Pilot study to validate scRNA sequencing and CyTOF analysis in intestinal biopsies from patients with inflammatory bowel disease

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

Summary

ID

NL-OMON51051

Source
ToetsingOnline

Brief title
Validate scRNAseq and CyTOF in intestinal biopsies

Condition

- Gastrointestinal inflammatory conditions

Synonym
Inflammatory bowel disease

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: filantropisch fonds: The Leona M. and Harry B. Helmsley Charitable Trust (New York;USA)

Intervention

Keyword: biomarker, Biopsy, Inflammatory bowel disease

Outcome measures

Primary outcome

We hypothesize that with the mentioned biopsies we will acquire around 500.000

viable cells required for thorough analysis with scRNAseq and CyTOF analysis.

Secondary outcome

na

Study description

Background summary

Crohn*s disease (CD) and ulcerative colitis (UC) are chronic idiopathic diseases affecting the gastrointestinal tract. Unless highly effective therapies, the majority of patients experience disease progression that leads to tissue damaging and complications affecting patient*s quality of life, morbidity and mortality. Where ulcerative colitis is characterized by extensive and progressive inflammation of the colon, Crohn*s disease is known to affect the entire gastrointestinal tract. More than 30 % of patients with CD encounter complications such as fibrotic stenosis or fistulas in their life.
Because CD en UC involves many different pathological pathways (inflammatory, microbial and tissue remodelling mechanisms) we aim to investigate the mechanism of action of the different treatment modalities and biomarkers that will allow stratification to a more targeted approach.
In this pilot study we will assess whether intestinal mucosal biopsies from rectum and colon are suitable to conduct future research with single cell RNA sequencing (scRNAseq) and CyTOF (cytometry by time-of-flight, i.e. mass cytometry). Most experience with scRNAseq and CyTOF has been performed with peripheral blood mononuclear cells (PBMC) obtained from blood. It is not known how many biopsies must be obtained with endoscopy to harvest enough viable cells to perform the analysis to obtain new biomarkers. Therefore, a pilot study is needed to assess the quantity of viable cells obtained by biopsies

during colonoscopy to ensure future study protocols can be formed.

Study objective

In this pilot study we will validate intestinal mucosa biopsies for usage in scRNA sequencing and CyTOF analysis for future research in patients with CD and UC. Key in this validation is the number of viable cells in mucosal biopsies and the number of inflammation related cells (CD45 +ve). Some biopsies will be taken from inflamed mucosa to account for the supposed higher cell count in inflamed tissue than in healthy tissue.

Study design

Cross-sectional study to acquire data for future research at the Amsterdam UMC, not meant to be published. We will collect 5 biopsies from rectal and/or colonic mucosa in addition to clinically required biopsies during standardized follow-up colonoscopies. These *fresh* biopsies will be analysed by FACS (i.e. flowcytometry), CyTOF and scRNAseq to assess cell count, viable cell count and CD45 +ve and CD45 -ve cell count and perform proof of principle analysis on single cell proteomic and transcriptomic analysis. To account for potential altering variables we ask the patients to collect additional serum and a stool sample to their clinically indicated blood and stool collection. Clinical data will be collected as far as disease entity, progression, location and current and past treatment.

Study burden and risks

Endoscopic biopsies taken during colonoscopy include a minimal risk of complication, mainly bleeding or perforation (< 1: 10.000). In case complication occurs, endoscopic treatment (hemostasis/clipping) is effective in most cases during the same session. Rarely, hospital admission with/without a second endoscopy or surgical intervention, antibiotic therapy and/or blood transfusion can be required. Peripheral blood is sampled with a negligible risk and low burden.
Patients participating in this pilot study undergo additional biopsies to clinically required biopsies, we do not expect this to be a significant extra burden.

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

All adult patients (*18y/o) with legal capacities and a diagnosis of IBD (CD or ulcerative colitis) undergoing a standardized care follow-up colonoscopy can be enrolled after giving written informed consent to enrolment.

Exclusion criteria

Patients are not eligible to participate when they have an ongoing malignancy, history of previous colonic surgery or serious concomitant inflammatory diseases and/or anti-inflammatory treatment(s) that may impair the interpretability of the biomarker analysis, per investigators* interpretation.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	17-12-2020
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO

Date:	15-12-2020
Application type:	First submission
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
CCMO	NL75341.018.20