Vedolizumab in PSC and concurrent IBD: Searching for the missing link between the gut and the liver and exploration of biomarkers for development of colorectal carcinoma.

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To test the hypothesis that vedolizumab has chemopreventive properties with regard to colorectal neoplasia in the high-risk group of patients with PSC/IBD.

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

Summary

ID

NL-OMON55753

Source
ToetsingOnline

Brief title
VIP study

Condition

- Gastrointestinal inflammatory conditions
- Hepatic and hepatobiliary disorders
- Gastrointestinal neoplasms malignant and unspecified

Synonym
Inflammatory bowel disease, Primair Scleroserende Cholangitis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Colorectal Carcinoma, Primary Sclerosing Cholangitis, Vedolizumab

Outcome measures

Primary outcome

Differences in expression of previously identified potential biomarkers with

regard to copy number changes, cancer-relevant gene mutations, methylation

status, as well as MIF expression in patients with PSC/IBD versus IBD,

stratified by vedolizumab treatment.

Secondary outcome

IIa) Evaluation of potential markers in peripheral blood samples in order to

evaluate clinical applicability of the potential markers.

IIb) Differences between PSC/IBD and IBD in the identified gene alterations.

Study description

Background summary

Primary sclerosing cholangitis (PSC) is a rare chronic inflammatory disease of the biliary tree of unknown cause. Therapy is still limited to treatment of complications, and ultimately leading to bile duct destruction and liver failure. PSC has a strong association with inflammatory bowel disease (IBD), especially ulcerative colitis (UC). The gut homing lymphocyte paradigm offers a plausible explanation linking the gut and liver in PSC, stating that gut-primed t-lymphocytes (expressing α4β7) can migrate into the liver because of aberrantly expressed adhesion molecules (like MAdCAM-1) and chemokines in the liver. Vedolizumab is a humanized monoclonal antibody, that specifically binds to the lymphocyte integrin α4β7, thereby impairing the migration of gut-homing lymphocytes into gastrointestinal mucosa and possibly into the liver.

The risk of developing colorectal carcinoma (CRC) is elevated in patients with PSC and concomitant IBD compared to patients with IBD alone, with an estimated cumulative risk of 13% after 30 years. This mandates annual colonoscopic surveillance from the date of diagnosis of PSC, which is a burden for the patients. A clinically useful biomarker assay for early detection of the dysplasia-carcinogenesis sequence could help in surveilling these patients. Previous research showed an increased expression of Macrophage Migration Inhibitory Factor (MIF) in right colonic mucosal tissue of PSC/IBD patients as opposed to IBD-patients. In gastrointestinal cancers, an increase of this inflammatory cytokine is seen. Blocking T-cell influx into the colonic tissue could possibly decrease MIF levels in the colonic mucosa, vedolizumab may play a role in this process.

Study objective

To test the hypothesis that vedolizumab has chemopreventive properties with regard to colorectal neoplasia in the high-risk group of patients with PSC/IBD.

Study design

Prospective observational study.

Study burden and risks

Patients will be recruited from the outpatient clinic and followed for 3 years. During surveillance colonoscopies (2 or 3 subsequent time points, depending on the planned colonoscopies), an additional 8 biopsies will be obtained in addition to routine serial biopsies. Prior to the first colonoscopy, blood will be drawn. Faeces will be collected prior to each colonoscopy.
Colon biopsies taken during colonoscopy include a minimal risk (risk of complications <1:1000). In case of a complication, such as a perforation or bleeding, the consequence is hospital admission, antibiotic therapy or blood transfusion.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Group 1:
- Diagnosis of Primary Sclerosing Cholangitis and concommitant diagnosis of Inflammatory bowel disease, Group 2:
- Diagnosis of inflammatory bowel disease
- 10 patients with routine vedolizumab treatment, 10 patients without vedolizumab treatment , Both groups:
- Age 18 years and older, either male or female
- Ability to give informed consent
- Groups will be stratified for the use of thiopurines
- Groups will be stratified for UC, CD and IBDU

Exclusion criteria

- Medical history of proctocolectomy
- Use of biologic therapy other than vedolizumab within 8 weeks of enrolment
- Inability to give informed consent

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-01-2018
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	22-02-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-03-2018
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

ID: 26884
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL59904.018.16
OMON	NL-OMON26884