Personalized AZithromycin/metronidAZole, in combination with standard induction therapy, to achieve a fecal microbiome community structure and metagenome changes associated with sustained remission in pediatric Crohn’s Disease (CD): a pilot study

Gepubliceerd: 01-06-2021 Laatst bijgewerkt: 18-08-2022

The study hypothesis is that adjunctive antibiotic therapy will improve clinical response to standard of care (SOC) induction therapy in a subgroup of CD patients with a relapse-associated microbiome profile.

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON24884

Bron
NTR

Verkorte titel
PAZAZ

Aandoening

Crohn's Disease

Ondersteuning

Primaire sponsor: Amsterdam UMC, location AMC
Overige ondersteuning: CCFA, Wetenschappelijke Adviesraad Emma Kinderziekenhuis

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

- To evaluate the feasibility of a multicenter trial on different continents with treatment allocation at week 4 depending on stool sample results at baseline
- To evaluate the potential efficacy of personalized adjunctive antibiotic therapy in maintaining clinical remission in pediatric subjects undergoing SOC induction therapy for mild to moderate Crohn’s disease who have a relapse-associated microbiome profile

Toelichting onderzoek

Achtergrond van het onderzoek

This is a multi-center, randomized, controlled open-label add-on design trial pilot study to evaluate the efficacy of personalized adjunctive antibiotic (azithromycin + metronidazole) therapy in pediatric subjects with mild to moderate Crohn’s disease (CD) who have a relapse-associated microbiome profile.

The study hypothesis is that adjunctive antibiotic therapy will improve clinical response to standard of care (SOC) induction therapy with Crohn's Disease Exclusion Diet (CDED) in a subgroup of CD patients with a relapse-associated microbiome profile. This is an add-on design trial for subjects already receiving SOC induction therapy (CDED); there will be no placebos.

Prior to starting SOC induction therapy at week 0, subjects will provide a baseline stool sample that will be screened for microbiome profiles associated with risk of relapse according to an established statistical model.
At week 4, subjects with a relapse-associated microbiome will be randomized into either a control arm that will continue to receive SOC induction therapy for an additional 8 weeks, or a treatment arm that will receive adjunctive antibiotic therapy in addition to continuing to receive SOC induction therapy for an additional 8 weeks. Subjects who do not have a relapse-associated microbiome will enter a separate control arm that will continue to receive SOC induction therapy and will have data collected for exploratory objectives. Subjects who are not in clinical remission by week 4 will receive antibiotic therapy regardless of microbiome signature at baseline. Subjects will be monitored for an additional 40 weeks after the treatment period (52 weeks total).

Doel van het onderzoek

The study hypothesis is that adjunctive antibiotic therapy will improve clinical response to standard of care (SOC) induction therapy in a subgroup of CD patients with a relapse-associated microbiome profile.

Onderzoeksopzet

week 0, week 4, week 12, week 24, week 36, week 52

Onderzoeksproduct en/of interventie

Antibiotics will be administered orally for an 8-week period. Azithromycin will be administered at a dose of 7.5mg/kg to a maximum of 500mg/day for 5 consecutive days per week for the first 4 weeks and then 3 consecutive days/week for 4 weeks. Metronidazole will be administered 10mg/kg twice daily to a maximum of 1000mg/day for 8 weeks.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Provision of signed and dated informed consent form (and assent form, as applicable)
2. Stated willingness to comply with all study procedures and availability for the duration of

the study
3. Male or female, aged 3 to 17 years
4. Diagnosed with CD according to standard clinical and histological criteria, within 36 months of week 0
5. Exhibiting mild to moderate symptoms of active disease, as determined by a PCDAI score >10 (or >7.5
excluding the height item) and ≤37.5
6. Evidence of active inflammation based on either: fecal calprotectin level >=250 microgram/g (local laboratory or
pre-arranged sponsor testing) within 30 days prior to week 0 visit; or according to accepted endoscopic and
histologic evidence obtained during an endoscopy procedure completed within 30 days prior to Week 0 Visit.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1.Current or previous use of anti-TNF or other biologic therapy
2.Presence of stricturing, penetrating (intestinal or perianal) and/or fistulizing CD.
3.Pregnancy or lactation
4.Have undergone intestinal resection
5.Laboratory diagnosis of Clostridium Difficile Infection (CDI), if performed for clinical indication
6.Treatment with another investigational drug or other intervention within 30 days before week 0
7.Risk factors for arrhythmia including history of prolonged QTc, hypokalemia or hypomagnesemia, resting
bradycardia, or concurrent treatment with other drugs with potential for QT prolongation.
8.History of Cockayne syndrome
9.Prior diagnosis of any hematologic condition/blood dyscrasia which may result in leukopenia (even if leukocyte
count is normal at screening)
10.Known allergy or intolerance to azithromycin or metronidazole
11.Subjects who received IV anti-infective within 35 days prior to week 0 visit or oral anti-infectives within 14 days
prior to the week 0 visit.
12.Subject on oral aminosalicylates who has not been on stable doses for greater than, or discontinued within, at
least 14 days prior to week 0.
13.Subject on cyclosporine, tacrolimus or mycophenolate mofetil. Stable doses (no change within 14 days prior to
week 0) of Azathioprine, 6-mercaptopurine or MTX are not a reason for exclusion.
14.Subject who received fecal microbial transplantation within 35 days prior to week 0 visit.
15.Screening laboratory and other analyses show any of the following abnormal results:
o AST, ALT > 2 X upper limit of the reference range (as determined locally at each site)

o Urea, Creatinine > 1.5X upper limit of the reference range (as determined locally at each site)
o White blood cell (WBC) count < 3.0 X 109/L
o Total bilirubin >= 20 micromol/liter (1.17mg/dl); except for subjects with isolated elevation of indirect bilirubin
relating to Gilbert syndrome
o Hemoglobin < 80 gram/liter
o Platelets < 100,000/µL

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-07-2021
Aantal proefpersonen:	20
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	01-06-2021
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL9512
Ander register	METC AMC : METC2020-803

Resultaten