An open label, long term, safety and tolerability extension to a randomized, double-blind, placebo controlled study of LCQ908 in subjects with Familial Chylomicronemia Syndrome

Published: 02-10-2012
Last updated: 26-04-2024

The purpose of this study is to determine long-term safety and tolerability, and continued efficacy in lowering triglycerides of LCQ908 in subjects FCS.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lipid metabolism disorders
Study type	Interventional

Summary

ID

NL-OMON41457

Source
ToetsingOnline

Brief title
LCQ908 extension study

Condition

- Lipid metabolism disorders

Synonym
Familial Chylomicronemia Syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis

Intervention

Keyword: Familial Chylomicronemia Syndrome, LCQ908, Open-label, Triglycerides

Outcome measures

Primary outcome

Number of patients with adverse and serious adverse events

Secondary outcome

Changes in lipid and lipoprotein profiles from baseline up to week 12, week 24

and week 52

Changes from baseline in triglyceride levels up week 12, week 24 and week 52

Study description

Background summary

Familial Chylomicronemia Syndrome (FCS) is a rare genetic disease due to loss of capacity to hydrolyze triglycerides (TG) circulating in TG-rich lipoproteins (primarily chylomicrons) resulting in severe hypertriglyceridemia (>8.4 mmol/L) in both the post-prandial and fasting state. The most severe consequence of FCS is acute pancreatitis, which can be severe and life-threatening LCQ908 is a potent and selective DGAT1 inhibitor. DGAT catalyzes the final step in TG synthesis. LCQ908 may reduce plasma TG levels and chylomicrom synthesis in patients with FCS and may therefore have a beneficial effect on the pathophysiology of chylomicronemia.

Study objective

The purpose of this study is to determine long-term safety and tolerability, and continued efficacy in lowering triglycerides of LCQ908 in subjects FCS.

Study design

This is a multicentre open-label trial consisting of 2 parts:
Part A:
Week 1 to 8: Patients will receive LCQ908 10mg/day
Week 9 to 16: LCQ 10 mg/ day may be possibly uptitrated with 10 mg. Durring this period patients may receive 10 mg/day or 20 mg/day LCQ908 Week 16 to 52: LCQ intake may possibly be uptitrated with 10 mg or 20 mg LCQ. During this period patients may receive 10 mg/day, 20 mg/day LCQ908 or 40 mg/dag LCQ908.
Part B:
week 52 to week 130: patients continue the study medication dose from part A

Intervention

Intervention consists of LCQ908 10 mg, LCQ908 20 mg or LCQ908 40 mg

Study burden and risks

This study will last for 130 weeks. During each visit a fasting blood sample will be taken and vital signs will be assessed. The EQ-5D questionnaire will be assessed during 4 visits, ECG measurements will be assessed during 3 visits and physical exams will be performed during 3 visits.

LCQ908 has been given to humans in single doses up to 300 mg and in multiple doses up to 20 mg for 12 weeks. All dose levels have been found to be safe. Over 1000 humans have been treated, including approximately 400 healthy volunteers, 600 patients with Type 2 diabetes, and 6 patients with FCS. In general, a dose-dependent occurrence of watery diarrhea was found that was generally mild. Adverse events also included nausea and abdominal discomfort. Draft preliminary results of the study with 6 FCS patients indicate that LCQ908 use for 21 days was safe and well tolerated at 10, 20 & 40 mg, with no clinically significant laboratory abnormalities or clinical findings attributed to LCQ908. There were some mild gastrointestinal adverse events recorded, but the frequency and duration was less than in healthy volunteer studies. There is a risk of hypersensitivity to sunlight at LCQ908 intake, although this has not been observed in humans.

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. Subjects that either discontinue prematurely or complete the CLCQ908B2302 study after 52 weeks or FCS subjects who have previously completed study CLCQ908A2212

Exclusion criteria

1. Subjects discontinued from the CLCQ908B2302 study for serious, potentially study drug related adverse events
2. Subjects from the CLCQ908B2302 study who have developed any other contraindication to participation (for example, renal failure)
3. Subjects with type 1 diabetes mellitus or type 2 diabetes mellitus if HbA1C is * 8.5%.
4. Treatment with fish oil preparations within 4 weeks prior to randomization
5. Treatment with bile acid binding resins (i.e. colesevelam etc) within 4 weeks prior to randomization
6. Treatment with fibrates within 8 weeks prior to randomization.
7. eGFR < 45 ml/min/1.73m2 or history of chronic renal disease
8. Glybera [alipogene tiparvovec (AAV1-LPLS447X)] gene therapy exposure within two years prior to screening
9. Pregnant or nursing (lactating) women.
10. Women of child-bearing potential not using highly effective methods of contraception during dosing and for 100 days after discontinuation of investigational study drug.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-10-2013
Enrollment:	4
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	LCQ908
Generic name:	LCQ908

Ethics review

Approved WMO Date:	02-10-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-12-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-11-2013
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-11-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-11-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-04-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-04-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-08-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-09-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-04-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-05-2015
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	EUCTR201200080232-NL
CCMO	NL41484.018.12

Study results

Date completed: 30-05-2015

Actual enrolment: 9

Summary results
Trial is onging in other countries