# An open-label interventional phase 4 study to evaluate efficacy , safety and mucosal healing of early versus late use of vedolizumab in Crohn's disease: the LOVE-CD study (LOw countries VEdolizumab in CD study)

Published: 08-01-2015
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Primary ObjectiveThe primary objective of this prospective open label study is to assess the ability of vedolizumab to promote clinical, endoscopic and histological remission in patients with active Crohn's disease in an 'early' and a...

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|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Gastrointestinal inflammatory conditions |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON53012

**Source**
ToetsingOnline

**Brief title**
LOVE-CD

### Condition

- Gastrointestinal inflammatory conditions

**Synonym**
Crohn's disease, Inflammatory bowel disease

**Research involving**

Human

## Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum
**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** Crohn's disease, vedolizumab

## Outcome measures

### Primary outcome

The primary endpoint is the proportion of patients with clinical and endoscopic

remission at Week 26 and 52-54, defined as CDAI of 150 or lower and SES-CD < 4.

### Secondary outcome

Secondary endpoints for this study are:

Proportion of patients with absence of ulcers at Weeks 26 and 52-54

- Proportion of patients with endoscopic response (SES-CD reduction by >= 50 %)

at Weeks 26 and 52

- Proportion of patients with 25% and 75% reduction of SES-CD at Weeks 26 and 52

- Proportion of patients with clinical response (CDAI decrease of >= 70 points

from baseline) at all time points

- Proportion of patients with clinical remission (CDAI <=150) at all time other

points

- Proportion of patients with corticosteroid- free clinical remission (CDAI

<=150) at all other time points

- Proportion of patients with normalized serum CRP at all time points

- Proportion of patients with no granulocytes in the biopsies at Weeks 26 and

52.

- Proportion of patients with 25%, 50% and 75% reduction in the Geboes

histology score at Weeks 26 and 52.

- Proportion of patients with sustained clinical response (response at all time

points after week 10)

- Proportion of patients with sustained clinical remission (remission at all

time points after week 10)

- Proportion of patients with draining fistulas

- Proportion of patients that need to be hospitalized

- Quality of life measured by IBDQ and Euroquol

- Work productivity Index

- WHO Disability Index

- Serum concentrations of vedolizumab and antibodies to vedolizumab before

every infusion

# Study description

**Background summary**

Crohn's disease (CD) is a chronic inflammatory disease of the small bowel and colon. Symptoms commonly include bloody diarrhea, abdominal pain, weight loss, and fever. There is no known cause or cure for CD. The aim of current CD treatments is to induce and maintain remission, to reduce the need of corticosteroids and avoid resections and fistulas.
Treatment options include systemic and/or topical corticosteroids, purine analogues (6-mercaptopurine and azathioprine), anti-TNF antibodies and surgery.
In 2013, results from the GEMINI II, phase 3, randomized controlled trial demonstrated the efficacy of vedolizumab (VDZ) in inducing and maintaining remission in adult patients with active CD.
VDZ (MLN0002, LDP-2 or MLN02), inhibits the interaction between α4β7 integrin on memory T and B cells and mucosal addressin cell adhesion molecule-1

expressed on the vascular endothelium of the gut and has been shown to be effective in both inducing and maintaining clinical remission in UC. The ideal positioning of vedolizumab in the therapeutic armamentarium for CD remains unknown. With other (anti-TNF) biologics, outcomes have usually been better if the treatment was started earlier in the disease course and if the patients had not been exposed to prior antibody treatments. Therefore, it appears appropriate and desirable to test the potency of vedolizumab in an earlier phase of CD.
Indeed, also with vedolizumab patients previously exposed to biologics appear to have lower success rates with vedolizumab, so a position earlier in the disease course would most likely lead to better outcomes.
This is an investigator-initiated open label study of VDZ therapy in 2 distinct populations of CD patients with active disease: 1. patients who have been diagnosed < 2 years ago and who only been exposed to aminosalicylates, corticosteroids and thiopurines and 2. patients who have been diagnosed > 2 years and exposed to immunomodulators and/or anti-TNF agents in addition to steroids and aminosalicylates.

## Study objective

Primary Objective

The primary objective of this prospective open label study is to assess the ability of vedolizumab to promote clinical, endoscopic and histological remission in patients with active Crohn's disease in an 'early' and a 'late' disease population after 54 weeks of treatment.

Secondary Objectives

Measures of clinical disease activity (including clinical response and remission) over the 1 year study period will be described. The mucosal healing capacity of vedolizumab treatment will be observed by assessing the endoscopic and histopathologic response to treatment over the 1 year study period.

## Study design

Open label, observational and multicenter

## Intervention

Entyvio (vedolizumab ) treatment (300 mg intravenous). Patients with a SES-CD score of less that 50 % at the week 26 endoscopy will receive vedolizumab 4 weekly. An extra vedolizumab dose will be given at week 34, 42 and 50.

## Study burden and risks

The endoscopy procedure can cause abdominal discomfort and due to biopsies there is an extreme small risk of perforation (1 in 10.000) of the bowel.
Blood drawing can cause discomfort , bruising or local pain.
PML :
Progressive mulitfocal leucoencephalopathy (PML) is a rare infection of the brain caused by the John- Cunningham-virus (JC-virus). Subjects with severely impaired immune systems are more likely to develop this disease. This disease was diagnosed in a few patients who were treatment with a medication called natalizumab (Tysabri®). The overall risk of developing PML is estimated as less than 1 in 1,000. Up to now, no known cases of PML have been reported by patients who have been, or are currently treated with vedolizumab . However, development of PML symptoms in patients who are receiving vedolizumab have to be assessed. All subject will be assessed for symptoms of PML prior to infusion.

# Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)

## Inclusion criteria

- Moderately to severely active CD (Crohn disease activity index (CDAI) 220-450) with objective evidence of ulcerations visualized on endoscopy., -Anti-TNF discontinued for at least 4 weeks prior to baseline, -Age 18 to 80, -GROUP 1 (EARLY CD):, Diagnosis of CD < 24 months prior to enrollment , Demonstrated failure to respond to topical or systemic corticosteroids or intolerance to corticosteroids,
and additionally, but not mandatory, lack of efficacy or intolerance to thiopurines (azathioprine, 6-mercaptopurine or 6-thioguanine)(any duration). Patients using thiopurines must have been using the agent for > 3 months (last 4 weeks at stable dose)., GROUP 2 (LATE CD), Demonstrated failure to respond to at least 3 months of thiopurines or intolerance to thiopurines and: failure to respond to at least 1 anti-TNF or intolerance to anti-TNF or loss of response to at least 1 anti-TNF.

## Exclusion criteria

- Prior treatment with vedolizumab, alpha4beta7 anti-bodies, beta7 antibodies and anti MADCAM-1
- History of colonic dysplasia or colonic cancer
- Presence of stoma
- subjects with a pouch
- Received other biologics within the last 4 weeks of baseline
- subjects with ALT or AST 3x the upper limit of normal measured at screening
- Use of 5-ASA or corticosteroid enemas/suppositories within 2 weeks of enrollment
- Chronic hepatitis B or C infection
- Evidence of or treatment for C. difficile infection or other intestinal pathogen at screening within 4 weeks prior to enrollment
- Active or latent tuberculosis
- Early CD group: previous exposure to any anti-TNF

# Study design

## Design

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|---|---|
| Study phase: | 4 |
| Study type: | Interventional |
| Masking: | Open (masking not used) |

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|---|---|
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 27-08-2015 |
| Enrollment: | 130 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | Entyvio |
| Generic name: | vedolizumab |
| Registration: | Yes - NL intended use |

## Ethics review

Approved WMO

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|---|---|
| Date: | 08-01-2015 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |

Approved WMO

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|---|---|
| Date: | 29-06-2015 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |

Approved WMO

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|---|---|
| Date: | 17-07-2015 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

Approved WMO

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|---|---|
| Date: | 23-03-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

Approved WMO

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|---|---|
| Date: | 05-04-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 20-01-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 07-03-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 28-02-2018 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 30-05-2018 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 04-04-2019 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 08-04-2019 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 20-08-2019 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 29-08-2019 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO | |

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|---|---|
| Date: | 11-12-2019 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 31-01-2020 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 24-09-2021 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 08-10-2021 |
| 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 | EUCTR2014-005376-29-NL |
| ClinicalTrials.gov | NCT02646683 |
| CCMO | NL51800.018.14 |