Transfer of feces in ulcerative colitis 2; improving efficacy

Published: 25-05-2018
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To study the efficacy and safety of FMT augmented by donor selection and repetitive dual route administration.To study microbiota composition, functional and metabolic changes as a result of dietary modulation and FMT.

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

Summary

ID

NL-OMON52507

Source
ToetsingOnline

Brief title
TURN 2 trial

Condition

- Gastrointestinal inflammatory conditions

Synonym
inflammatory bowel disease, Ulcerative colitis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Perspectum Inc.,Stichting AIO;MLDS & Spinoza Grant prof. Willem de Vos;Perspectum Inc.

Intervention

Keyword: Faecal transplantation, FMT, IBD, Ulcerative colitis

Outcome measures

Primary outcome

The primary endpoint is the proportion of study subjects in clinical and endoscopic remission per adapted Mayo: stool frequency subscores (SFS) <= 1, rectal bleeding subscore (RBS)=0 and endoscopic subscore <= 1

Secondary outcome

- Proportion of patients with a clinical response per Adapted Mayo at week 8: decrease from baseline >= 2 points and >= 30% plus a decrease in RBS >= 1 or an absolute RBS <= 1

- Proportion of patients with >=1 point reduction in summed endoscopic Mayo score of both the rectum and sigmoid at week 8.

- Proportion of patients in sustained steroid-free remission per adapated mayo at week 12: stool frequence subscore (SFS) <= 1, rectal bleeding subscore (RBS) = 0 and endoscopic subscore <= 1 and no need for rescue therapy until week 8.

- Proportion of patients in clinical response per partial adapted Mayo (without endoscopy) at week 8: decrease from Baseline >1 points and >30% plus a decrease in RBS >1 or an absolute RBS <= 1

- Proportion of patients in clinical remission per full mayo at week 8 : Full mayo score <= 2 with no subscore > 1

- Proportion of patients with:

o Endoscopic improvement: Endoscopic subscore of 0 or 1 at week 8

o Endoscopic remission: endoscopic subscore = 0 at week 8

o Histological Remission: Geboes score of < 2,0 at week 8, change in Robarts

histopathology index

o Change in IBDQ-control from baseline to week 2,4,8,18,39 and week 52

o Change in SSCAI from baseline to week 1,2,3,4,8,18,39 and week 52

o Change in Partial Mayo from baseline to week 1,2,3,4,8,18,39 and 52.

o Occurrence of adverse events

Study description

Background summary

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) of the colon that affects approximately 40,000 individuals in The Netherlands. Complaints such as abdominal pain, cramps and bloody diarrhoea usually start in early adulthood and lead to life-long substantial morbidity. The cause of UC is unknown, but the prevailing hypothesis is that there is a disproportionate immune response to the host gut microbiota. Many observational studies have shown a dysbiosis of the gut microbiota in UC. An attractive way to modulate this interaction is to radically reset the microbiota by fecal microbiota transplantation -or transfer- (FMT) from a healthy individual to a patient. We recently completed a randomized trial comparing FMT from a healthy donor with infusion of autologous feces in UC patients. In this phase 2a proof-of-concept trial, there was no statistically significant difference in clinical and endoscopic remission between patients with UC who received fecal transplants from healthy donors (30.4%) and those who received their own fecal microbiota (20.0%), which may be due to limited numbers. However, the microbiota of responders had distinct features from that of nonresponders, warranting further study. We next found that patients who received donor feces from a healthy individual rich in certain Clostridium clusters IV and XIVa and with a low abundance of Ruminococcus gnavus, had a high chance of sustained clinical remission. We hypothesize that by preselecting favorable donors, augmenting engraftment by rigorous prior bowel cleansing and dual and repetitive administration of :25 gr of feces per donation we can boost the treatment efficacy of FMT in UC patients.

Study objective

To study the efficacy and safety of FMT augmented by donor selection and repetitive dual route administration.

To study microbiota composition, functional and metabolic changes as a result of dietary modulation and FMT.

Study design

Randomized, double-blind, placebo controlled, multicenter, parallel group phase II trial with open label extension possibility.

Intervention

One group will be treated with faecal transplantation from a healthy donor, the other group will be treated with autologous faeces as a placebo.

Study burden and risks

FMT will be administered by nasojejunal tube at week 0 and week 3 as well as by retention enema at week 0, 1, 2, and 3. Nasojejunal tube placement will be performed by a Cortrak procedure. This procedure is routine in all participating centers and is associated with a very small risk of complications. The same holds for sigmoidoscopies, which patients will have to undergo three times with biopsies (for the non-responder group this will be four times).
Total follow-up time will be 52 weeks, during which 11 study visits are planned. From our earlier trials we know that nasojejunal FMT administration is well tolerated. In TURN1 out of 100 administrations vomiting was seen on two occasions. Most patients complained of transient borborygmi and in two patients transient fever was seen. No serious adverse events attributable to FMT have been encountered in a total experience with nasojejunal FMT administration in over 500 study subjects in the AMC. Donors and patients will be asked to fill in an dietary questionnaire.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Age >=18 and <70
• Ability to give informed consent
• Established ulcerative colitis with known involvement of the left colon according to the Lennard-Jones criteria
• Full Mayo score 5-9
• Endoscopic Mayo score of >= 2 in either the rectum or sigmoid upon screening sigmoidoscopy
• Stable dose of thiopurines, 5-ASA, in preceding 8 weeks, stable budesonide use in preciding 2 weeks, prednisone use <=15mg/day in preceding 2 weeks with a mandatory taper of 5mg per week from week 4
• Women need to use reliable contraceptives during participation in the study
* Alkaline phosphatase >1.5x ULN in the subgroup of PSC/UC patients

Exclusion criteria

• Condition leading to profound immunosuppression
o For example: HIV, infectious diseases leading to immunosuppression, bone marrow malignancies
o Use of systemic chemotherapy
o Child-Pugh B liver cirrhosis
• Anti-TNF treatment in preceding 2 months
Vedolizumab, tofacitinib and/or ustekinumab treatment in preceding 2 months
• Cyclosporine treatment in preceding 4 weeks
• Use of Methotrexate in preceding 2 months

• Prednisolone dose > 15 mg/day in preceding 2 weeks
• Use of topical therapy in preceding 2 weeks
• Life expectancy < 12 months
• Difficulty with swallowing
• Use of systemic antibiotics in preceding 4 weeks
• Use of probiotic treatment in preceding 4 weeks
• Positive stool cultures for common enteric pathogens (Salmonella, Shigella, Yersinia, Campylobacter, enteropathogenic e coli)
• Positive C. Difficile stool test
• Positive dual faeces test for pathogenic parasites e.g. Dientamoeba histolytica, Giardia Lamblia, Dientamoeba fragilis..
• Positive serological test for HIV
• History of surgery:
o presence of a pouch
o presence of stoma
• Known intra-abdominal fistula
• Pregnancy or women who give breastfeeding
• Vasopressive medication, icu stay
• Signs of ileus, diminished passage
• Allergy to macrogol or substituents, eg peanuts, shellfish
* Allergy to gadolinium iv contrast agent in the subgroup of patients who will be scheduled for MRI liver.
• Crohn*s disease
* Subject who has any conditions that in the opinion of the investigator, would compromise the safety of the subject or the quality of the data and is an unsuitable candidate for the study

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-12-2018
Enrollment:	76
Type:	Actual

Ethics review

Approved WMO Date:	25-05-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-08-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-05-2020

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-10-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-10-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-06-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-10-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 20218
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL65069.018.18
OMON	NL-OMON20218