Top-Down Infliximab Study in Kids with Crohn's disease (TISKids)

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

Summary

ID

NL-OMON52984

Source
ToetsingOnline

Brief title
Top-down Infliximab Study in Kids with Crohn's disease (TISKids)

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn's disease, Inflammatory bowel disease

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: NWO (ZonMW),Hospira

Intervention

Keyword: Crohn's disease, infliximab, pediatric, top-down

Outcome measures

Primary outcome

Clinical remission at 52 weeks without need for additional CD related therapy or surgery.

Secondary outcome

Secondary efficacy endpoints

* Clinical response (decrease in wPCDAI >17.5) and remission (wPCDAI <12.5) rates at week 10

* Mucosal healing rates at week 10 assessed by endoscopy (absence of ulcers) and calprotectin (<100 µg/g), and at week 52 assessed by endoscopy (performed on a voluntary basis, or if clinically indicated) and/or calprotectin

* Growth (change in height and BMI Z-scores, bone age and pubertal development)

* Quality of life at week14 and 52 (IMPACT III)

* Therapy failure rates over time (primary non-response, loss of response and medication intolerance)

* Cumulative therapy use (steroids, immunomodulators, biologicals, etc)

Secondary safety endpoints

* Adverse events rates

* Complication rate at 52 weeks (fistulas, abscesses, strictures, surgery, extra-intestinal manifestations)

Long-term follow-up endpoints (5 years)

* Yearly clinical remission rates without need for additional CD-related therapy or surgery
* Yearly clinical response, clinical remission and mucosal healing rates
* Number of flairs
* Quality of life at 5 years
* Cumulative therapy use (steroids, immunomodulators, biologicals, etc)
* Adverse events rate
* Complication rate (fistulas, abscesses, strictures, surgery, extra-intestinal manifestations)

Subanalyses

* Correlation between clinical disease activity, fecal calprotectin and endoscopic disease severity
* Comparing efficacy and safety endpoints between the two step-up treatment options (prednisolon+AZA vs EEN+AZA)

Additional objectives

* Determination of PK/PD properties of IFX in children
* Identification of predictive biomarkers of response to IFX
* Comparing cost-efficacy of top-down versus step-up

Study description

Background summary

Crohn*s disease (CD) is an incurable, debilitating inflammatory bowel disorder (IBD) which presents during childhood and adolescence in 25% of its patients. CD requires lifelong medication and is accompanied by severe complications. The use of anti-TNF antibodies has significantly improved CD management. Infliximab (IFX) is the first anti-TNF antibody registered for pediatric CD. Currently, IFX is reserved for immunomodulator refractory patients. We hypothesize that top-down IFX use (instead of the current step-up approach) with introduction of IFX at an early stage of disease, is more effective in the treatment of pediatric CD patients.

Study objective

The primary objective of our study is to determine the efficacy and safety of top-down IFX treatment in moderate-to-severe pediatric CD. Secondary objectives are determination of the pharmacokinetic/-dynamic profile of IFX and finding predictors of response to IFX in pediatric CD.

Study design

An international multicenter open-label randomised controlled trial

Intervention

Patients will be randomised to either top-down IFX treatment or conventional step-up treatment.
Treatment arm 1: Top-down IFX treatment will consist of a total of 5 IFX infusions of 5 mg/kg (IFX induction at week 0, 2 and 6, followed by 2 maintenance infusions every 8 weeks) combined with oral azathioprine (AZA) 2-3 mg/kg once daily. AZA therapy will continue after the last IFX infusion to maintain remission.
Treatment arm 2: Step-up treatment will consist of standard induction treatment by either oral prednisolone 1 mg/kg (maximum 40 mg) once daily for 4 weeks, followed by tapering in 6 weeks until stop, or exclusive enteral nutrition (EEN) with polymeric feeding for 6 to 8 weeks after which normal foods are gradually reintroduced within 2-3 weeks. Prednisolone and EEN will be combined with oral AZA 2-3 mg, once daily, as maintenance treatment.

Study burden and risks

In total, approximately 8 study visits will take place. In 5 of these visits, additional blood will be drawn for study purposes during routine blood draws and in case of disease relapse. Patients are requested to collect 3 stool samples and an additional sample in case of disease relapse. At week 10, patients will undergo an additional ileocolonoscopy, during which mucosal

biopsies of the ileum and colon will be taken.
The short-term risks of IFX treatment are the risk of infections and immunogenicity. The
long-term risks of IFX treatment are currently unknown. Some of the patients randomised to conventional therapy may eventually require and receive IFX, but in a later stage of the disease.
Top-down treated patients may benefit from increased therapy efficacy with increased chance of mucosal healing, as demonstrated by earlier studies in adult CD patients. Increased mucosal healing rates may result in decreased rates of complications. Since a short disease history and a younger age at diagnosis have been related to increased IFX efficacy in adults, children may benefit more from top-down IFX treatment

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)

Children (2-11 years)

Inclusion criteria

Diagnosed with Crohn's disease,
Moderate-to-severe disease activity
Aged 3-17
Untreated

Exclusion criteria

Need for surgery
Severe comorbidity or severe infection
Active perianal fistulas
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):	07-04-2015
Enrollment:	30
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	12-02-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-04-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-06-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-07-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-08-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-09-2015
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-12-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-01-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-03-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-04-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-02-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-02-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-07-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	14-08-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-12-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-11-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-11-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-07-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-09-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-03-2023
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	EUCTR2014-005702-37-NL
CCMO	NL52030.078.15