An Open-Label Study to Evaluate the Pharmacokinetics, Pharmacodynamics, and Safety of Bempedoic Acid in Pediatric Patients (6 to 17 Years of Age) with Heterozygous Familial Hypercholesterolemia

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This study has been transitioned to CTIS with ID 2024-515864-30-00 check the CTIS register for the current data. Primary Objectives:• To assess the pharmacokinetics (PK) of bempedoic acid (ETC-1002 and ESP15228) in pediatric patients (6 to 17 years...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Metabolic and nutritional disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON53717

Source
ToetsingOnline

Brief title
Esperion 1002-041

Condition

- Metabolic and nutritional disorders congenital

Synonym
Familial Hypercholesterolemia, Heterozygous Familial Hypercholesterolemia

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Bempedoic Acid, Familial Hypercholesterolemia, HeFH, Heterozygous Familial Hypercholesterolemia

Outcome measures

Primary outcome

• Observed trough plasma concentration of ETC-1002 following 8 weeks of

steady-state dosing of bempedoic acid

• Model-based PK parameters including steady-state estimates of:

* area under the plasma concentration-time curve (AUCss),

* average plasma concentration (Cavg,ss) and

* maximum plasma concentration (Cmax,ss)

Secondary outcome

Secondary Endpoints

• Observed trough plasma concentration of ESP15228 (active metabolite)

following 8 weeks of steady-state dosing of bempedoic acid

• Plasma concentration at 4 hours (C4hr) of ETC-1002 and ESP15228 following

first dose

• ETC-1002 dose and exposure/LDL-C-lowering response relationship.

• Percent and absolute change from baseline to Weeks 8 and 16 in LDL-C, TC,

non-HDL-C, and hsCRP.

• Evaluation of acceptability (taste and ease of swallowing) of the

age-appropriate formulations.

Safety Endpoints

• Adverse events;

• Clinical safety laboratories (hematology, clinical chemistry, and urinalysis);

• Vital signs;

• Electrocardiogram (ECG) readings;

• Physical examinations (PEs)

Study description

Background summary

HeFH is a disorder resulting in elevated bad cholesterol levels from birth onward. Exposure to elevated bad cholesterol at a young age is a risk factor for atherosclerotic cardiovascular disease (ASCVD). Despite the use of available lipid-lowering therapies (such as statin therapy), some children with HeFH fail to achieve their lipid goals. These children may benefit from additional non-statin lipid-lowering therapies. The availability of new lipid-modifying treatments could be beneficial for children with elevated bad cholesterol due to FH who are not meeting their bad cholesterol goals with currently available therapies.

Bempedoic acid is a medicine that lowers levels of bad cholesterol in the blood when used along with diet, alone or with other lipid-lowering drugs for the treatment of adults with HeFH. It is currently not being used as therapy in children and adolescents with HeFH. This open-label, dose-escalation study will be to evaluate the blood levels of bempedoic acid in pediatric patients with HeFH on stable statin therapy with or without ezetimibe.

Study objective

This study has been transitioned to CTIS with ID 2024-515864-30-00 check the CTIS register for the current data.

Primary Objectives:
• To assess the pharmacokinetics (PK) of bempedoic acid (ETC-1002 and ESP15228)

in pediatric patients (6 to 17 years of age) with heterozygous familial hypercholesterolemia (HeFH) treated for 8 weeks.

Secondary Objectives:
• To assess bempedoic acid exposure/low-density lipoprotein cholesterol (LDL-C)-lowering response relationship.
• To assess the percent and absolute change from baseline to Weeks 8 and 16 in LDL-C, total cholesterol (TC), non-high-density lipoprotein cholesterol (non-HDL-C), and high-sensitivity C-reactive protein (hsCRP).
• To monitor the acceptability (taste and ease of swallowing) of the age-appropriate formulations.
• To assess the safety and tolerability of bempedoic acid in pediatric patients with HeFH treated.

Study design

This is a Phase 2, open-label, uncontrolled, multicenter study of bempedoic acid administered for 8 and 16 weeks in pediatric patients (6 to 17 years of age) with HeFH and LDL-C >= 130 mg/dL (3.4 mmol/L) and who are on an optimal dose of statin.

Study burden and risks

Subjects will visit the study center 6 or 9 times and receive 1 or 2 phone calls - depending on the group they are allocated to - over the course of 4 or 6 months. The most important tests include blood draw, urine collection, ECG and evaluation of sexual maturity. Subjects are asked to adhere to the provided diet and exercise counselling, fill in a daily diary and questionnaires during the visits.

Common side effects include anemia, gout and pain in shoulders, arms, or legs. There is a rare but serious risk for an allergic reaction.

Nonclinical and clinical data indicate that bempedoic acid has a favorable risk-benefit profile in indicated patients, as it may achieve LDL-C lowering responses.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

1. The patient*s parent(s)/guardian(s) must be willing to provide written informed consent and the patient must provide informed assent before any study-specific procedures are performed;
2. The patient must be aged 6-17 years old;
3. The patient must weigh at least 16 kg;
4. The patient must have a diagnosis of HeFH per MEDPED criteria by meeting at least one of the following clinical criteria*
a. Documented diagnosis of HeFH determined by positive genetic testing; or
b. Documented LDL-C or TC meeting one or more of the following criteria:
i. LDL-C >200 mg/dL (5.2 mmol/L) or total cholesterol (TC) >270 mg/dL (7.0 mmol/L), with no first- second- or third-degree relative with documented FH diagnosis (general population); or
ii. LDL-C >155 mg/dL (4.0 mmol/L) or TC >220 mg/dL (5.7 mmol/L), and also having a first-degree relative with documented familial hypercholesterolemia (FH) diagnosis; or
iii. LDL-C >165 mg/dL (4.3 mmol/L) or TC >230 mg/dL (5.9 mmol/L), and also having a second-degree relative with documented FH diagnosis; or
iv. LDL-C >170 mg/dL (4.4 mmol/L) or TC >240 mg/dL (6.2 mmol/L), and also having a third-degree relative with documented FH diagnosis

5. Current treatment with approved stable LMTs, including optimal dose of statin +/- other LMT(s), at stable dose for at least 4 weeks prior to screening Visit S1 (6 weeks for fibrates; however, gemfibrozil is not allowed in patients taking a statin as per co-administration instructions defined in the statin label) and must remain on that stable dose throughout the duration of the trial.
6. The patient must have a fasting LDL-C level >=130 mg/dL (3.4 mmol/L);
7. The patient may be male or female. Females must not be pregnant (or planning to become pregnant within 30 days after the last dose of investigational medicinal product [IMP]) breastfeeding and must be sexually inactive or willing to use 1 acceptable method of birth control. The minimal requirement for use of acceptable contraception is from the time the informed consent form (ICF) is signed, during the study period, and for at least 30 days after the last dose of IMP.

Exclusion criteria

1. The patient has a diagnosis of HoFH or compound HeFH;
2. The patient has a fasting triglyceride (TG) level >=400 mg/dL (4.5 mmol/L);
3. The patient has uncontrolled hypothyroidism, including a value for thyroid-stimulating hormone (TSH) < lower limit of normal (LLN) or >1.5 × the upper limit of normal (ULN);
4. The patient has liver disease or dysfunction, including:
a. positive serology for hepatitis B surface antigen (HBsAg) and/or hepatitis C virus antibodies (HCV-AB), or
b. serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) value >=2 × ULN and/or serum total bilirubin (TB) value >=2 × ULN. If the serum TB value is >=1.2 × ULN, a reflex indirect (unconjugated) bilirubin will be obtained and, if consistent with Gilbert*s disease or if the patient has a history of Gilbert*s disease, the patient may be enrolled in the study.
5. The patient has renal dysfunction or glomerulonephritis, including an estimated glomerular filtration rate (eGFR) <75 mL/min/1.73 m2 (as determined by the central laboratory using the Revised [*Bedside*] Schwartz formula);
6. The patient has Stage 2 hypertension (based on gender, age and height;
7. The patient has a gastrointestinal condition that may affect drug absorption;
8. The patient has a history of hematologic or coagulation disorders, anemia, or a hemoglobin (Hgb) level <11.5 g/dL;
9. The patient has type 1 or type 2 diabetes, or newly diagnosed impaired glucose tolerance (within 3 months of Screening);
10. The patient had an active malignancy, including those requiring surgery, chemotherapy, and/or radiation, in the past 5 years. Nonmetastatic basal or squamous cell carcinoma of
the skin and cervical carcinoma in situ are allowed;
11. The patient has an unexplained (ie, not associated with recent trauma or

physically strenuous activity) serum creatine kinase (CK) value >3 × ULN at any time before randomization. Patients with an explained elevation in serum CK must have single repeat serum CK value <=3 × ULN before enrollment;
12. The patient has a history of drug or alcohol abuse within the last 2 years or is unwilling to refrain from alcohol consumption for the duration of the study, or uses any illicit drugs, or has a history of amphetamine or derivatives abuse or cocaine abuse. Patients who are using amphetamine derivatives prescribed by and who are under the care of a health care practitioner can be enrolled after evaluation by the Investigator;
13. The patient has donated blood, undergone multiple blood draws in a clinical study, experienced major trauma, received a blood transfusion, or undergone surgery, with or without blood loss, within 30 days before enrollment;
14. The patient has used any experimental or investigational drugs within 30 days before screening and throughout the trial;
15. The patient has previously participated in a clinical study of bempedoic acid;
16. The patient is taking any of the following medications or therapies, except as indicated below:
a. Mipomersen or lomitapide (current or within 6 months of Screening).
b. PCKS9 inhibitors including evolocumab or alirocumab (current or within 3 months of Screening).
c. Lipid apheresis (current or within 8 weeks of Screening or intends to have lipid apheresis treatments throughout the trial).
d. Systemic corticosteroids (current or within 4 weeks prior to enrollment; topical and inhaled corticosteroids are allowed).
e. Red yeast rice extract (also known as monascus purpureus extract or Cholestin) containing products (current or within 4 weeks of Screening);
f. Lipid altering nutritional supplements including berberine, psyllium (Metamucil®), green tea extract, sitostanol (found in oral nutritional supplements and some margarines, such as Benecol), beta-sitosterol (found in oral nutritional supplements and some margarines, such as Promise Activ), pantothine and policosanol (current or within 4 weeks of Screening);
g. Bile acid sequestrants, fibrates, omega 3 fatty acids, or niacin, unless the dose has been stable for >=6 weeks and will remain stable throughout the trial.
h. Simvastatin >20 mg or pravastatin >40 mg (current or within 4 weeks of Screening).
17. The patient has a history or evidence of any other clinically significant condition, or planned or expected procedure that in the opinion of the Investigator, may compromise the patient*s safety or ability to complete the study;
18. The patient has a situational (ie, geographical) finding that, in the Investigator*s opinion, may compromise the patient*s safety or ability to complete the study;
19. The patient is an employee or contractor of the facility that is conducting the study or is a family member of the Investigator, sub-Investigator, or any Sponsor personnel.

Study design

Design

Study phase:	2
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-03-2023
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	bempedoic acid
Generic name:	bempedoic acid
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	26-09-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-01-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-03-2023

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-04-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-11-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-11-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-02-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-04-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-06-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-06-2024
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
EU-CTR	CTIS2024-515864-30-00
EudraCT	EUCTR2018-004084-31-NL
CCMO	NL81847.018.22