Tofacitinib in the treatment of chronic, recurrent and/or antibiotic refractory pouchitis: a multi-omics approach

Published: 02-09-2020
Last updated: 08-04-2024

To assess efficacy and safety of tofacitinib in the treatment of chronic, recurrent and/or antibiotic refractory pouchitis.

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

Summary

ID

NL-OMON52963

Source
ToetsingOnline

Brief title
TOFA-Pouchitis

Condition

- Gastrointestinal inflammatory conditions

Synonym
inflammation of the pouch reservoir, Pouchitis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Pfizer

Intervention

Keyword: Antibiotic refractory pouchitis, Chronic Pouchitis, Tofacitinib, Ulcerative Colitis

Outcome measures

Primary outcome

The primary endpoint is the proportion of patients in clinical and endoscopic remission at week 8.

Secondary outcome

The main secondary endpoints are changes in histologic disease activity, immune cell infiltration, gene expression of inflammatory cytokines and changes in the microbiome.

Study description

Background summary

Ileal pouch-anal anastomosis (IPAA) is the standard of care for patients with ulcerative colitis (UC) who require colectomy. Up to 50% of these IPAA patients will develop at least one episode of pouchitis(1, 2) 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(3). Furthermore, pouchitis accounts for 24% of all late-onset pouch failures as current therapies are not always effective(4). 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(5). 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(6), 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.

Study objective

To assess efficacy and safety of tofacitinib in the treatment of chronic, recurrent and/or antibiotic refractory pouchitis.

Study design

This study will be a single-arm, open-label, proof of concept trial.

Intervention

Treatment with Tofacitinib 10mg, two times a day, for 8 weeks.

Study burden and risks

Patients will have a total follow-up time of 12 weeks, in which five outpatient clinic visits and one telephone consult are scheduled. Blood samples will be drawn five times. Endoscopic assessment of the pouch will be done at baseline and at week 8. During this procedure, biopsies will be taken. A pouchoscopy is regarded as a safe procedure with a very small risk of complications. Tofacitinib will be given to patients included in this trial. In previous research, tofacitinib proved to be effective in the treatment of moderately to severely active UC(5). Tofacitinib has been studied for more than 10 years in patients with rheumatoid arthritis. In these studies, tofacitinib showed a similar safety profile as biologic agents, apart from a higher incidence rate of herpes zoster infection(7, 8).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Subject has a history of ileal pouch anal anastomosis (IPAA) for UC, all stages completed at least 6 months prior to day one of the start of the study.
2. Subject has chronic, recurrent and/or antibiotic refractory pouchitis, defined as a PDAI >= 7 (or mPDAI >= 5 if histology is pending) , with either
- >= 2 recurrent pouchitis episodes within 1 year prior to screening, necessitating treatment with antibiotics or other prescription, or;
- 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.

Exclusion criteria

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 pouchitis on endoscopy and histology).
4. Mechanical complications of the pouch (e.g. pouch stricture or pouch fistula).
5. Diverting ileostomy.
6. Positive stool sample for C. difficile, enteric pathogens, pathogenic ova or parasites at screening.
7. Active herpes zoster infection or history of disseminated zoster infection.
8. Evidence of an active infection during screening, or known history of chronic HBV, HCV, HIV infection, or if subject is immunodeficient.
9. Active or latent infection with Mycobacterium tuberculosis (TB), regardless of treatment history.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-09-2021
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Xeljanz
Generic name:	Tofacitinib
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	02-09-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-10-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-07-2021

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-07-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-04-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-05-2022
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2020-002695-12-NL
CCMO	NL71383.018.20

Study results

Date completed:	05-07-2023
Actual enrolment:	13