A prospective Pilot Intervention Study: Near-infrared fluorescence molecular endoscopy for elucidating the mechanism of action and predicting response to vedolizumab in IBD using labelled vedoLizumab-8000CW.

Published: 04-06-2019
Last updated: 09-04-2024

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

Summary

ID

NL-OMON54932

Source
ToetsingOnline

Brief title
NIR-FME with vedolizumab-800CW in IBD.
VISION study

Condition

- Gastrointestinal inflammatory conditions

Synonym
Inflammatory bowel disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Europese Unie

Intervention

Keyword: Endoscopy, Fluorescence, Inflammatory Bowel Disease, Vedolizumab-800CW

Outcome measures

Primary outcome

• Quantification of fluorescent signal after a microdose of vedolizumab-800CW in inflamed and non-inflamed tissue in patients with IBD.

• Correlation between the fluorescent signal and the clinical response and remission to regular vedolizumab treatment in individual patients with IBD.

• Correlation with response and remission to vedolizumab treatment and the composition of immune cells in the mucosal microenvironment.

• Correlation with response and remission to vedolizumab treatment and the composition of immune cells in the peripheral blood compartment.

• The safety of vedolizumab-800CW through monitoring vital signs, the injection site and evaluating possible tracer-related (severe) adverse events (SAE/AEs).

Secondary outcome

• Difference in vivo and ex vivo fluorescent signal between inflamed and non-inflamed tissue

• Identification of vedolizumab target cells (innate vs. lymphocytes) in both inflamed and non-inflamed tissue.

• Gain insight in target engagement in patients treated with vedolizumab

therapy for at least 14 weeks.

• Investigate autofluorescence signals in normal and inflamed tissue by including patients without tracer administration.

Response to treatment:

- Clincal response to vedolizumab treatment using worldwide approved clinical scoring methods, (SCCAI for UC and HBI for CD). Clinical induction response is defined when patients reached halved the clinical score at week 14 compared to week 0 due to vedolizumab treatment.
- Biochemical response to vedolizumab treatment is defined when people reached normalization of C-reactive protein and leukocytes thanks to vedolizumab.
- Endoscopic response to vedolizumab treatment is defined when patients have a reduction of endoscopic disease activity using the worldwide approved scoring method: MAYO for UC and SES-CD score for CD.
- The correlation between responders versus non responders compared with fluorescence intensity to predict response to treatment.
- Elucidate the differences between vedolizumab distribution between CD and UC.

Study description

Background summary

Crohn*s Disease (CD) and Ulcerative Colitis (UC) are chronic idiopathic inflammatory bowel diseases (IBD). Symptoms consist of (bloody) diarrhea, abdominal and perianal pain. Current drugs are partly effective and have major limitations. Vedolizumab is a humanized monoclonal antibody against α4β7

integrin capable of blocking the migration of several immune cells across the endothelium expressing MAdCAM-1. Vedolizumab is less cost effective than Infliximab (anti-TNFα inhibitor) and therefore, this antibody is only accepted as a second line biological therapy after anti-TNF failure. Vedolizumab is promised to be gut specific although until today the specific binding capacity of vedolizumab is unknown. The University Medical Center Groningen (UMCG) developed a fluorescent tracer for labeling vedolizumab. This study aims to gain insight into vedolizumab distribution and concentrations. The current study has the ambition to identify the vedolizumab target cells in the inflamed gut inflammation using near-infrared fluorescence molecular endoscopy (NIR-FME). By gaining insight in local vedolizumab concentrations, distribution and discovering target cells, we aim to optimize vedolizumab dosing and predicting response in individual patients.

Study objective

The primary objective of this pilot intervention study is to gain insight into vedolizumab distribution and to identify vedolizumab target cells in the inflamed gut, by performing in- and ex-vivo imaging using a tracer consisting of fluorescently labeled vedolizumab. We further aim to elucidate the mechanism of action of vedolizumab and use our findings to predict response to treatment.

Study design

The current study is a non-randomized, non-blinded, prospective, single center phase I intervention study. Patients, with an established diagnosis of UC or CD with active inflammation, who are scheduled to start vedolizumab therapy, will be administered with vedolizumab-800CW before the initiation of the vedolizumab regimen. The tracer will be administered in our study at a microdose level (4.5mg/30 nmol of fluorescent antibody). Near-infrared (NIR) imaging will be performed during endoscopic intervention, by the use of a NIR fiber-bundle and spectroscopy probe, which will be inserted through the working channel of the standard therapeutic white light endoscope (WLE). Additionally, biopsies of non-inflamed gut mucosa, inflamed tissue and of surrounding fluorescent tissue (if present) will be taken. Standardized fluorescence readings will be validated against histopathology on biopsied specimen from normal mucosa, inflamed mucosa (based on WLE conclusions) and areas exhibiting increased fluorescence signal during FME. Ex-vivo CITE-seq will be performed to elucidate vedolizumab which cells can bind vedolizumab. An interim analysis of the primary endpoint results will be performed after 5 patients haven been included, before continuing the study. In case of insufficient fluorescent signal, the follow-up of the study will include a dose-optimization part, in which tracer dose can be increased, and/or a non-labeled blocking dose can be added. All groups in all arms within the dose-escalation study will contain the same amount of patients. During the interim analysis the safety will be evaluated, the dose escalation study will only start if the tracer has been

found safe.
After the study procedures, patients will be treated with vedolizumab following the standard clinical care.

Negative control arm:
Five patients will not receive vedolizumab-800CW prior to the FME procedure. These patients will be included to investigate the autofluorescent signals of in the gut.

Therapy arm
During the interim analysis, safety and fluorescence intensity will be evaluated. In case no adverse events are seen and the fluorescence intensity is considered to be optimal we will continue inclusion. After the interim analysis, 10 patients on vedolizumab therapy will be included in the study. Patients must be treated for at least 14 weeks before they can be included in this study-arm. Both, patients already included in the study prior to vedolizumab therapy and patients who were not included prior to vedolizumab therapy can be included.
According to clinical standard care an IBD patient treated with vedolizumab will be sheduled for a follow-up endoscopic procedure between week 10 to week 30 weeks of treatment. The exact date is dependent of (clinical) response to treatment, not the current study or the involved researchers, but the medical doctor together with the patient will discuss the date for a follow-up endoscopic procedure. If patients are included they receive 2-4 days prior to the FME procedure 15mg vedolizumab, which is considerded the optimal dose.

Intervention

Patients will be, 2 to 4 days prior to the endoscopic procedure, intravenously administrerd with the tracer vedolizumab-800CW. Where after fluorescence endocopy, MDSFR/SFF spectroscopy and confocale laser endomicroscopy (CLE) will be perfomed endoscopically. Furthermore we will collect biopsies for research purposes. Patients will be sedated during the endoscopic prodedure following standard clinical care procedures.

Study burden and risks

For the participating patients, there is no diagnostic or treatment benefit related to the study. Participation may possibly produce useful scientific data for the future. Risks related to the administration of vedolizumab-800CW are described in the IMPD (version 2.0 June 2020). The risks of the fluorescence endoscopy procedure are comparable to a clinical endoscopy, and therefore found to be minimal and negligible.The biopsies taken at fluorescence endoscopy procedure have a small risk of causing superficial bleeding. Most bleedings coagulate spontaneously. If not, which is very uncommon, the gastroenterologist will coagulate the small bleeding. For an extensive structured risk analysis,

see section 13 of the protocol. The procudure will be extended due to the study with 15 minutes. Patients included in the current study will be sedated for a longer period compared to the clinical standard procedure. If the patient will be completely sedated, a team of anesthesiology collegues will monitor all the vitals during the procedure.

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

• Established diagnosis of IBD, or Ulcerative Colitis (UC) or Crohn*s Disease (CD).
• Severely affected and therefore a candidate for vedolizumab treatment or already treated with vedolizumab.
• Age: 18 years or older.

• Written informed consent.

Exclusion criteria

• Patients younger than 18 years old
• Prior vedolizumab treatment
• Pregnancy or breast feeding.

* For therapy arm vedolizumab treatment is no exclusion criterium

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-02-2020
Enrollment:	60
Type:	Actual

Medical products/devices used

Generic name:	A clinical therapeutic endoscope;a fiber bundle to perform fluorescence endoscopy;a MDSFR/SFF spectr
Registration:	No
Product type:	Medicine
Brand name:	NVT
Generic name:	Vedolizumab-800CW

Ethics review

Approved WMO Date:	04-06-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-09-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-03-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-06-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-07-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2019-002228-33-NL
ClinicalTrials.gov	NCT04112212
CCMO	NL69572.042.19

Study results

Date completed:	21-03-2023
Actual enrolment:	38