A 12-week, open-label, dose-escalating, phase 2 study to evaluate the effects of MBX-8025 in patients with Homozygous Familial Hypercholesterolemia (HoFH) (study CB8025-21427)

Published: 05-03-2015
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Primary:To evaluate the effect of MBX-8025 on LDL-C.Secondary:To evaluate the effects of MBX-8025 on other lipid parameters. To evaluate the safety and tolerability of MBX-8025. To evaluate steady-state trough plasma levels of MBX-8025 and its...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metabolic and nutritional disorders congenital
Study type	Interventional

Summary

ID

NL-OMON42421

Source
ToetsingOnline

Brief title
CB8025-21427 (CymaBay)

Condition

- Metabolic and nutritional disorders congenital
- Lipid metabolism disorders

Synonym
Homozygous familial hypercholesterolemia; elevated cholesterol

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Familial, Homozygous, Hypercholesterolemia, MBX-8025

Outcome measures

Primary outcome

LDL-C.

Secondary outcome

Total cholesterol, HDL-C, VLDL-C, non-HDL-cholesterol, apolipoprotein B,

apolipoproteïi A-l, lipoprotein (a), triglycerides, apolipoprotein C-lll,

RLP-cholesterol. Adverse events. Steady-state trough plasma levels of MBX-8025

and its metabolites.

Study description

Background summary

Homozygous Familial Hypercholesterolemia (HoFH) is a rare, severe clinical disorder characterized by very high LDL-C levels (usually of more than 12.9 mmol/L), cutaneous and tendionous xanthomata, and early onset of cardiovascular disease. The main cause of HoFH is a substantial reduction in LDL receptor function. Conventional therapies such as statins and ezetimibe are the most commonly used drugs for HoFH. However, due to their mechanism of action, their result in LDL-cholesterol reductions ranges between 15% to 25%. Consequently, plasma LDL apheresis is still considered the treatment of choice for HoFH. Apheresis is a selective mechanical filtration of blood to remove LDL, but it is a complex and inconvenient procedure that is not widely available. Apheresis transiently reduces LDL-C levels and must be repeated every 1 to 2 weeks. Recently two additional drugs, lomitapide (US and EU) and mipomersen sodium (US) have been available for the treatment of HoFH. Both compounds have demonstrated potent LDL-C lowering properties in HoFH subjects. However, not all HoFH subjects are able to decrease their LDL-C to recommended levels,

either due to incomplete efficacy or poor tolerability and significant safety issues. Both lomitapide and mipomersen carry the risk of hepatotoxicity. MBX-8025 has an effect on lowering LDL-C through mechanisms that may not involve the LDL-C receptor, MBX-8025 has been shown to decrease LDL-C, while also leading to improvements in TG, HDL-C, TC and FFA. The use of MBX-8025 to treat HoFH represents an important opportunity to address an unmet clinical need in healthcare.

Study objective

Primary:
To evaluate the effect of MBX-8025 on LDL-C.
Secondary:
To evaluate the effects of MBX-8025 on other lipid parameters. To evaluate the safety and tolerability of MBX-8025. To evaluate steady-state trough plasma levels of MBX-8025 and its metabolites, M1, M2 and M3.

Study design

Open-label, single arm study, non-controlled, dose ascending (MBX-8025 OD, 50 mg/day, 100 mg/day and 200
mg/day). Dose increase every 4 weeks. Screening max. 2 weeks, run-in period 2 weeks, treatment period 12 weeks, follow-up 2 weeks.
MBX-8025 will be added to the existing therapy.
Approx. 8 patients, 3 in NL.
Independent DSMB.

Intervention

Treatment with MBX-8025.

Study burden and risks

Risk: side effects of study medication..
Burden: 10 visits in approx. 18 weeks. Duration 1-2 hours..
Diet.
3 times physical examination.
9 times blood tests (approx. 150 ml blood, 5-25 mL/visit).
6 times ECG.

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

1. Written informed consent.
2. Male or female with HoFH confirmed by genotype (two mutant alleles at the LDL-Receptor gene locus)
3. 18 years of age or older
4. Existing lipid lowering therapies (statins, cholesterol absorption inhibitors, bile acid sequestrants, nicotinic acid and their combinations, LDL-C apheresis) on a stable regimen for at least four weeks before Screening Visit.
5. Stable lipid lowering diet compatible with a Step I diet of the American Heart Association.
6. Fasting LDL-C > 4.8 mmol/L during screening.
7. For females or males of reproductive potential, use of at least one barrier contraceptive and a second effective birth control method during the study and for at least two weeks after the last dose.

Exclusion criteria

1. Treatment with lomitapide or mipomersen within two months of screening.
2. Heart Failure NYHA class lll-IV or LVEF <30%.

3. Uncontrolled cardiac arrhythmia during the pastthree months of screening.
4. Myocardial infarction, unstable angina, PCI, CABG orstroke during the pastthree months prior to screening.
5. Planned cardiac surgery, or revascularization, in the next four months.
6. Uncontrolled hypertension.
7. AST or ALT >3 times the ULN.
8. Unexplained CK >5 times the ULN.
9. For females, pregnancy or breast-feeding.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-04-2015
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	MBX-8025
Generic name:	MBX-8025

Ethics review

Approved WMO

Date:	05-03-2015

Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-04-2015
Application type:	First submission
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	EUCTR2014-004856-68-NL
CCMO	NL52715.060.15