The TURN 2 trial, transplantation of feces in ulcerative colitis; improving efficacy

No registrations found.

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

Summary

ID

NL-OMON28664

Source
Nationaal Trial Register

Brief title
The TURN 2 trial

Health condition

Ulcerative colitis, colitis ulcerosa, IBD, Primary Sclerosing Cholangitis

Sponsors and support

Primary sponsor: Academical Medical Center (AMC)
Source(s) of monetary or material Support: Stichting auto-immuun onderzoek (SAIO), MLDS, Spinoza Grant Prof. Willem de Vos

Intervention

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

1. Proportion of patients with a clinical response per Adapted Mayo at week 8
2. Proportion of patients with ≥1 point reduction in summed endoscopic Mayo score of both the rectum and sigmoid at week 8.
3. Proportion of patients in sustained steroid-free remission per adapted mayo at week 8
4. Proportion of patients in clinical response per partial adapted Mayo (without endoscopy) at week 8
5. Proportion of patients in clinical remission per full mayo at week 8
6. Change in microbiota signature from baseline to week 2, week 8 and week 52
7. Change in IBDQ-control from baseline to week 1,2,3,4, 8,18 and week 52
8. Change in SSCAI from baseline to week 1,2,3 4,8, 18 and week 52
9. Change in MRI liver images (with post-processing analysis techniques MRCP+ and cT1) from baseline to week 8.

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 (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, anaerobic fecal collection, augmenting engraftment by rigorous prior bowel cleansing and dual and repetitive administration of >60 gr of feces per donation, we can boost the treatment efficacy of FMT in UC patients. Furthermore, IBD is associated with primary sclerosing cholangitis (PSC) and a a recent pilot study described promising results in liver enzymes levels in PSC/UC patients.Therefore, we hypothesize that FMT can affect disease activity, captured by MRI liver images and post-processing analysis, of PSC in patiënts with PSC/UC.

Study objective

We hypothesize that the treatment efficacy of FMT in UC can be augmented by anaerobic stool collection, appropriate donor selection based on their microbiota profile and by enhancing the engraftment by dual route administration. Furthermore, we hypothesize that FMT can affect disease activity of PSC, captured by MRI liver images and post-processing analysis, in patiënts with PSC/UC.

Study design

Week -4,0,1,2,3,4,8,18,39,52

Intervention

Arm 1: Patients will be treated with faecal transplantation, processed for duodenal and rectal administration.
Arm 2: Patients will be treated with their own faeces (placebo), processed for duodenal and rectal administration.
PSC/UC subgroup will undergo a MRI liver at baseline and 8 weeks after faecal transplantation.

Contacts

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Eligibility criteria

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
• Partial mayo score of ≥ 3 and calprotectin > 250
• 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, or budesonide in preceding 8 weeks, prednisone use ≤15mg/day in preceding 2 weeks, stable dose of 5-ASA or corticosteroid containing enemas in preceding 2 weeks
• Women need to use reliable contraceptives during participation in the study
• Alkaline phosphatase > 1.5 x ULN in the subgroup of PSC/UC patients.

Exclusion criteria

• Condition leading to profound immunosuppression
• For example: HIV, infectious diseases leading to immunosuppression, bone marrow malignancies
• Use of systemic chemotherapy
• Child-Pugh B liver cirrhosis
• Anti-TNF 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, Blastocystis hominis only if microscopically many or very many blastocysts are seen.
• Positive serological test for HIV
• History of surgery:
• presence of a pouch
• 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
• 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

• Known allergy to iv gadolinium in the subgroup of patients who would be scheduled for MRI liver

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	05-12-2018
Enrollment:	76
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N/A

Ethics review

Positive opinion

Date:	03-06-2019
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	NL7770
Other	METC AMC : MET 2018_057

Study results

Summary results
N/A