids in the standard care arm. Risk of subcutaneous administration with an auto-injection device is limited and consist of mild pain or purpura after injection. There is a small risk to hit a nerve with increased pain, or for an injectionside reactions (swelling, pruritus and redness) all of these are local and self-limiting. There might be discrete scarring or dimpling of the skin from a subcutaneous injection. Both

corticosteroids and adalimumab are immunosuppressive and the main adverse effects therefore infection, however the risk for severe infectious complications is higher for corticosteroids compared to anti-TNF monotherapy. Anti-TNF is generally well tolerated while side effects (weight gain, hyperglycemia, psychological complaints and development of striae) of corticosteroid occur in up to 50% of the patients. All the patients in the trial have a colonoscopy at week 24. Colonoscopy is an invasive uncomfortable procedure with a time-consuming preparation. Diagnostic ileocolonoscopy without biopsies has a 1/1000 risk for bowel perforation. In recent international guidelines performing an endoscopy, to assess the effect of treatment and to adjust treatment if persistent endoscopic inflammation is present is recommended (1). Patients have a second MRI-enterography after 96 week, this is not standard care. Participant have to drink contrast fluid as preparation for this examination and MRI-enterography yield a small risk for allergic reactions to intravenous administered contrast

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Inclusion criteria

- Newly diagnosed CD patients or patients with a flare of an established diagnosis visiting the outpatient clinic or endoscopy ward of the participating centres.
- CD diagnosis according to ECCO-guidelines including complete ileo-colonoscopy (last endoscopy <12 months ago) + complete small bowel imaging at diagnosis (MRI or CT-enterography)
- naïve to biologicals
- Sufficient knowledge Dutch language
- 18 years old <= 70 years old
- Smartphone with internet access
- Use of myIBDcoach

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Use of prednisone for longer than 4 weeks in the year before screening
- Use of budesonide (>=6 mg daily) for a duration longer than 3 months in the year before screening
- Use of thiopurines in the 3 years before screening
- Indication for primary treatment with biologicals or surgery
- Malignancy in 5 years before treatment. Exception adequately treated non-melanoma skin cancer
- Contra-indication for an TNF-blocker or immunosuppressant treatment. (Contra-indications are: a symptomatic stricture, an abscess, a history of tuberculosis or other granulomatous infection, a positive chest radiograph or Quantiferon or tuberculin skin test with purified protein derivative, a recent history of an opportunistic infection (within the previous 6 months), active infection with hepatitis B or C, infection with the human immunodeficiency virus, multiple sclerosis, cancer (except adequately treated non melanoma skin cancer)).
- Contra-indication for MRI-and CT-enterography
- Patients with short bowel syndrome or an ostomy

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):	23-12-2019
Enrollment:	158
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	21-08-2019
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	10-09-2019
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	25-03-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	26-03-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	26-05-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	27-05-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	18-02-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	25-02-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
EU-CTR	CTIS2024-516002-33-01
EudraCT	EUCTR2017-004588-11-NL
ClinicalTrials.gov	NCT03917303
CCMO	NL64005.068.18