A Randomized, Double-Blind, Double-Dummy, Multicenter, Active-Controlled Study to Evaluate the Efficacy and Safety of Vedolizumab IV Compared to Adalimumab SC in Subjects With Ulcerative Colitis

Published: 30-09-2015
Last updated: 19-04-2024

Primary:* To determine the effect of vedolizumab IV compared to adalimumab SC on clinical remission at Week 52.Secondary:* To evaluate the effect of vedolizumab IV compared to adalimumab SC on mucosal healing at Week 52.* To evaluate the effect of...

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

Summary

ID

NL-OMON43558

Source
ToetsingOnline

Brief title
Vedolizumab vs. Adalimumab in Ulcerative Colitis

Condition

- Gastrointestinal inflammatory conditions

Synonym
inflammatory bowel disease, ulcerative colitis

Research involving

Human

Sponsors and support

Primary sponsor: Takeda
Source(s) of monetary or material Support: Industry

Intervention

Keyword: Ulcerative Colitis, Vedolizumab IV

Outcome measures

Primary outcome

The primary endpoint for the study is proportion of subjects achieving clinical remission (defined as a complete Mayo score of *2 points and no individual subscore >1 point) at Week 52.

Secondary outcome

Secondary endpoints for this study are:

* Proportion of subjects achieving mucosal healing (defined as Mayo endoscopic subscore *1 point) at Week 52.

* Proportion of subjects using oral corticosteroids at Baseline who have discontinued corticosteroids and are in clinical remission at Week 52.

Study description

Background summary

Current treatments have been effective for many patients with UC but have numerous limitations for patients with moderately to severely active disease. These limitations indicate that there is a significant need for safer and more effective therapies. Vedolizumab (also called MLN0002) is a humanized immunoglobulin (Ig) G1 mAb developed as a treatment for UC and CD that acts as

a gut-selective immunomodulator. The aim of the current study is to evaluate the efficacy and safety of vedolizumab IV compared with adalimumab SC in the treatment of subjects with moderately to severely active UC.

Study objective

Primary:

* To determine the effect of vedolizumab IV compared to adalimumab SC on clinical remission at Week 52.

Secondary:

* To evaluate the effect of vedolizumab IV compared to adalimumab SC on mucosal healing at Week 52.
* To evaluate the effect of vedolizumab IV compared to adalimumab SC on corticosteroid-free remission at Week 52.

Study design

This is a phase 3b randomized, double-blind, double-dummy, multicenter, active-controlled study to evaluate the efficacy and safety of vedolizumab compared to adalimumab over a 52 week Treatment Period followed by 18-week Follow-up Period. The study will be conducted globally and will include 658 subjects with moderately to severely active ulcerative colitis (UC).

Intervention

On Day 1, subjects who meet the inclusion criteria and who meet none of the exclusion criteria will be randomly assigned in a 1:1 ratio to double-blind medication for 50 weeks.

Subjects in the vedolizumab treatment group will receive a 300 mg intravenous (IV) infusion on Day 1 and Weeks 2, 6, 14, 22, 30, 38, and 46, as well as placebo subcutaneous (SC) injection on Day 1, Week 2, and once every 2 weeks (Q2W) thereafter until Week 50.

Subjects in the adalimumab treatment group will receive a 160 mg SC injection on Day 1 (4 40 mg injections in 1 day or 2 40 mg injections per day for 2 consecutive days), 80 mg at Week 2 (2 40 mg injections in 1 day), then 40 mg Q2W thereafter until Week 50, as well as a placebo IV infusion at Day 1 and Weeks 2, 6, 14, 22, 30, 38, and 46.

Study burden and risks

Including screening and follow-up the study will consist of 29 visits (12 at the hospital, the remaining at home) over a period of 72 weeks. Additionally, subjects will be required to participate in a long-term follow-up (LTFU) safety survey by telephone 6 months after the last dose of study drug.
During the treatment period subjects will receive 8 infusions and 26 injections over a period of 50 weeks. Subjects will need to maintain a daily electronic diary throughout the study up until week 52 and complete an IBDQ questionnaire at 3 study visits. Procedures will among others include 3 flexible sigmoidoscopies (with biopsy), 2 ECGs and collection of blood (10x), stool (5x) and urine (2x) samples. As part of the study screening subjects will be tested for TB, HIV and Hepatitis B/C and be informed of any positive result.

The most common side effects of the study drug, reported in more than 10% of patients, include common cold, headache, joint pains and worsening of Crohn*s disease in patients with Crohn*s disease. To address the theoretical risk of the development of PML in subjects treated with vedolizumab, a Risk Minimization Action Plan for PML will be implemented.

Contacts

Public
Takeda

Aldwich 61
London WC2B 4AE
GB
Scientific
Takeda

Aldwich 61
London WC2B 4AE
GB

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* The subject has a diagnosis of UC established at least 3 months prior to enrollment, by clinical and endoscopic evidence and corroborated by a histopathology report.;* The subject has moderately to severely active UC as determined by a complete Mayo score of 6-12 with an endoscopic subscore *2 within 14 days prior to randomization.;* The subject has evidence of UC extending proximal to the rectum (*15 cm of involved colon).;* a. The subject has had previous treatment with tumor necrosis factor*alpha (TNF-*) antagonists without documented clinical response to treatment (eg, due to lack of response [primary nonresponders], loss of response, or intolerance [secondary nonresponder], or
b. Has previously used a TNF-alpha antagonist (except adalimumab), and discontinued its use due to reasons other than safety.;* The subject is naïve to TNF-alpha antagonist therapy but is failing current treatment (ie, corticosteroids, 5-aminosalicylate, or immunomodulators).

Exclusion criteria

* The subject has had extensive colonic resection, subtotal or total colectomy.;* The subject has any evidence of an active infection during Screening. ;* The subject has a positive progressive multifocal leukoencephalopathy (PML) subjective symptom checklist at Screening or before the administration of study drug at Day 1. ;* The subject has received any investigational or approved biologic or biosimilar agent (other than those listed below) within 60 days or 5 half lives prior to screening (whichever is longer).;* The subject has had prior exposure to vedolizumab, natalizumab, efalizumab, adalimumab, etrolizumab, AMG-181, anti-mucosal addressin cell adhesion molecule-1 (MAdCAM-1)-antibodies or rituximab.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-01-2016
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Entyvio
Generic name:	Vedolizumab IV
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Humira
Generic name:	Adalimumab SC
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	30-09-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-01-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-02-2016

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-07-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-07-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-07-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-08-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-09-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-09-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-06-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	27-09-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2015-000939-33-NL
ClinicalTrials.gov	NCT02497469
CCMO	NL54690.056.15