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

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24884

Source
NTR

Brief title
PAZAZ

Health condition

Crohn's Disease

Sponsors and support

Primary sponsor: Amsterdam UMC, location AMC
Source(s) of monetary or material Support: CCFA, Wetenschappelijke Adviesraad Emma Kinderziekenhuis

Intervention

Outcome measures

Primary outcome

- 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

Secondary outcome

- To evaluate the potential efficacy of personalized adjunctive antibiotic therapy in improving PRO, components of established disease activity measures in remission, as well as ‘biochemical’ remission in pediatric subjects undergoing SOC induction therapy for mild to moderate Crohn’s disease who have a relapse-associated microbiome profile
- To investigate relationship between changes in subject microbiome composition and changes in disease activity over time.

Study description

Background summary

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).

Study objective

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.

Study design

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

Intervention

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.

Contacts

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Eligibility criteria

Inclusion criteria

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.

Exclusion criteria

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

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2021
Enrollment:	20
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	01-06-2021
Application type:	First submission

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
NTR-new	NL9512
Other	METC AMC : METC2020-803

Study results