A Multicenter Open-label Extension (OLE) Study to Assess the Long-term Safety and Efficacy of Bempedoic Acid (ETC-1002) 180 mg

Published: 07-03-2017
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Primary:* To characterize the safety and tolerability of long-term administration of bempedoic acid (ETC-1002) 180 mgSecondary:* To characterize the efficacy of long-term administration of bempedoic acid 180 mg/day as assessed by changes in low-…

Ethical review	Approved WMO
Status	Completed
Health condition type	Cardiac disorders, signs and symptoms NEC
Study type	Interventional

Summary

ID

NL-OMON47830

Source
ToetsingOnline

Brief title
Esperion 3481/0013 (1002-050)

Condition

- Cardiac disorders, signs and symptoms NEC
- Lipid metabolism disorders

Synonym
cardiovascular disease hyperlipidemia

Research involving
Human

Sponsors and support

Primary sponsor: Esperion Therapeutics, Inc.
Source(s) of monetary or material Support: Esperion Therapeutics Inc

Intervention

Keyword: Bempedoic Acid, Hyperlipidemia, Open-label extension study (OLE), Phase 3

Outcome measures

Primary outcome

Patient incidence of adverse events (AEs)

Secondary outcome

* Percent change from baseline in LDL-C at Weeks 52 and 78

* Change from baseline in LDL-C at Weeks 52 and 78

* Percent change from baseline in non-HDL-C at Weeks 52 and 78

* Percent change from baseline in TC at Weeks 52 and 78

* Percent change from baseline in ApoB at Weeks 52 and 78

* Percent change from baseline in hs-CRP at Weeks 52 and 78

* Percent change from baseline in TG at Weeks 52 and 78

* Percent change from baseline in HDL-C at Weeks 52 and 78

Study description

Background summary

Bempedoic acid is a first-in-class small molecule inhibitor of ACL, an enzyme upstream of HMG-CoA in the cholesterol biosynthesis pathway. Bempedoic acid is a prodrug that requires activation in liver to ETC-1002-co-enzyme A (ETC-1002-CoA), which mediates competitive inhibition of ACL. Inhibition of ACL by ETC-1002-CoA decreases cholesterol synthesis in liver leading to increased LDLR expression and LDL particle clearance from the blood. Therefore, inhibition of ACL by ETC-1002-CoA reduces LDL-C via the same pathway as HMG-CoA

reductase inhibition by statins.

Bempedoic acid has been evaluated in 21 completed clinical studies, with over 1000 subjects/patients receiving bempedoic acid doses from 2.5 mg/day up to 240 mg/day (multiple doses). All multiple-dose studies have demonstrated consistent, clinically meaningful LDL-C lowering with bempedoic acid treatment and have shown a positive safety profile.

This is a multicenter open-label extension (OLE) study designed to assess the long-term safety and efficacy of bempedoic acid 180 mg. All patients will receive open-label bempedoic acid 180 mg for up to 1.5 years after rolling over from Study 1002-040 (parent study) followed by a follow-up period off study drug for 4 weeks. The total duration in the study will be 19 months.

Bempedoic acid in this study is currently being evaluated as an add-on to lipid-modifying therapy in high-risk CV patients (ie, those with HeFH and/or ASCVD) who have not achieved their LDL-C goal despite maximally tolerated lipid-modifying therapy.

The primary clinical hypothesis is that long-term exposure of bempedoic acid (ETC-1002) 180 mg will be safe and well tolerated.

Study objective

Primary:
* To characterize the safety and tolerability of long-term administration of bempedoic acid (ETC-1002) 180 mg

Secondary:
* To characterize the efficacy of long-term administration of bempedoic acid 180 mg/day as assessed by changes in low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), non-high-density lipoprotein cholesterol (non-HDL-C), apolipoprotein B (ApoB), total cholesterol (TC), triglycerides (TG), and high-sensitivity C-reactive protein (hs-CRP) in patients with hyperlipidemia

Study design

This is a multicenter open-label extension study designed to assess the long-term safety and efficacy of bempedoic acid (ETC-1002) 180 mg. All patients will receive open-label bempedoic acid 180 mg for up to 1.5 years after rolling over from the parent study (Study 1002-040) followed by a follow-up period off study drug for 4 weeks. Investigators, site staff, patients, and the study team will be masked to study lipid levels until the Week 12 study visit, after which time lipid values will be made available to sites. While this is an open-label study where all patients will receive active treatment with bempedoic acid,

blinding of the treatment that patients received during the parent study must be maintained for all patients unless, in the opinion of the Investigator, the safety of the patient may be at risk.

Patients will have visits every 3 months. Patients will be required to visit the site at baseline (end of study [EOS] parent), Week 12, Week 52, Week 78 and Week 82. Phone visits will occur at Weeks 24, 36, and 64.

Patients who withdraw from investigational medicinal product (IMP) treatment will be asked to continue to be followed for safety using the protocol-specified visit schedule. For details of study assessments, see the Schedule of Events in Appendix 1 of the protocol.

Intervention

All patients will receive open-label bempedoic acid 180 mg for up to 1.5 years after rolling over from parent study (Study 1002-040). Bempedoic acid (180 mg) will be ingested once daily with or without food. On clinic days patients will come to the clinic in the fasted state and study drug will be administered after laboratories are obtained.

Study burden and risks

To date, the nonclinical and clinical data indicate that bempedoic acid has a favorable risk-benefit profile. The ability of bempedoic acid to achieve clinically meaningful LDL-C-lowering responses while demonstrating a favorable tolerability profile in a variety of patient populations supports continued development of bempedoic acid, an oral ACL inhibitor, in Phase 3 studies.

Please refer to the most recent IB for additional information regarding previous human experience.

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

Each patient must meet the following criteria to be enrolled in this study:
Successfully completed the parent study (1002-040) and meet both of the following criteria:
* The patient was compliant with the parent study requirements including study visits, procedures, and investigational medicinal product (IMP) in the opinion of the principal investigator.
* The patient was able to tolerate IMP through the end of the parent study.

Exclusion criteria

1. Female patient is not willing to use at least 1 acceptable method of birth control during treatment and for an additional 30 days after the end of treatment unless patient is sterilized or postmenopausal;
a. Menopause is defined as greater than 55 years and *1 year without menses, less than 55 years and *1 year without menses with follicle-stimulating hormone (FSH) *40.0 IU/L, or surgically sterile (including hysterectomy and/or bilateral oophorectomy);
b. Acceptable methods of birth control include: oral birth control medications; placement of an intrauterine device (IUD) with or without hormones; barrier methods including condom or occlusive cap with spermicidal foam or spermicidal jelly; vasectomized male partner who is the sole partner for this patient; or true abstinence where it is the preferred and usual lifestyle of the patient (not including periodic abstinence such as calendar, ovulation, symptothermal, postovulation methods, or withdrawal).
2. Patient is pregnant or breastfeeding, or might become pregnant during treatment and/ or within 30 days after the end of treatment

3. Unreliability as a study participant based on the investigator*s (or designee*s) knowledge of the patient (eg, inability or unwillingness to adhere to the protocol) 4. Experienced a treatment-related SAE that led to study drug discontinuation in the parent study
5. Disorder that would interfere with understanding and giving informed consent or compliance with protocol requirements
6. Have any medical condition that in the opinion of the investigator may affect patient safety or ability to complete scheduled assessments
7. Patient*s medical condition requires lipid measurement and/or adjustment of background lipid-regulating therapy during the first 12 weeks of study participation
8. Known sensitivity to any of the products to be administered during dosing
9. Currently enrolled in another investigational device or drug study (excluding ETC-1002-040), or less than 30 days since ending another investigational device or drug study(s),or receiving or planning to receive other investigational agent(s) during this study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	14-08-2017
Enrollment:	120
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	NA
Generic name:	Bempedoic acid

Ethics review

Approved WMO Date:	07-03-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-07-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-11-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-02-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-04-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-02-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-03-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	05-04-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-04-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2016-004115-12-NL
CCMO	NL60616.100.17

Study results

Date completed:	19-09-2019
Results posted:	28-10-2020
Actual enrolment:	108

First publication
21-08-2020