Risk-stratified randomized controlled trial in paediatric Crohn*s Disease: Methotrexate versus azathioprine or adalimumab for maintaining remission in patients at low or at high risk for aggressive disease course, respectively * a treatment strategy

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To compare the effectiveness of weekly subcutaneously administered MTX for maintaining relapse-free sustained steroid/EN-free 1-year remission compared with:- daily oral AZA/6MP in low risk paediatric CD- subcutaneously administered adalimumab in...

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

Summary

ID

NL-OMON55661

Source
ToetsingOnline

Brief title
REDUCE-RISK in CD-PIBD-TRIAL

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn's disease, Inflammatory bowel disease

Research involving
Human

Sponsors and support

Primary sponsor: PIBD-NET
Source(s) of monetary or material Support: horizon2020

Intervention

Keyword: Crohn's Disease, Pediatric, Randomized, Reduce risk

Outcome measures

Primary outcome

Rate of sustained steroid/EEN-free remission at month 12, where sustained remission is defined as wPCDAI *12.5 and CRP *1,5, fold the normal upper limit without a relapse since week 12.

Secondary outcome

Comparison between the two treatment arms per risk group (high risk vs low risk for aggressive disease evolution) (and inter-risk group analysis for MTX-treated patients) plus analysis of adalimumab-treated patients from inclusion (TOP-down) versus patients switched to adalimumab due to failure of immunomodulator therapy (STEP-up).

Study description

Background summary

Crohn's disease (CD) is a chronic recurrent inflammatory disorder, which can cause tissue and bowel damage leading to major disability if not treated adequately. The recent ECCO-ESPGHAN guidelines indicate that children/adolescents with a moderate to severe form of Crohn's disease should receive a more potent treatment regimen allowing to positively influence the subsequent evolution of the disease. The ultimate aim of treatment is the

control of all inflammation, including at the mucosal level (mucosal healing). Recent studies suggest that obtaining mucosal healing offers a unique chance for patients to stop the natural evolution and progression of the disease. This may translate to a new way of treating CD. A more "aggressive" treatment at disease onset increases the likelihood of deep remission thereby improving long term outcomes. Experience with immunomodulators exists for more than 40 years in the treatment of IBD, and over 15 years with anti-TNF drugs. However, it is unclear which drug should be used as first line maintenance therapy and for which patient. A treatment strategy-based clinical trial using a risk-algorithm to identify high risk patients for progressive disease could address this question.

Study objective

To compare the effectiveness of weekly subcutaneously administered MTX for maintaining relapse-free sustained steroid/EN-free 1-year remission compared with:
- daily oral AZA/6MP in low risk paediatric CD
- subcutaneously administered adalimumab in high risk paediatric CD

Study design

Multicenter, phase IV, prospective, randomized treatment strategy with PROBE (prospective randomized open blind end-point) evaluation

Intervention

After initial diagnosis of moderate to severe Crohn's disease and an open induction therapy (exclusive enteral nutrion (orally or by NGT) and/or steroid therapy) patients are included in this treatment strategy-RCT by week 3 +/-1 and allocated to the high or low risk group for progressive and aggressive disease course.
In the low risk group: patients are 1:1 randomized to methotrexate versus azathioprine/6mercaptopurine as maintenance therapy until month 12
In the high risk group: patients are 1:1 randomized to methotrexate versus adalimumab as maintenance therapy until month 12

Study burden and risks

NA

Contacts

Public

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-Children 6-17, with a new-onset CD diagnosed < 6months using established criteria (28, 29), requiring a steroid-based or EN based induction therapy
-At initial diagnosis, wPCDAI >40 or CRP>2 times upper limit at diagnosis
-all wPCDAI scores (0-120) are possible at inclusion (patients in remission and patients with active disease)
-Luminal active CD (B1) with or without B2 and/or B3 disease behavior
-Initial exposure to 5-ASA and derivate is tolerated
-Exposure to antibiotics is tolerated

Exclusion criteria

*Patients with wPCDAI<42,5 at initial diagnosis, except if CRP>2 times upper limit
*No induction therapy with steroids or enteral nutrition

*Previous therapy with any IBD-related medications other than induction therapy as detailed in this protocol (except 5-ASA).

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:	Recruitment stopped
Start date (anticipated):	01-04-2019
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Humira
Generic name:	Adalimumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Imuran
Generic name:	Azathioprine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Mercaptopurine
Generic name:	purinethol

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

Ethics review

Approved WMO Date:	03-07-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-12-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-12-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-03-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-01-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-02-2020
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	EUCTR2016-000522-18-NL
CCMO	NL59161.078.17