Filgotinib in the treatment of patients with ulcerative colitis: towards precision medicine (TOPS study)

Published: 28-02-2023
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Primary objective: identifying biomarkers for response to filgotinib in patients with UC.Secondary objective: To establish a biobank which can be used for future inquiries into UC.

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

Summary

ID

NL-OMON53453

Source
ToetsingOnline

Brief title
TOPS

Condition

- Gastrointestinal inflammatory conditions

Synonym
Ulcerative colitis; inflammatory bowel disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Farmaceutisch bedrijf,Galapagos NV

Intervention

Keyword: Filgotinib, Systems Medicine, Ulcerative colitis

Outcome measures

Primary outcome

Clinical response at 24 weeks, defined as a corticosteroid-free reduction of 3 or more points in the Mayo Clinical Score and at least 30% from induction baseline with an accompanying decrease in rectal bleeding subscore of 1 point or more, or an absolute rectal bleeding subscore of 0 or 1.

Secondary outcome

Not applicable

Study description

Background summary

Rationale: The traditional step-up strategy of treatment for inflammatory bowel disease is changing rapidly with the introduction of new treatment modalities. Two newly approved drugs inhibiting Janus kinase (JAK) - tofacitinib and filgotinib- have been shown to be efficacious in inducing and maintaining remission in patients with ulcerative colitis (UC). In the SELECTION study, filgotinib 200mg once daily, performed significantly better than placebo for inducing remission in both biological naïve and biological experienced patients with UC (26.1% versus 15.3% and 11.5% versus 4.2%, respectively), while remission rates at week 58 were 37.2% versus 11.2% in the respective placebo group1. To date, head-to-head studies comparing efficacy and safety of different classes of drugs and biomarkers enabling precision medicine are presently lacking. Therefore, therapeutic choices are mostly based on comorbidity, potential side effects, the need for a rapid onset of action and costs. In the present study, we aim to identify and validate biological predictors of clinical response to filgotinib in patients with UC. Furthermore, we will establish a biobank, the TOPS Biobank, with the biological material of patients, that will enable future inquiries into UC without subjecting subjects to additional study measures.

Study objective

Primary objective: identifying biomarkers for response to filgotinib in patients with UC.
Secondary objective: To establish a biobank which can be used for future inquiries into UC.

Study design

Observational, longitudinal, multicentre study with establishment of a biobank.

Study procedures
Endoscopy: Before initiating a step-up therapy, colonoscopy or flexible sigmoidoscopy is routinely performed to confirm the presence of inflammation. In addition, endoscopy is routinely performed after a follow-up of 20-24 weeks and in case of a flare to assess mucosal healing or newly developed inflammation. Whether a sigmoidoscopy or colonoscopy is chosen is decided by the treating physician. During endoscopies eight mucosal biopsies will be obtained for research purposes. Additionally, the patient will be asked to undergo an additional proctoscopy with biopsies at week 10 (optional).

Blood/faeces: During treatment with filgotinib, blood and fecal samples are routinely collected to monitor the treatment effect (CRP and fecal calprotectin levels). Participation in the study will not result in more frequent blood sampling. However additionally to the routine assessments, 42ml of blood and two fecal samples will be collected at each time point. Time points will be at baseline, at 4 weeks, at 10 weeks, at 24 weeks and 52 weeks or in case of a flare.

Questionnaires: Patients will be asked to complete a short and validated questionnaire (Mayo) for assessment of disease activity at each follow-up moment (max.10 minutes, 5 times in total).

If the participant gives his/her consent, blood-, fecal- and tissue samples will be stored in the TOPS Biobank.

Study burden and risks

Burden: Minimal as the endoscopies and blood sampling are part of the standard of care. Additonal burden comes from filling in the quality of life questionnaires which is minimal. If the participant agrees to partake in the optional rectoscopy, a short and relatively burdenless procedure is added to the standard of care.

Risks: Blood withdrawal carries a negligible risk of complications. The risk of bleeding or perforation following the taking of biopsies during colonoscopy is very low, approximately 1 per 1000 colonoscopies.

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

- Previously (>=3 months) documented diagnosis of ulcerative colitis
- Moderately to severe ulcerative colitis, defined as a Mayo score of 6-12.
- Age >= 18 years
- Indication for the start of filgotinib, as determined by the treating physician(s)

Exclusion criteria

- No informed consent has been obtained
- The patient is diagnosed with Crohn*s disease
- The concomitant use of biological medication

- Previous failure of a JAK-inhibitor
- Recent (<4 weeks) start or intensification of other topical or systemic treatments for UC
- Immunodeficiency (e.g. HIV, SCID)
- Acute severe ulcerative colitis
- Pregnancy or lactating female

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-06-2023
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	28-02-2023
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	09-01-2025
Application type:	Amendment
Review commission:	METC NedMec

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
CCMO	NL82056.041.22