Treatment of chronic, recurrent and/or antibiotic refractory pouchitis with tofacitinib

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We hypothesize there is an immunological component underlying chronic pouchitis which might be similar to that seen in UC. Therefore, we believe tofacitinib might be an effective treatment for these patients as well.

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON23800

Bron
NTR

Verkorte titel
TOFA-Pouchitis

Aandoening

Chronic pouchitis, antibiotic refractory pouchitis, recurrent pouchitis, ulcerative colitis, inflammatory bowel disease

Ondersteuning

Primaire sponsor: Amsterdam UMC, location AMC
Overige ondersteuning: Pfizer

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

To assess the safety and efficacy of 8 weeks of treatment with tofacitinib in chronic, recurrent and/or antibiotic refractory pouchitis, based on clinical, endoscopic, and histologic response.

Toelichting onderzoek

Achtergrond van het onderzoek

Up to 50% of UC patients with an Ileal pouch-anal anastomosis (IPAA) will develop at least one episode of pouchitis, and up to 20% will develop a chronic phenotype. The aetiology of pouchitis remains unknown. An overlap with recurrence of UC has been suggested, since pouchitis is rarely seen in patients with IPAA for other indications, such as familial adenomatous polyposis (FAP). With symptoms such as increased stool frequency, urgency and abdominal cramps, quality of life in pouchitis patients is considerably impaired. Furthermore, pouchitis accounts for 24% of all late-onset pouch failures as current therapies are not always effective. Therefore, new therapies that can offer symptom resolution as well as endoscopic and histologic remission are essential. Tofacitinib, an oral small molecule JAK1 and JAK3 inhibitor, is effective for induction and maintenance of remission in UC. Considering the immunological component of chronic pouchitis, in which the inflammatory pathway might be similar to that seen in UC since pouchitis rarely occurs in FAP patients, effective immunosuppressant drugs such as tofacitinib potentially offer a new treatment modality for this treatment refractory population.
The aim of this proposal is to assess the efficacy of tofacitinib in the treatment of chronic, recurrent and/or antibiotic refractory pouchitis, as well as observing changes in endoscopic and histologic appearance and in multi-omics analyses before and after treatment with tofacitinib.

Doel van het onderzoek

We hypothesize there is an immunological component underlying chronic pouchitis which might be similar to that seen in UC. Therefore, we believe tofacitinib might be an effective treatment for these patients as well.

Onderzoeksopzet

-4, 0, 2, 4, 8, 12

Onderzoeksproduct en/of interventie

Tofacitinib 20mg a day, for 8 weeks

Contactpersonen

Publiek

Amsterdam UMC, location AMC
Djuna de Jong

020-5661260

Wetenschappelijk

Amsterdam UMC, location AMC
Djuna de Jong

020-5661260

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1) Subject must be at least 18 years of age.
2) Subject has a history of an IPAA for UC, all stages completed at least 6 months prior to day one of the start of the study.
3) Subject has chronic, recurrent and/or antibiotic refractory pouchitis, defined as a PDAI ≥ 7 , with either
a) ≥ 2 recurrent pouchitis episodes within 1 year prior to screening, necessitating treatment with antibiotics or other prescription, or;
b) Requiring maintenance antibiotic therapy for ≥ 4 weeks to maintain clinical remission and a history of at least two attempts in the last 24 months to stop this therapy, resulting in a relapse of the pouchitis episodes.
4) Female subjects of childbearing potential, defined as biologically capable of having children and is sexually active, must agree to use a highly effective method of contraception throughout the study and for at least 4 weeks after the last dose of assigned treatment.
5) Female subjects of childbearing potential must have a negative pregnancy test prior to enrolment in the study.
6) Written informed consent must be obtained and documented.

Belangrijkste redenen om niet deel te kunnen nemen

(Exclusiecriteria)

1) Pouchitis due to surgery related conditions (such as an abscess, fistula, or sinus of the pouch).
2) Absence of a previous pelvic MRI to assess secondary causes of pouchitis.
3) Irritable pouch syndrome (symptoms without evidence of inflammation on endoscopy and histology).
4) Mechanical complications of the pouch (e.g. pouch stricture or pouch fistula).
5) Crohn's disease of the pouch.
6) Patients with signs of severe systemic inflammation (at least two of the following symptoms: temperature > 38.5 ^{0}C, tachycardia > 100 bpm (after rehydration), systolic blood pressure < 100 mmHg).
7) Diverting ileostomy.
8) Chronic treatment for pouchitis with antibiotics. All antibiotics should be discontinued 4 weeks prior to baseline.
9) Positive stool sample for C. difficile, enteric pathogens, pathogenic ova or parasites at screening.
10) Subjects with clinically significant infections currently or within 6 months of baseline (e.g., those requiring hospitalization or parenteral antimicrobial therapy or opportunistic infections), a history of any infection requiring antimicrobial therapy within 2 weeks of baseline, or a history of any infection otherwise judged by the investigator to have the potential for exacerbation by participation in the study.
11) Active herpes zoster infection or history of disseminated zoster infection.
12) Evidence of an active infection during screening, or known history of chronic HBV, HCV, HIV infection, or if subject is immunodeficient.
13) Active or latent infection with Mycobacterium tuberculosis (TB), regardless of treatment history.
14) Subjects who have been vaccinated with live or attenuated vaccine within 6 weeks of baseline or scheduled to receive these vaccines during study period or within 6 weeks after last dose of study medication. Subjects with history of any lymphoproliferative disorder (such as EBV-related lymphoproliferative disorder, as reported in some subjects on other immunosuppressive drugs), history of lymphoma, leukaemia, myeloproliferative disorders, multiple myeloma, or signs and symptoms suggestive of current lymphatic disease.
15) Subjects with a history of pulmonary embolism and/or deep venous thrombosis.
16) Subjects with malignancies or a history of malignancies, with the exception of adequately treated or excised non-metastatic basal cell or squamous cell cancer of the skin.
17) Subjects with a history of bowel surgery within 6 months prior to baseline.
18) Subjects with significant trauma or major surgery within 4 weeks of screening visit.
19) Subjects likely to require any type of surgery during the study period.
20) Subjects with the following laboratory values at screening:
a) Hemoglobin levels <5.5 mmol/L or hematocrit <30%.
b) An absolute white blood cell (WBC) count of <3.0 x 109/L (<3000/mm3) or absolute neutrophil count of <1.2 x 109/L (<1200/mm3), or an absolute lymphocyte count of <0.5 x 109/L (<500/mm3).
c) Thrombocytopenia, as defined by a platelet count <100 x 109/L (<100,000/mm3).
d) Subjects with estimated GFR <50 ml/min.

e) Subjects with total bilirubin, AST or ALT more than 1.5 times the upper limit of normal.
21) Subjects with evidence of or suspected liver disease i.e., liver injury due to methotrexate or primary sclerosing cholangitis.
22) Subjects with current or recent history of severe, progressive, or uncontrolled renal, hepatic, hematological, gastrointestinal, metabolic (including uncontrolled hypercholesterolemia), endocrine, pulmonary, cardiac or neurological disease.
23) Subjects with any condition possibly affecting oral drug absorption (e.g., gastrectomy, clinically significant diabetic gastro-enteropathy, or certain types of bariatric surgery such as gastric bypass). Procedures such as gastric banding that simply divide the stomach into separate chambers are NOT exclusionary.
24) Women who are pregnant or lactating, or planning to become pregnant during the study period.
25) History of alcohol or drug abuse with less than 6 months of abstinence prior to baseline.
26) Donation of blood in excess of 500 mL within 8 weeks prior to baseline.
27) Subjects with a first-degree relative with a hereditary immunodeficiency.
28) Subjects who have previously participated in any study of tofacitinib or any other JAK-inhibitor.
29) Subjects who have received any investigational drug or device within 3 months prior to baseline.
30) Subject who has any condition 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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-10-2020
Aantal proefpersonen:	12
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

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	NL8879
Ander register	METC AMC : 2020_147

Resultaten