AN OPEN-LABEL EXTENSION AND SAFETY MONITORING STUDY OF PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN*S DISEASE PREVIOUSLY ENROLLED IN THE ETROLIZUMAB PHASE III PROTOCOL GA29144

Published: 16-04-2015
Last updated: 15-04-2024

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…

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

Summary

ID

NL-OMON47567

Source
ToetsingOnline

Brief title
ETRO-GA29145

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn's disease, inflammatory bowel disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Crohn□s disease, Etrolizumab, inflammatory bowel disease

Outcome measures

Primary outcome

The efficacy outcome measures for this study are as follows:

• CDAI remission assessed at 12-week intervals during Part 1 (OLE)

• PRO2 remission assessed at 12-week intervals during Part 1 (OLE)

The safety outcome measures for Part 1 of this study are as follows:

• Incidence and severity of adverse events

• Incidence of serious adverse events

• Incidence, rate per subject-year, 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 and rate per subject-year of malignancies

• Incidence of ATAs to etrolizumab

• Incidence and severity of hypersensitivity reactions

The safety outcome measure for Part 2 of this study is as follows:

• Incidence of suspected or confirmed PML events

Secondary outcome

NA

Study description

Background summary

So far, there is no cure for CD. The treatment goals for CD are to induce and maintain symptom improvement, induce mucosal healing, avoid surgery, and improve quality of life. Etrolizumab, a subcutaneously administered mAb, is a novel anti-integrin that, like vedolizumab, targets the α4β7 receptors that regulates trafficking of T-cell subsets in the intestinal mucosa, but unlike vedolizumab, etrolizumab also targets the αEβ7 receptors that regulate retention of T-cell subsets in the intestinal mucosa. Thus, etrolizumab offers the potential of an additive therapeutic effect in CD via a dual mechanism of action (MOA) without generalized immunosuppression.

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 in patients who have stopped study treatment
Safety Objectives
The other safety objectives for this study are as follows:
Part 1 (OLE)
• To evaluate the incidence, rate per subject-year, and severity of infection-related adverse events
• To evaluate the incidence and rate per subject-year 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 etrolizumab, 105 mg subcutaneous (SC), will be administered every 4 weeks (Q4W) followed by a 12-week safety follow-up post-treatment.
• Part 2 is the 92-week PML SM for all patients, during which no etrolizumab will be administered.
Patients who are enrolled in Part 1 (OLE) should participate in Part 2 (SM).
There may be patients from Study GA29144 who are ineligible for or choose not to participate in Part 1 (OLE) who will be asked to directly enroll in Part 2 (SM).

Intervention

Every 4 weeks an SC-injections with etrolizumab

Study burden and risks

The current therapeutic options available for CD include corticosteroids, immunosuppressants, and biological agents. These treatments reduce symptoms and improve quality of life; however, patients often stop responding to treatments and the goals of maintaining clinical remission and healing mucosal inflammation are not achieved. Moreover, these therapies are associated with adverse effects including diabetes (reported with corticosteroid use; Peyrin-Boulet et al. 2010), systemic toxicities such as leucopenia and thrombocytopenia (reported with immunosuppressant use; Prefontaine et al. 2009), and an increased risk for lymphoma and serious and opportunistic infections (reported with immunosuppressant and anti-TNF use when given as monotherapy or in combination; Siegal and Melmed 2009).
The anti-integrins are another class of biologics approved for the treatment of CD. The reported efficacy of the recently licensed anti-integrin vedolizumab, an intravenously administered anti-α4β7 mAb, in CD demonstrates a role for α4β7 in the pathobiology of this disease (Sandborn et al. 2013). In addition to demonstrating efficacy compared with placebo, vedolizumab had an acceptable safety profile in two Phase III trials for CD (Sandborn et al. 2013; Sands et al. 2014). Although long-term safety data for vedolizumab is still being collected and is not yet published, to date no cases of PML have been reported.

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

Patients must meet the following criteria for study entry:
Part 1 (OLE)
• Patients who were previously enrolled in Study GA29144 and experienced any of the following:
Disease worsening in the Induction Phase of Study GA29144, defined as both CDAI and PRO2 scores at Week 10 or later in the Induction Phase being greater than the patient*s baseline (Week 0) score
Did not achieve CDAI-70 response at Week 14 in Study GA29144
A clinical relapse in Study GA29144, defined as >= 100-point increase in CDAI score from the Week 14 CDAI score on two consecutive visits (which may include unscheduled visits) and a CDAI score >= 220 points
Completed the Maintenance Phase including the Week 74 clinic visit in Study GA29144
• Ability and willingness to provide written informed consent and comply with the requirements of the OLE-SM protocol.
• For women who are not postmenopausal (at least 12 months of non-therapy-induced amenorrhea) or surgically sterile (absence of ovaries and/or uterus): agreement to remain abstinent or to use a highly effective method of contraception during the treatment period and for at least 24 weeks after the last dose of study drug.

Abstinence is acceptable only if it is in line with the preferred and usual lifestyle of the patient. Periodic abstinence (e.g., calendar, ovulation, symptothermal, or postovulation methods) and withdrawal are not acceptable methods of contraception.
• For men: agreement to remain abstinent or to use a condom during the treatment period and for at least 24 weeks after the last dose of study drug
Abstinence is acceptable only if it is in line with the preferred and usual lifestyle of the patient. Periodic abstinence (e.g., calendar, ovulation, symptothermal, or postovulation methods) and withdrawal are not acceptable methods of contraception.
PART 2 (SM)
• Patients who participated in Study GA29144 and are not eligible or chose not to enroll in Part 1 (OLE)
• Patients who participated in Part 1 (OLE) of this protocol
• Ability and willingness to provide written informed consent and comply with the requirements of Part 2 (SM) of the OLE-SM protocol
All patients must have completed the 12-week safety follow-up prior to entering Part 2 (SM).

Exclusion criteria

Patients who meet any of the following criteria will be excluded from study entry:
Part 1 (OLE)
• Patients who leave Study GA29144 before Week 10
• Patients who do not perform the Week 14 visit in Study GA29144 , except for those escaping between Weeks 10 and 14 for disease worsening
• Patients who discontinue study drug in the Induction Phase of Study GA29144, except for those escaping between Weeks 10 and 14 due to disease worsening
• Patients who received rescue therapy in the absence of disease worsening during the Induction Phase of Study GA29144
• Patients who received rescue therapy in the absence of clinical relapse during the Maintenance Phase of Study GA29144 will not be eligible for Part 1 (OLE) until completing the Week 74 visit in Study GA29144
• Patients who received medications that are prohibited in conjunction with etrolizumab (see protocol)
• Patients participating at U.S investigational sites who require continued use of immunosuppressant therapy beyond a total of 14 weeks of co-administration with study drug in Study GA29144 are ineligible for Part 1 (OLE).
• Inability to comply with the study protocol, in the opinion of the investigator
• Pregnancy or lactation
• Patients who developed an anaphylactic/anaphylactoid or severe allergic reaction to study medication during Study GA29144
• Patients who have an untreated or unresolved serious infection event

• Patients who experienced a de novo or reactivated serious viral infection such as hepatitis B virus (HBV), hepatitis C virus (HCV), or HIV during Study GA29144
• Patients who developed life-threatening infections during Study GA29144
• Patients who developed a malignancy (with the exception of non-serious local and resectable basal or squamous cell carcinoma of the skin) or who develop adenocarcinoma in situ (AIS), high-grade squamous intraepithelial lesions (HSIL), or cervical intraepithelial neoplasia (CIN) of Grade > 1 on cervical Pap smear or who develop colonic dysplasia during Study GA29144
• Receipt of the following since commencement of Study GA29144:
Any investigational treatment, including investigational vaccines
Use of T or B cell depleting agents (e.g., rituximab, alemtuzumab or visilizumab)
Use of cyclosporine, tacrolimus, sirolimus, or mycophenolate mofetil (MMF)
Use of natalizumab, vedolizumab, or efalizumab
Use of TNF antagonists
Immunization with a live/attenuated vaccine
• In the opinion of the investigator, any new (since enrolling in Study GA29144), significant, uncontrolled comorbidity, such as neurological, cardiac (e.g., moderate to severe heart failure New York Heart Association [NYHA] Class III/IV), pulmonary, renal, hepatic, endocrine, or gastrointestinal (GI) disorders (excluding CD)
• Any patient who developed PML in Study GA29144
• Any patient with neurological symptoms where suspected PML has not been ruled out
Part 2 (SM)
• No exclusion criteria

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):	08-07-2016
Enrollment:	23
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	NA
Generic name:	Etrolizumab

Ethics review

Approved WMO Date:	16-04-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-09-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-12-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-06-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-07-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	22-05-2017
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:	10-01-2018
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:	01-05-2018
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:	27-08-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	10-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-12-2020
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:	26-03-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-12-2021
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:	05-05-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-09-2022
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	EUCTR2014-003855-76-NL
CCMO	NL52292.018.15