Prospective Analysis of Pharmacokinetic Infliximab data in Paediatric Inflammatory Bowel Disease patients

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This study has been transitioned to CTIS with ID 2023-507352-72-00 check the CTIS register for the current data. The primary study objective of our study is to assess the efficacy of an IFX intensified induction scheme vs. a standard dosing schedule...

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

Summary

ID

NL-OMON51805

Source
ToetsingOnline

Brief title
PRO-RAPID

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: Ministerie van OC&W,Kiddy Goodpills

Intervention

Keyword: Crohn's disease, Infliximab, Paediatric, Pharmacokinetics

Outcome measures

Primary outcome

Proportion of patients with IFX TL >= 5 µg/mL at week 12 without treatment escalation.

Secondary outcome

• Proportion of patients with IFX TL >= 5 µg/mL at week 24 without the need for treatment escalation

• Clinical and biochemical remission at weeks 4, 12, and 24 without the need for treatment escalation in patients with TL >= 5 µg/mL and in patients with TL < 5 µg/mL

• Predictors of IFX TLs at weeks 4, 12, and 24. Factors included in this analysis will be sex, age, body mass index (BMI), wPCDAI, IBD laboratory values, ATI, dose, and interval of IFX infusions

• Development of ATI until week 24

• Prediction of patients who will respond vs. those who will not despite adequate TLs at weeks 12 and 24 based on proteomics analysis by OLINK

• Evaluation of quality of life at baseline, week 12, and 24 in all patients

• Adverse event rate over time

Study description

Background summary

Crohn*s disease (CD) is a chronic, debilitating inflammatory bowel disease (IBD) which is diagnosed during childhood in up to one in ten patients. CD requires lifelong medication and is accompanied by severe complications. The use of anti-tumor necrosis factor (TNF)-α agents has significantly ameliorated CD management. Infliximab (IFX) is the first anti-TNF-α agent registered for pediatric CD. The current dosing recommendation of IFX is extrapolated from adult studies, and it is a weight-based dose (5 mg/kg) delivered during induction (infusion at weeks 0, 2, and 6) and maintenance (every 8 weeks). However, paediatric patients have a 25-40% lower drug exposure compared to adults, particularly children under 10 years of age, resulting in diminished efficacy and an increased risk of developing a complicated disease course. We hypothesize that an IFX intensified induction scheme (instead of the current dosing recommendation) is more effective in the treatment of pediatric CD patients.

Study objective

This study has been transitioned to CTIS with ID 2023-507352-72-00 check the CTIS register for the current data.

The primary study objective of our study is to assess the efficacy of an IFX intensified induction scheme vs. a standard dosing schedule in improving drug exposure (=therapeutic trough levels) without treatment escalation in pediatric CD patients.

Study design

An international, multicenter, prospective, open-label trial.

Intervention

IFX will be given intravenously at 10 mg/kg at week 0, and 5 mg/kg at weeks 2, 4, and 8 to all patients (induction). Maintenance will start at week 12, and then ideally continue every 6 weeks till week 24 (end of study). IFX trough levels will be measured at weeks 4, 12, and 24. During the maintenance, the IFX dose and/or interval adjustments, the IFX discontinuation or the start of a co-medication (i.e., an immunomodulator) will be possible on indication (i.e., primary nonresponse, secondary loss of response, intolerance to study medication) at the physicians* discretion. Follow-up will continue for the duration of the study (week 24).

Study burden and risks

In total, approximately 7 study visits will take place. In 4 of these visits, additional blood will be drawn for study purposes during routine blood draws. Patients are requested to collect 3 stool samples. No additional radiological

investigations or ileocolonoscopy will be performed for the study purposes. The short-term risk of IFX treatment are the risk of infections and immunogenicity. However, higher IFX trough levels are not associated with more severe adverse events. The long-term risks of IFX treatment are currently unknown. As a result of this study, dosing schedules for IFX could be more effectively used in pediatric patients with CD, with both improved short- and long-term outcomes. Moreover, this could lead to a decrease in hospitalizations and surgical treatments, resulting in a cost reduction over time and an improvement in quality of life.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Children (2-11 years)
Babies and toddlers (28 days-23 months)

Inclusion criteria

Diagnosed with Crohn's disease, age 1-15, anti-TNF naive, indication to start Infliximab

Exclusion criteria

Established monogenetic disease, perianal/fistulizing disease, severe comorbidity (not related to IBD)

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-08-2023
Enrollment:	49
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Inflectra
Generic name:	Infliximab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	22-11-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-01-2023
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-01-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-02-2024
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
EU-CTR	CTIS2023-507352-72-00
EudraCT	EUCTR2022-002648-35-NL
ClinicalTrials.gov	NCT05552287
CCMO	NL81536.078.22