Clinical trial results:
A Randomized, Double-blind, Placebo Controlled Study to Assess Efficacy, Safety and Tolerability of LCQ908 in Subjects With Familial Chylomicronemia Syndrome

Summary

EudraCT number	2011-005535-68
Trial protocol	DE NL GB ES
Global end of trial date	28 May 2014

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	27 July 2015

Trial information

Trial identification

Sponsor protocol code	CLCQ908B2302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01514461
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 May 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 May 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this clinical trial was to demonstrate the superiority of LCQ908 20 mg or LCQ908 40 mg compared to placebo in reducing fasting triglycerides after 12 weeks of treatment in subjects with FCS.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 July 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 16
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Netherlands: 10
Country: Number of subjects enrolled	South Africa: 3
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	45
EEA total number of subjects	22

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	42
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Among 63 screened patients, 45 (71.4%) patients completed the screening/dietary lead-in phase and got randomized.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

In period II (0-12 weeks) double-blind treatment: one LCQ908 placebo matching to 40mg tablet + one LCQ908 placebo matching to 20mg tablet, once daily. In period III (12-52 weeks) double blind treatment: Without down titration, the period II dosing regimen was followed. Following decision to down titrate: one LCQ908 placebo matching to 40mg tablet + one LCQ908 placebo matching to 20mg tablet + one LCQ908 placebo matching to 10mg tablets, once daily. A low fat diet was followed and recorded in patient diary.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo of LCQ908 10 mg, 20 mg and 40 mg

Arm title	LCQ908 20 mg

Arm description:

In period II (0-12 weeks) double-blind treatment: one LCQ908 20 mg active tablet + one LCQ908 placebo matching to 40mg tablet, once daily. No dose titration allowed. In period III (12-52 weeks) double blind treatment: Without down titration, the period II dosing regimen was followed. Following decision to down titrate: one LCQ908 10 mg active tablet + one LCQ908 placebo matching to 40 mg tablet + one LCQ908 placebo matching to 20 mg tablets, once daily. A low fat diet was followed and recorded in patient diary.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo of LCQ908 10 mg, 20 mg and 40 mg

Investigational medicinal product name	pradigastat
Investigational medicinal product code	LCQ908
Other name	
Pharmaceutical forms	Tablet

Routes of administration	Oral use

Dosage and administration details:

LCQ908 20 mg taken once daily

Arm title	LCQ908 40 mg

Arm description:

In period II (0-12 weeks) double-blind treatment: one LCQ908 40 mg active tablet + one LCQ908 placebo matching to 20mg tablet, once daily. No dose titration allowed. In period III (12-52 weeks) double blind treatment: Without down titration, the period II dosing regimen was followed. Following decision to down titrate: one LCQ908 20 mg active tablet + one LCQ908 placebo matching to 40 mg tablet + one LCQ908 placebo matching to 10mg tablets, once daily. A low fat diet was followed and recorded in patient diary.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo of LCQ908 10 mg, 20 mg and 40 mg

Investigational medicinal product name	pradigastat
Investigational medicinal product code	LCQ908
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

LCQ908 20 mg taken once daily

Number of subjects in period 1	Placebo	LCQ908 20 mg	LCQ908 40 mg
Started	15	15	15
Completed	10	12	11
Not completed	5	3	4
Adverse event, serious fatal	1	-	-
Physician decision	1	1	-
Adverse event, non-fatal	2	1	3
Patient/guardian decision	1	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
In period II (0-12 weeks) double-blind treatment: one LCQ908 placebo matching to 40mg tablet + one LCQ908 placebo matching to 20mg tablet, once daily. In period III (12-52 weeks) double blind treatment: Without down titration, the period II dosing regimen was followed. Following decision to down titrate: one LCQ908 placebo matching to 40mg tablet + one LCQ908 placebo matching to 20mg tablet + one LCQ908 placebo matching to 10mg tablets, once daily. A low fat diet was followed and recorded in patient diary.	
Reporting group title	LCQ908 20 mg
Reporting group description:	
In period II (0-12 weeks) double-blind treatment: one LCQ908 20 mg active tablet + one LCQ908 placebo matching to 40mg tablet, once daily. No dose titration allowed. In period III (12-52 weeks) double blind treatment: Without down titration, the period II dosing regimen was followed. Following decision to down titrate: one LCQ908 10 mg active tablet + one LCQ908 placebo matching to 40 mg tablet + one LCQ908 placebo matching to 20 mg tablets, once daily. A low fat diet was followed and recorded in patient diary.	
Reporting group title	LCQ908 40 mg
Reporting group description:	
In period II (0-12 weeks) double-blind treatment: one LCQ908 40 mg active tablet + one LCQ908 placebo matching to 20mg tablet, once daily. No dose titration allowed. In period III (12-52 weeks) double blind treatment: Without down titration, the period II dosing regimen was followed. Following decision to down titrate: one LCQ908 20 mg active tablet + one LCQ908 placebo matching to 40 mg tablet + one LCQ908 placebo matching to 10mg tablets, once daily. A low fat diet was followed and recorded in patient diary.	

Reporting group values	Placebo	LCQ908 20 mg	LCQ908 40 mg
Number of subjects	15	15	15
Age categorical Units: Subjects			
Adults (18-64 years)	12	15	15
From 65-84 years	3	0	0
Age Continuous | Units: Years			
arithmetic mean	52.9	42.3	42.7
standard deviation	± 10.9	± 13.61	± 10.94
Gender, Male/Female Units: Participants			
Female	8	7	4
Male	7	8	11

Reporting group values	Total		
Number of subjects	45		
Age categorical Units: Subjects			
Adults (18-64 years)	42		
From 65-84 years	3		
Age Continuous | Units: Years			
arithmetic mean			
standard deviation	-		

Gender, Male/Female Units: Participants			
Female	19		
Male	26		

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

In period II (0-12 weeks) double-blind treatment: one LCQ908 placebo matching to 40mg tablet + one LCQ908 placebo matching to 20mg tablet, once daily. In period III (12-52 weeks) double blind treatment: Without down titration, the period II dosing regimen was followed. Following decision to down titrate: one LCQ908 placebo matching to 40mg tablet + one LCQ908 placebo matching to 20mg tablet + one LCQ908 placebo matching to 10mg tablets, once daily. A low fat diet was followed and recorded in patient diary.

Reporting group title	LCQ908 20 mg

Reporting group description:

In period II (0-12 weeks) double-blind treatment: one LCQ908 20 mg active tablet + one LCQ908 placebo matching to 40mg tablet, once daily. No dose titration allowed. In period III (12-52 weeks) double blind treatment: Without down titration, the period II dosing regimen was followed. Following decision to down titrate: one LCQ908 10 mg active tablet + one LCQ908 placebo matching to 40 mg tablet + one LCQ908 placebo matching to 20 mg tablets, once daily. A low fat diet was followed and recorded in patient diary.

Reporting group title	LCQ908 40 mg

Reporting group description:

In period II (0-12 weeks) double-blind treatment: one LCQ908 40 mg active tablet + one LCQ908 placebo matching to 20mg tablet, once daily. No dose titration allowed. In period III (12-52 weeks) double blind treatment: Without down titration, the period II dosing regimen was followed. Following decision to down titrate: one LCQ908 20 mg active tablet + one LCQ908 placebo matching to 40 mg tablet + one LCQ908 placebo matching to 10mg tablets, once daily. A low fat diet was followed and recorded in patient diary.

Primary: Percent change in fasting triglycerides from baseline to 12 weeks

End point title	Percent change in fasting triglycerides from baseline to 12 weeks

End point description:

Blood samples were collected for a fasting lipid panel, including triglycerides. If the 12-week value was missing, the measurement value at 12 weeks or the last available post-baseline measurement value during the double-blind treatment period was analyzed. Baseline is defined as the average of fasting triglyceride values taken at day -3 and day 1. Adjusted geometric means are calculated by back-transforming the adjusted means from the model and expressing as a percentage change from baseline.

End point type	Primary

End point timeframe:

Baseline to 12 weeks

End point values	Placebo	LCQ908 20 mg	LCQ908 40 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	14	12	
Units: percent change				
geometric mean (confidence interval)	45.6 (6.8 to 98.7)	3.7 (-24.3 to 42.1)	-13.9 (-38.9 to 21.3)	

Statistical analyses

Statistical analysis title	LCQ908 20 mg Vs Placebo
Comparison groups	Placebo v LCQ908 20 mg
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0538 [1]
Method	Mixed models analysis
Parameter estimate	% change from reference treatment
Point estimate	-28.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-55.69
upper limit	14.46

Notes:

[1] - Adjusted 1-sided p-value calculated using Dunnett's step down method.

Statistical analysis title	LCQ908 40mg Vs Placebo
Comparison groups	Placebo v LCQ908 40 mg
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0182 [2]
Method	Mixed models analysis
Parameter estimate	% change from reference treatment
Point estimate	-40.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-63.99
upper limit	-2.94

Notes:

[2] - Adjusted 1-sided p-value calculated using Dunnett's step down method.

Secondary: Percentage of patients responding to investigational treatment by achieving fasting triglycerides (TG) of at least 40% from baseline or final fasting TG < 8.4 mmol/L (750 mg/dL)

End point title	Percentage of patients responding to investigational treatment by achieving fasting triglycerides (TG) of at least 40% from baseline or final fasting TG < 8.4 mmol/L (750 mg/dL)

End point description:

Percentage calculated as (m/n)*100 where m = number of patients who respond; n = the number of patients with non-missing fasting triglyceride.

End point type	Secondary

End point timeframe:

Baseline, 12 weeks, 24 weeks, 52 weeks

End point values	Placebo	LCQ908 20 mg	LCQ908 40 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	15	
Units: Percentage of participants				
number (not applicable)				
Week 12 (n = 14, 14, 12)	14.3	21.4	50	
Week 24 (n = 13, 14, 12)	30.8	35.7	33.3	
Week 52 (n = 11, 14, 11)	18.2	21.4	27.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients responding to investigational treatment by achieving final fasting triglycerides < 8.4 mmol/L (750 mg/dL)

End point title	Percentage of patients responding to investigational treatment by achieving final fasting triglycerides < 8.4 mmol/L (750 mg/dL)

End point description:

Percentage calculated as (m/n)*100 where m = number of patients who respond; n = the number of patients with non-missing fasting triglyceride.

End point type	Secondary

End point timeframe:

12 weeks, 24 weeks, 52 weeks

End point values	Placebo	LCQ908 20 mg	LCQ908 40 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	15	
Units: Percentage of participants				
number (not applicable)				
Week 12 (n = 14, 14, 12)	14.3	14.3	33.3	
Week 24 (n = 13, 14, 12)	30.8	14.3	16.7	
Week 52 (n = 11, 14, 11)	18.2	14.3	18.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients responding to investigational treatment by achieving fasting triglycerides (TG) of at least 40% from baseline

End point title	Percentage of patients responding to investigational treatment by achieving fasting triglycerides (TG) of at least 40% from baseline

End point description:

Percentage calculated as (m/n)*100 where m = number of patients who respond; n = the number of

patients with non-missing fasting triglyceride.

End point type	Secondary

End point timeframe:

Baseline, 12 weeks, 24 weeks, 52 weeks

End point values	Placebo	LCQ908 20 mg	LCQ908 40 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	15	
Units: Percentage of participants				
number (not applicable)				
Week 12 (n = 14, 14, 12)	0	14.3	25	
Week 24 (n = 13, 14, 12)	15.4	28.6	16.7	
Week 52 (n = 11, 14, 11)	0	14.3	27.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients achieving fasting triglycerides (TG) target thresholds

End point title	Percentage of patients achieving fasting triglycerides (TG) target thresholds

End point description:

Percentage of patients reaching target values of <1000 mg/dL or target values of < 2000 mg/dL for fasting triglycerides is reported. Pecentage calculated as (m/n)*100; where 'm' The number of patients who reach target values for fasting triglyceride, 'n' the number of patients with non-missing fasting triglyceride.

End point type	Secondary

End point timeframe:

12 weeks, 24 weeks, 52 weeks

End point values	Placebo	LCQ908 20 mg	LCQ908 40 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	15	
Units: Percentage of patients				
number (not applicable)				
TG < 1000 mg/dL, week 12 (n=14,14,12)	14.3	21.4	33.3	
TG < 1000 mg/dL, week 24 (n=13,14,12)	30.8	21.4	25	
TG < 1000 mg/dL, week 52 (n=11,14,11)	27.3	14.3	36.4	
TG < 2000 mg/dL, week 12 (n=14,14,12)	35.7	50	83.3	
TG < 2000 mg/dL, week 24 (n=13,14,12)	38.5	57.1	58.3	

TG < 2000 mg/dL, week 52 (n=11,14,11)	36.4	50	63.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline in fasting triglycerides

End point title	Percent change from baseline in fasting triglycerides

End point description:

End point type	Secondary

End point timeframe:

Baseline, 24 weeks, 52 weeks

End point values	Placebo	LCQ908 20 mg	LCQ908 40 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	15	
Units: Percent change				
geometric mean (confidence interval)				
Week 24 (n=13, 14, 12)	4.9 (-26.6 to 50.1)	-15.8 (-40.5 to 19.3)	5.5 (-28 to 54.5)	
Week 52 (n=11, 14, 11)	15.2 (-23 to 72.5)	-6.7 (-36.4 to 36.9)	4.9 (-31.2 to 60)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline for postprandial triglycerides following the standardized meal tolerance test at Week 12

End point title	Percent change from baseline for postprandial triglycerides following the standardized meal tolerance test at Week 12

End point description:

Post prandial peak triglycerides – maximum triglyceride value over 0-24 hours Post prandial triglycerides AUC0-24 – area under the time curve for triglycerides over 0-24 Adjusted geometric means are calculated by back-transforming the adjusted means from the model and expressed as a percentage change from baseline. hours

End point type	Secondary

End point timeframe:

0-24 hours at Baseline, Week 12

End point values	Placebo	LCQ908 20 mg	LCQ908 40 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	15	
Units: Percent change				
geometric mean (confidence interval)				
Triglycerides (Peak 0-24h) [n=12, 12, 11)	56.9 (6.9 to 130.2)	8.6 (-24.8 to 56.8)	6.3 (-30.3 to 62.2)	
Triglycerides (AUC 0-24h) [n=12, 12, 11)	44.5 (-1.3 to 111.5)	0.8 (-30.1 to 45.1)	2.8 (-32.4 to 56.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics of LCQ908 - Trough Concentration (Cmin) and Observed maximum blood concentration (Cmax)

End point title	Pharmacokinetics of LCQ908 - Trough Concentration (Cmin) and Observed maximum blood concentration (Cmax)[3]

End point description:

Lowest observed blood concentration (Cmin) and observed maximum blood concentration (Cmax) following drug administration derived from non-compartmental analysis using scheduled sampling time for the whole dataset.

End point type	Secondary

End point timeframe:

0, 1, 2, 3, 4, 6, and 24 hours at Week 12

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK parameters are only analyzed on study drug (LCQ908), not on placebo.

End point values	LCQ908 20 mg	LCQ908 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	9		
Units: ng/mL				
arithmetic mean (standard deviation)				
Cmin	312 (± 120)	426 (± 224)		
Cmax	603 (± 244)	745 (± 408)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics of LCQ908- Area under the plasma concentration time curve AUC (0-24hour)

End point title	Pharmacokinetics of LCQ908- Area under the plasma concentration time curve AUC (0-24hour)[4]

End point description:

The area under the concentration-time curve from time zero to 24 hours after drug administration was calculated by using linear trapezoidal rule.

End point type	Secondary

End point timeframe:

0, 1, 2, 3, 4, 6, and 24 hours at Week 12

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK parameters are only analyzed on study drug (LCQ908), not on placebo.

End point values	LCQ908 20 mg	LCQ908 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	9		
Units: ng/mL *hr				
arithmetic mean (standard deviation)	11000 (± 4100)	14300 (± 7390)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics of LCQ908- Time to reach maximum concentration following drug administration Tmax (hours)

End point title	Pharmacokinetics of LCQ908- Time to reach maximum concentration following drug administration Tmax (hours)[5]

End point description:

End point type	Secondary

End point timeframe:

0, 1, 2, 3, 4, 6, and 24 hours at Week 12

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK parameters are only analyzed on study drug (LCQ908), not on placebo.

End point values	LCQ908 20 mg	LCQ908 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	9		
Units: hours				
median (full range (min-max))	6 (0 to 24)	8 (0 to 24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics of LCQ908- Average observed blood concentration (Cavg)

End point title	Pharmacokinetics of LCQ908- Average observed blood concentration (Cavg)[6]

End point description:

Average observed blood concentration measured by (AUC0-24)/24.

End point type	Secondary

End point timeframe:

0, 1, 2, 3, 4, 6, and 24 hours at Week 12

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: PK parameters are only analyzed on study drug (LCQ908), not on placebo.

End point values	LCQ908 20 mg	LCQ908 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	9		
Units: ng/mL				
arithmetic mean (standard deviation)	459 (± 171)	597 (± 308)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients reported with any adverse event, serious adverse event and death

End point title	Number of patients reported with any adverse event, serious adverse event and death

End point description:

End point type	Secondary

End point timeframe:

52 weeks

End point values	Placebo	LCQ908 20 mg	LCQ908 40 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	14	
Units: Participants				
At least one adverse events	15	15	14	
At least one serious adverse event	6	6	3	
Death	1	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

In period II (0-12 weeks) double-blind treatment: one LCQ908 placebo matching to 40mg tablet + one LCQ908 placebo matching to 20mg tablet, once daily. In period III (12-52 weeks) double blind treatment: Without down titration, the period II dosing regimen was followed. Following decision to down titrate: one LCQ908 placebo matching to 40mg tablet + one LCQ908 placebo matching to 20mg tablet + one LCQ908 placebo matching to 10mg tablets, once daily. A low fat diet was followed and recorded in patient diary.

Reporting group title	LCQ908 40mg

Reporting group description:

In period II (0-12 weeks) double-blind treatment: one LCQ908 40 mg active tablet + one LCQ908 placebo matching to 20mg tablet, once daily. No dose titration allowed. In period III (12-52 weeks) double blind treatment: Without down titration, the period II dosing regimen was followed. Following decision to down titrate: one LCQ908 20 mg active tablet + one LCQ908 placebo matching to 40 mg tablet + one LCQ908 placebo matching to 10mg tablets, once daily. A low fat diet was followed and recorded in patient diary.

Reporting group title	LCQ908 20mg

Reporting group description:

In period II (0-12 weeks) double-blind treatment: one LCQ908 20 mg active tablet + one LCQ908 placebo matching to 40mg tablet, once daily. No dose titration allowed. In period III (12-52 weeks) double blind treatment: Without down titration, the period II dosing regimen was followed. Following decision to down titrate: one LCQ908 10 mg active tablet + one LCQ908 placebo matching to 40 mg tablet + one LCQ908 placebo matching to 20 mg tablets, once daily. A low fat diet was followed and recorded in patient diary.

Serious adverse events	Placebo	LCQ908 40mg	LCQ908 20mg
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 15 (40.00%)	3 / 14 (21.43%)	6 / 15 (40.00%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
HEPATIC ENZYME INCREASED			

subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
MALIGNANT PALATE NEOPLASM			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
INCISIONAL HERNIA			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
FEMORAL ARTERY OCCLUSION			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
CARDIAC ARREST			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
CEREBRAL HAEMORRHAGE			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL DISORDER			

subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS			
subjects affected / exposed	2 / 15 (13.33%)	1 / 14 (7.14%)	3 / 15 (20.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS ACUTE			
subjects affected / exposed	2 / 15 (13.33%)	1 / 14 (7.14%)	2 / 15 (13.33%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
HYPERTRANSAMINASAEMIA			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
PULMONARY EMBOLISM			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
PNEUMONIA			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	LCQ908 40mg	LCQ908 20mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)	14 / 14 (100.00%)	15 / 15 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
LIPOMA			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
NEOPLASM SKIN			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
PAPILLOMA			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Vascular disorders			
PERIPHERAL ARTERIAL OCCLUSIVE DISEASE			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
HOT FLUSH			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
CYST			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
ASTHENIA			
subjects affected / exposed	0 / 15 (0.00%)	2 / 14 (14.29%)	1 / 15 (6.67%)
occurrences (all)	0	2	1
FATIGUE			
subjects affected / exposed	2 / 15 (13.33%)	0 / 14 (0.00%)	2 / 15 (13.33%)
occurrences (all)	2	0	2
PYREXIA			
subjects affected / exposed	1 / 15 (6.67%)	1 / 14 (7.14%)	2 / 15 (13.33%)
occurrences (all)	1	1	2
MALAISE			

subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Immune system disorders			
ALLERGY TO ARTHROPOD STING			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
FOOD ALLERGY			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
ALLERGY TO PLANTS			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA			
subjects affected / exposed	3 / 15 (20.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0
COUGH			
subjects affected / exposed	2 / 15 (13.33%)	4 / 14 (28.57%)	3 / 15 (20.00%)
occurrences (all)	2	4	3
SINUS CONGESTION			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	2 / 15 (13.33%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	2
NASAL CONGESTION			
subjects affected / exposed	2 / 15 (13.33%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	2	1	0
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			

DEPRESSION			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
INSOMNIA			
subjects affected / exposed	2 / 15 (13.33%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
STRESS			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Investigations			
BLOOD GLUCOSE INCREASED			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
HEPATIC ENZYME INCREASED			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
HAEMOGLOBIN DECREASED			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
CAROTID BRUIT			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
WEIGHT DECREASED			
subjects affected / exposed	0 / 15 (0.00%)	2 / 14 (14.29%)	2 / 15 (13.33%)
occurrences (all)	0	2	2
WEIGHT INCREASED			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	1 / 15 (6.67%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
CONTUSION			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
CHEST INJURY			

subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
LIGAMENT SPRAIN			
subjects affected / exposed	1 / 15 (6.67%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
LIMB INJURY			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
MUSCLE RUPTURE			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
SCAR			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
RIB FRACTURE			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
POST PROCEDURAL COMPLICATION			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
SPORTS INJURY			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
TOOTH FRACTURE			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
CARDIAC ARREST			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
PALPITATIONS			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
CORONARY ARTERY STENOSIS			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0

CARDIAC FAILURE			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
SUPRAVENTRICULAR EXTRASYSTOLES			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	3 / 15 (20.00%)	1 / 14 (7.14%)	3 / 15 (20.00%)
occurrences (all)	4	1	3
DYSGEUSIA			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
LETHARGY			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
HEADACHE			
subjects affected / exposed	1 / 15 (6.67%)	1 / 14 (7.14%)	4 / 15 (26.67%)
occurrences (all)	1	1	4
SCIATICA			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	2 / 15 (13.33%)
occurrences (all)	0	1	2
SYNCOPE			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
LEUKOPENIA			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
ANAEMIA			
subjects affected / exposed	2 / 15 (13.33%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			

DEAFNESS			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Eye disorders			
CONJUNCTIVAL HAEMORRHAGE			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
BLEPHARITIS			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 15 (0.00%)	2 / 14 (14.29%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
ABDOMINAL RIGIDITY			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	2 / 15 (13.33%)
occurrences (all)	0	1	3
ABDOMINAL PAIN			
subjects affected / exposed	1 / 15 (6.67%)	1 / 14 (7.14%)	7 / 15 (46.67%)
occurrences (all)	1	2	14
BARRETT'S OESOPHAGUS			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
CHANGE OF BOWEL HABIT			
subjects affected / exposed	1 / 15 (6.67%)	1 / 14 (7.14%)	2 / 15 (13.33%)
occurrences (all)	1	1	2
DENTAL CARIES			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
DEFAECATION URGENCY			

subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
CONSTIPATION			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
DIARRHOEA			
subjects affected / exposed	10 / 15 (66.67%)	10 / 14 (71.43%)	12 / 15 (80.00%)
occurrences (all)	13	34	56
DIVERTICULUM			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
ENTERITIS			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
DYSPEPSIA			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
DRY MOUTH			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
FAECES DISCOLOURED			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
FREQUENT BOWEL MOVEMENTS			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
FLATULENCE			
subjects affected / exposed	1 / 15 (6.67%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
FAECES SOFT			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	0	1	2
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	2 / 15 (13.33%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0

HYPERCHLORHYDRIA			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
PANCREATITIS			
subjects affected / exposed	0 / 15 (0.00%)	2 / 14 (14.29%)	3 / 15 (20.00%)
occurrences (all)	0	6	7
NAUSEA			
subjects affected / exposed	1 / 15 (6.67%)	4 / 14 (28.57%)	5 / 15 (33.33%)
occurrences (all)	1	6	9
INGUINAL HERNIA			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	3
TOOTHACHE			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
VOMITING			
subjects affected / exposed	0 / 15 (0.00%)	4 / 14 (28.57%)	6 / 15 (40.00%)
occurrences (all)	0	7	11
Hepatobiliary disorders			
CHOLELITHIASIS			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
SKIN LESION			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
ROSACEA			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
ALOPECIA			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
XANTHOMA			

subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
ACNE			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Renal and urinary disorders			
RENAL FAILURE ACUTE			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
DYSURIA			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	3 / 15 (20.00%)
occurrences (all)	0	1	3
BACK PAIN			
subjects affected / exposed	1 / 15 (6.67%)	3 / 14 (21.43%)	1 / 15 (6.67%)
occurrences (all)	1	3	1
BURSITIS			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
MUSCLE FATIGUE			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
MUSCLE SPASMS			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
MUSCULOSKELETAL PAIN			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
PAIN IN EXTREMITY			

subjects affected / exposed	2 / 15 (13.33%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0
NECK PAIN			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
MYOPATHY			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
MYALGIA			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
TENDONITIS			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	3 / 15 (20.00%)
occurrences (all)	0	0	3
SJOGREN'S SYNDROME			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	1 / 15 (6.67%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
CONJUNCTIVITIS			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
ERYSIPELAS			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
EAR INFECTION			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
CYSTITIS			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
GASTROENTERITIS			
subjects affected / exposed	3 / 15 (20.00%)	1 / 14 (7.14%)	2 / 15 (13.33%)
occurrences (all)	3	1	3

GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
INFLUENZA			
subjects affected / exposed	3 / 15 (20.00%)	4 / 14 (28.57%)	0 / 15 (0.00%)
occurrences (all)	3	4	0
HORDEOLUM			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
HAND-FOOT-AND-MOUTH DISEASE			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
JOINT ABSCESS			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
LARYNGITIS			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
PHARYNGITIS			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
NASOPHARYNGITIS			
subjects affected / exposed	3 / 15 (20.00%)	4 / 14 (28.57%)	2 / 15 (13.33%)
occurrences (all)	3	6	4
LOCALISED INFECTION			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
PNEUMONIA			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
RHINITIS			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	3
TINEA INFECTION			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
TOOTH ABSCESS			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
TOOTH INFECTION			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	3 / 15 (20.00%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	3	1	1
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
DIABETES MELLITUS			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
HYPERGLYCAEMIA			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
HYPOCALCAEMIA			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
HYPOKALAEMIA			

subjects affected / exposed	2 / 15 (13.33%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
IRON DEFICIENCY			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
VITAMIN D DEFICIENCY			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 April 2012	Amendment 1 Version 1 : This protocol amendment introduced two key secondary objectives to the study protocol: a. To assess the effect of LCQ908 as compared to placebo on fasting triglycerides after 24 and 52 weeks. b. To assess the effect of LCQ908 as compared to placebo on post-prandial triglycerides after 12 weeks.
20 June 2012	Amendment 1 Version 2 : To incorporate the rational for the amendment 1 version 1 into the body of the protocol, rather than a stand-alone document to meet the requirements of certain Health Authorities.
23 January 2013	Amendment 2 Version 3: This amendment introduced modifications to three exclusion criteria. Additionally, the reporting of SAEs was updated to reflect the current reporting procedure.
02 May 2013	Amendment 3 Version 4: This amendment introduced modifications based on feedback from the FDA regarding previous amendment of the CLCQ908B2302 study protocol in which the exclusion criterion associated with diabetes mellitus (type 1 and 2) was deleted. The modification allowed a more representative patient population to be recruited into the study but has also raised concern at the agency with regard to the potential hypoglycemic events that could be associated with the use of pradigastat in uncontrolled diabetes. Additional information about potential hypoglycemic events was therefore, collected in the case report forms.
07 November 2013	Amendment 4 Version 5: This amendment incorporated FDA feedback on need to follow the recommendations of the National Research council on the Prevention and Treatment of Missing Data in Clinical Trials. FDA suggested that an alternative method of dealing with missing data in the primary analysis should be defined. Following the changes to the primary analysis required to alter the method of handling missing data, an alternative methodology to the original approach for controlling the family wise type I error rate was also specified in order to reduce the operational burden on statistical programming.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported