A randomised controlled trial comparing FMT (Fecal Microbiota Transplantation) after budesonide or placebo in patients with active ulcerative colitis

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Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20218

Source
Nationaal Trial Register

Brief title
FECBUD

Health condition

Ulcerative colitis

Sponsors and support

Primary sponsor: Vedanta
Source(s) of monetary or material Support: Vedanta

Intervention

Outcome measures

Primary outcome

The primary outcome is engraftment of donor microbiota at 1,2, 4 and 8 weeks after the last FMT in patients pretreated with budesonide or placebo assessed with metagenomics/deep sequencing of the gut microbiota.

Secondary outcome

Secondary endpoints are: clinical response at 4 and 8 weeks after FMT, donor dependent efficacy and safety

Study description

Background summary

Despite an increasing number of active drugs against Inflammatory Bowel Disease (IBD) (ulcerative colitis and Crohn's disease), treatment results are disappointing far a subset of patients. In general, patients with ulcerative colitis are treated with with mesalazine (with or without prednisolone as induction). If mesalazine alone appears insufficient, a thiopurine (azathioprine or purinethol) is added as maintenance treatment. In a subset of patients, treatment with biologicals is required. Investigations of dysbiosis of the gut microbiota in patients with IBD may guide the development of new therapeutic strategies. IBD is characterized by a disturbed gut microbiota. Importantly, fecal microbiota transplantation (FMT) is able to induce remission in a small subset of patients with active ulcerative colitis (1-4). Interestingly, certain donors may be more effective, and patients with a response after FMT showed a change of their mlcrobiota profile towards that of their donor, pointing to the potential benefit of careful donor selection (1). So far, FM7 was been studied as induction therapy in patients with active inflammation without pre-treatment with antiinflammatory medication. The active inflammation may in part explain the side effects of FMT described ín IBO patients, such as fever, increased CRP and bacteraemia. Furthermore, the active inflammation may negatively influence engraftment of donor microbiota, which could possibly explain the limited efficacy of FMT in IBD patients. Our hypothesis is that the efficacy of FMT in patients with active ulcerative colitis can be increased by: 1. Pre treatment with budesonide (sortiment, which is a standard treatment approach in patients with activity of ulceratnre colitis) to enhance engraftment of donor microbiota in the recipient 2. Rational donor selection increases the effectiveness of FMT in patients with FMT

Study objective

Our hypothesis is that the efficacy of FMT in patients with active UC can be increased by: 1. Pretreatment with budesonide in patients with active UC, which may reduce inflammation

prior to infusion of the donor feces solution. This reduced inflammation may enable more effective engraftment of donor microbiota in the recipient, thereby increasing the efficacy of FMT. Treatment with cortiment is a standard treatment approach in patients with active ulcerative colitis. This study compares two different approaches in timing of FMT: (1) after initiation of anti-inflammatory therapy with budesonide or (2) without/before initiation of anti-inflammatory therapy with budesonide. 2. Rational donor selection. This might increase the power of FMT by preferentially transferring beneficial microbiota.

Study design

Baseline: randomization, starting with the pre-treatment (placebo vs. Budesonide), first visit at the outpatient clinic Week 3: FMT 1 Week 4: FMT 2 Week 5: FMT 3 Week 6: FMT 4 Week 7: collecting samples Week 8: collecting samples Week 10 (4 weeks after the last FMT): follow-up visit at the outpatient clinic Week 14 (8 weeks after the last FMT): follow-up visit at the outpatient clinic Week 15: Sigmoidoscopy

Intervention

Patients with active ulcerative colitis (n=24) will be randomized to a 3 weeks course of budesonide 9 mg once a day or placebo, followed by 4 infusions of a donor feces solution produced by the NDFB. The first FMT will be scheduled immediately after cessation of budesonide or placebo (t=3 weeks) and is delivered by a nasoduodenal tube. Three subsequent FMTs are scheduled weekly. Each individual patient receives donor feces infusion of one donor. Patients are treated with bowel lavage one day prior to the first FMT. Bowel lavage is not given prior to the 2nd, 3rd and 4th FMT Sigmoidoscopy will be performed 8 weeks after the 4th FMT, or earlier in case of clinical suspicion of persistent or recurrent activity.

Contacts

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Eligibility criteria

Inclusion criteria

Patients > 18 years old (n=24) with mild or moderate activity of ulcerative colitis despite previous maintenance therapy (mesalazine, or thiopurine, or anti-TNF) with a MA YO endoscopic score of I or II.

Exclusion criteria

CMV infection, pregnancy, recent use (<6 weeks) of antibiotics, recent (<2 months) use of oral corticosteroids, current need for systematic antibiotics or prophylactic antibiotic, recent intraabdominal surgery (<3 months), signs of active active infectious gastro-enteritis/enterocolitis or signs of infectious agents in stool sample, previous surgery for UC, abnormal renal function (eGFR <30ml/min), pre-existent leucopenia or thrombopenia (leucocyte count <2,000/mm3, or platelets <90,000/mm3, liver function tests abnormalities (>2 ULN), treatment with any investigational drug in another trial within 12 weeks of randomization, previous treatment with >2 biologicals, other significant medical illness that might interfere with this study.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-05-2019
Enrollment:	24
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	23-08-2021
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 52507
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL9858
CCMO	NL65069.018.18
OMON	NL-OMON52507

Study results