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

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

Samenvatting

ID

NL-OMON28664

Bron
Nationaal Trial Register

Verkorte titel
The TURN 2 trial

Aandoening

Ulcerative colitis, colitis ulcerosa, IBD, Primary Sclerosing Cholangitis

Ondersteuning

Primaire sponsor: Academical Medical Center (AMC)
Overige ondersteuning: Stichting auto-immuun onderzoek (SAIO), MLDS, Spinoza Grant Prof. Willem de Vos

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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

Onderzoeksproduct en/of interventie

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.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

• 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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

• 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

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	05-12-2018
Aantal proefpersonen:	76
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Toelichting
N/A

Ethische beoordeling

Positief advies

Datum:	03-06-2019
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	NL7770
Ander register	METC AMC : MET 2018_057

Resultaten

Samenvatting resultaten
N/A