AN OPEN LABEL EXTENSION AND SAFETY MONITORING STUDY OF MODERATE TO SEVERE ULCERATIVE COLITIS PATIENTS PREVIOUSLY ENROLLED IN ETROLIZUMAB PHASE III STUDIES

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The objectives of this open-label extension safety monitoring (OLE-SM) study are as follows:Part 1 (Open-Label Extension; OLE)• To assess the long-term safety and efficacy of etrolizumab in patients eligible for Part 1 (OLE)Part 2 (Safety Monitoring...

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

Summary

ID

NL-OMON53027

Source
ToetsingOnline

Brief title
ETRO - OLE (GA28951)

Condition

- Gastrointestinal inflammatory conditions

Synonym
inflammatory bowel disease, Ulcerative colitis

Research involving
Human

Sponsors and support

Primary sponsor: Hoffmann-La Roche
Source(s) of monetary or material Support: pharmaceutical industry

Intervention

Keyword: etrolizumab, extension study, safety, ulcerative colitis

Outcome measures

Primary outcome

The efficacy outcome measure for this study is as follows:

• To describe the long-term efficacy of etrolizumab (105 mg SC every 4 weeks)

by pMCS for patients with UC in Part 1 (OLE)

• To evaluate remission by MCS at Week 108 in Part 1 (OLE)

• To evaluate endoscopic remission by MCS at Week 108 in Part 1 (OLE)

• Incidence of adverse events

Secondary outcome

The safety outcome measures for this study are as follows:

Part 1 (OLE)

• Incidence and severity of adverse events

• Incidence of serious adverse events

• Incidence and severity of infection-related adverse events

• Incidence of serious infection-related adverse events

• Incidence and severity of injection-site reactions

• Incidence of adverse events leading to etrolizumab discontinuation

• Incidence of laboratory abnormalities

• Incidence of malignancies

• Incidence of anti-therapeutic antibodies (ATAs) to etrolizumab

• Incidence and severity of hypersensitivity reaction events

Part 2 (SM)

• Incidence of suspected or confirmed PML events

Study description

Background summary

UC is characterized by mucosal ulceration, rectal bleeding, diarrhea, and abdominal pain and may be complicated by severe bloody diarrhea and toxic megacolon, requiring major and sometimes urgent surgery.

The overall incidence of UC ranges from 6.3 to 24.3 cases per 100,000 persons per year, and prevalence ranges from 4.9 to 505.0 cases per 100,000 persons, with the highest estimates in European and Northern American populations.

The goals of treatment are to induce and maintain remission, decrease corticosteroid use (as measured by steroid-free remission), induce mucosal healing, reduce hospitalization and surgery, improve quality of life (QOL), and avoid disability.

The current treatments are associated with significant adverse events, resulting in low rates of sustained remission, or are highly invasive. Targeted therapy with an improved safety profile and ability to sustain remission and prevent long-term complications would provide a valuable therapeutic option for these patients. Consequently, the potential benefits of etrolizumab in this population warrant further investigation.

This study investigates the long-term safety of patients with UC who were initially treated in Phase III UC studies and includes long-term monitoring for progressive multifocal leukoencephalopathy (PML).

More information can be found in the protocol.

Study objective

The objectives of this open-label extension safety monitoring (OLE-SM) study are as follows:

Part 1 (Open-Label Extension; OLE)
• To assess the long-term safety and efficacy of etrolizumab in patients eligible for Part 1 (OLE)

Part 2 (Safety Monitoring; SM)
•Progressive multifocal leukoencephalopathy (PML) safety monitoring

Safety Objectives
The other safety objectives for this study are as follows:
Part 1 (OLE)
• To evaluate the incidence and severity of infection-related adverse events
• To evaluate the incidence of malignancies
• To evaluate the incidence and severity of hypersensitivity reactions
• To evaluate the incidence and the clinical significance of anti-therapeutic antibodies (ATAs)

Study design

This OLE-SM study is composed of two parts:
• Part 1 is the OLE for eligible patients, during which active etrolizumab, 105 mg subcutaneous (SC), will be administered every 4 weeks followed by a 12-week safety follow-up.
• Part 2 is the 92-week PML safety monitoring for all patients, during which no etrolizumab will be administered.

Patients who are enrolled in Part 1 (OLE) should participate in Part 1 (OLE) and Part 2 (SM). There may be patients who are ineligible for or choose not to participate in Part 1 (OLE) who will directly enroll in Part 2 (SM) only.

Intervention

Etrolizumab prefilled syringe (PFS): containing SC formulation, 105 mg given as 0.7 mL of a 150-mg/mL solution will be administered by SC injection every 4 weeks.

Study burden and risks

In this study etrolizumab is being assessed for induction and long-term maintenance therapy. Therefore, this study is being conducted to treat patients with etrolizumab in an open-label fashion in order to assess the long-term safety and efficacy.
The benifit of this design is that no patient will be exposed to risk of not receiving any treatment.

There may be side effects, risks, discomforts associated with etrolizumab, the study procedures or reproductive risks for patients participating in this trial. These can vary from person to person and can go from mild to very serious. Everyone taking part in the study will be watched carefully for any side effect.

Patients are asked to visit the clinic as indicated by the protocol and do the following procedures (amongst others):

- Pregnancy tests (if applicable)
- Physical exams
- PML neuro exams
- ECGs
- HBV test
- Completion of e-diary
- Blooddraws
- Examination of gastrointestinal tract
- Subcutaneous IP injections

For more details regarding the risks, side effects and study procedures please refer to the informed consent form.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Part 1 (Open-label Extension; OLE), - Patients previously enrolled in Phase III controlled studies who meet the eligibility criteria for open-label etrolizumab for those studies as described in the protocol, Part 2 (Safety Monitoring; SM),
- Patients who participated in one of the etrolizumab Phase III studies and are not eligible or chose not to enter Part 1 (OLE)
- Patients who transfer from Part 1 (OLE)
- Completion of the 12-week safety follow-up prior to entering., A complete list of inclusion criteria can be found in the protocol

Exclusion criteria

Part 1 (Open-label Extension; OLE), - Any new, significant, uncontrolled condition
- Receipt of the following since commencement of the Phase II OLE or Phase III controlled studies: Use of anti-adhesion molecules, Part 2 (Safety Monitoring; SM), - No exclusion criteria, A complete list of exclusion criteria can be found in the protocol

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-06-2015
Enrollment:	33
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	n/a
Generic name:	etrolizumab

Ethics review

Approved WMO Date:	04-08-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-01-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-05-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-11-2016
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-05-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-05-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-02-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-02-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-05-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-07-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-08-2018
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-09-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-01-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-05-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-04-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-07-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-09-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-11-2022
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	EUCTR2013-004435-72-NL
ClinicalTrials.gov	NCT02118584
CCMO	NL48053.018.14