



Clinical trial results:

An open label, 52-week, safety and tolerability extension to a randomized, double-blind, placebo controlled study of LCQ908 in subjects with Familial Chylomicronemia Syndrome.

Summary

EudraCT number	2012-000802-32
Trial protocol	DE GB ES NL
Global end of trial date	01 July 2015

Results information

Result version number	v1 (current)
This version publication date	03 July 2016
First version publication date	03 July 2016

Trial information

Trial identification

Sponsor protocol code	CLCQ908B2305
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01589237
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	01 July 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 July 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To establish the long-term safety and tolerability of pradigastat in a study with optional up titration, comparable to clinical practice, in patients with FCS (Familial Chylomicronemia Syndrome) (HLP type I) who discontinued (due to tolerability issues or for reasons other than serious study drug related AEs) or completed study CLCQ908B2302 after 52 weeks.

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	27 February 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 17
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	South Africa: 2
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	38
EEA total number of subjects	16

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)	35
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

100% patients who completed the screening phase were enrolled in the study.

Period 1

Period 1 title	Part A (52 weeks)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo of pradigastat (LCQ908) regimen

Arm description:

Part A: Patients who were randomized to placebo in study CLCQ908B2302/NCT01514461. In current study, patients initiated at 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.

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

Dosage and administration details:

starting dose: 10 mg/day pradigastat (LCQ908) with optional up-titration up to 40 mg

Arm title	20 mg pradigastat (LCQ908) regimen
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Arm description:

Part A: Patients who were randomized to LCQ908 20 mg in study CLCQ908B2302/NCT01514461. In current study, patients initiated at LCQ908 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.

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

Dosage and administration details:

starting dose: 10 mg/day pradigastat (LCQ908) with optional up-titration up to 40 mg

Arm title	40 mg pradigastat (LCQ908) regimen
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Arm description:

Part A: Patients who were randomized to LCQ908 40 mg in study CLCQ908B2302/NCT01514461. In current study, patients initiated at LCQ908 10 mg/day. After at least 8 weeks of treatment with a dose,

optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.

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

Dosage and administration details:

starting dose: 10 mg/day pradigastat (LCQ908) with optional up-titration up to 40 mg

Arm title	pradigastat (LCQ9908) regimen- from study A2212
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Arm description:

Part A: Patients who were randomized to LCQ908 in study CLCQ908A2212/NCT01146522. In current study, patients initiated at LCQ908 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.

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

Dosage and administration details:

starting dose: 10 mg/day pradigastat (LCQ908) with optional up-titration up to 40 mg

Number of subjects in period 1	Placebo of pradigastat (LCQ908) regimen	20 mg pradigastat (LCQ908) regimen	40 mg pradigastat (LCQ908) regimen
Started	11	12	10
Completed	9	9	8
Not completed	2	3	2
Subject/guardian decision	2	3	2

Number of subjects in period 1	pradigastat (LCQ9908) regimen- from study A2212
Started	5
Completed	5
Not completed	0
Subject/guardian decision	-

Period 2

Period 2 title	Part B (planned for 78 week-terminated)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo of pradigastat (LCQ908) regimen

Arm description:

Part A: Patients who were randomized to placebo in study CLCQ908B2302/NCT01514461. In current study, patients initiated at 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.

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

Dosage and administration details:

starting dose: 10 mg/day pradigastat (LCQ908) with optional up-titration up to 40 mg

Arm title	20 mg pradigastat (LCQ908) regimen
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Arm description:

Part A: Patients who were randomized to LCQ908 20 mg in study CLCQ908B2302/NCT01514461. In current study, patients initiated at LCQ908 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.

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

Dosage and administration details:

starting dose: 10 mg/day pradigastat (LCQ908) with optional up-titration up to 40 mg

Arm title	40 mg pradigastat (LCQ908) regimen
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Arm description:

Part A: Patients who were randomized to LCQ908 40 mg in study CLCQ908B2302/NCT01514461. In current study, patients initiated at LCQ908 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.

Arm type	Experimental
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Investigational medicinal product name	pradigastat
Investigational medicinal product code	LCQ908
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
starting dose: 10 mg/day pradigastat (LCQ908) with optional up-titration up to 40 mg	
Arm title	pradigastat (LCQ908) regimen- from study A2212

Arm description:

Part A: Patients who were randomized to LCQ908 in study CLCQ908A2212/NCT01146522. In current study, patients initiated at LCQ908 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.

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

Dosage and administration details:

starting dose: 10 mg/day pradigastat (LCQ908) with optional up-titration up to 40 mg

Number of subjects in period 2^[1]	Placebo of pradigastat (LCQ908) regimen	20 mg pradigastat (LCQ908) regimen	40 mg pradigastat (LCQ908) regimen
Started	5	6	4
Completed	0	0	0
Not completed	5	6	4
Physician decision	-	-	-
Study terminated by sponsor	5	5	4
Subject/guardian decision	-	1	-

Number of subjects in period 2^[1]	pradigastat (LCQ908) regimen- from study A2212
Started	4
Completed	0
Not completed	4
Physician decision	1
Study terminated by sponsor	3
Subject/guardian decision	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all patients who completed Part A consented to continue in Part B of the study.

Baseline characteristics

Reporting groups

Reporting group title	Placebo of pradigastat (LCQ908) regimen
Reporting group description:	
Part A: Patients who were randomized to placebo in study CLCQ908B2302/NCT01514461. In current study, patients initiated at 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.	
Reporting group title	20 mg pradigastat (LCQ908) regimen
Reporting group description:	
Part A: Patients who were randomized to LCQ908 20 mg in study CLCQ908B2302/NCT01514461. In current study, patients initiated at LCQ908 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.	
Reporting group title	40 mg pradigastat (LCQ908) regimen
Reporting group description:	
Part A: Patients who were randomized to LCQ908 40 mg in study CLCQ908B2302/NCT01514461. In current study, patients initiated at LCQ908 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.	
Reporting group title	pradigastat (LCQ9908) regimen- from study A2212
Reporting group description:	
Part A: Patients who were randomized to LCQ908 in study CLCQ908A2212/NCT01146522. In current study, patients initiated at LCQ908 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.	

Reporting group values	Placebo of pradigastat (LCQ908) regimen	20 mg pradigastat (LCQ908) regimen	40 mg pradigastat (LCQ908) regimen
Number of subjects	11	12	10
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			

Age Continuous Units: Years arithmetic mean standard deviation	52.9 ± 10.22	44.1 ± 14.26	43.6 ± 84.53
Gender, Male/Female Units: Participants			
Female	5	6	2
Male	6	6	8

Reporting group values	pradigastat (LCQ9908) regimen- from study A2212	Total	
Number of subjects	5	38	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age Continuous Units: Years arithmetic mean standard deviation	52.2 ± 12.72	-	
Gender, Male/Female Units: Participants			
Female	3	16	
Male	2	22	

End points

End points reporting groups

Reporting group title	Placebo of pradigastat (LCQ908) regimen
Reporting group description:	
Part A: Patients who were randomized to placebo in study CLCQ908B2302/NCT01514461. In current study, patients initiated at 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.	
Reporting group title	20 mg pradigastat (LCQ908) regimen
Reporting group description:	
Part A: Patients who were randomized to LCQ908 20 mg in study CLCQ908B2302/NCT01514461. In current study, patients initiated at LCQ908 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.	
Reporting group title	40 mg pradigastat (LCQ908) regimen
Reporting group description:	
Part A: Patients who were randomized to LCQ908 40 mg in study CLCQ908B2302/NCT01514461. In current study, patients initiated at LCQ908 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.	
Reporting group title	pradigastat (LCQ9908) regimen- from study A2212
Reporting group description:	
Part A: Patients who were randomized to LCQ908 in study CLCQ908A2212/NCT01146522. In current study, patients initiated at LCQ908 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.	
Reporting group title	Placebo of pradigastat (LCQ908) regimen
Reporting group description:	
Part A: Patients who were randomized to placebo in study CLCQ908B2302/NCT01514461. In current study, patients initiated at 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.	
Reporting group title	20 mg pradigastat (LCQ908) regimen
Reporting group description:	
Part A: Patients who were randomized to LCQ908 20 mg in study CLCQ908B2302/NCT01514461. In current study, patients initiated at LCQ908 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.	
Reporting group title	40 mg pradigastat (LCQ908) regimen
Reporting group description:	
Part A: Patients who were randomized to LCQ908 40 mg in study CLCQ908B2302/NCT01514461. In current study, patients initiated at LCQ908 10 mg/day. After at least 8 weeks of treatment with a dose,	

optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.

Reporting group title	pradigastat (LCQ908) regimen- from study A2212
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Reporting group description:

Part A: Patients who were randomized to LCQ908 in study CLCQ908A2212/NCT01146522. In current study, patients initiated at LCQ908 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained. Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.

Primary: Number of patients with any Adverse events, Serious Adverse events and death

End point title	Number of patients with any Adverse events, Serious Adverse events and death ^[1]
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End point description:

Safety set (SAF) - All subjects who received at least one dose of study drug and had at least one post-baseline safety assessment in this extension study.

End point type	Primary
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End point timeframe:

52 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There was no planned statistical analysis for this safety endpoint

End point values	Placebo of pradigastat (LCQ908) regimen	20 mg pradigastat (LCQ908) regimen	40 mg pradigastat (LCQ908) regimen	pradigastat (LCQ9908) regimen- from study A2212
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	10	5
Units: Participants				
At least one Adverse Event (any)	11	12	10	5
At least one serious AE	1	6	2	2
Death	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline in triglyceride levels up to 52 weeks

End point title	Changes from baseline in triglyceride levels up to 52 weeks
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End point description:

Blood samples were collected for a fasting lipid panel, including total triglycerides. Lipid measurements were collected after a 12 hour (overnight) fast. The maintenance of effect was assessed on triglyceride levels during continued therapy with LCQ908 for up to 52 weeks. For patients from LCQ908 arm of study

CLCQ908A2212, baseline was the assessment obtained at Week 0 of current study. For patients from study CLCQ908B2302, baseline is defined as the average of values taken Day -3 and Week 0 (randomization) in study CLCQ908B2302. The geometric mean for the percentage (%) change is calculated from back-transforming the mean of the log transformed ratio to baseline values: $(\exp(\text{mean of the log-transformed ratio to baseline values}) - 1) \times 100$. Full analysis set (FAS) – All subjects in the extension study who were in FAS in either study LCQ908A2212 or LCQ908B2302. At each time point post-baseline, only patients with a value at both baseline and the post-dose time point are included.

End point type	Secondary
End point timeframe:	
Baseline, Week 12, 24 and 52	

End point values	Placebo of pradiastat (LCQ908) regimen	20 mg pradiastat (LCQ908) regimen	40 mg pradiastat (LCQ908) regimen	pradiastat (LCQ9908) regimen- from study A2212
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	10	5
Units: percentage change				
geometric mean (geometric coefficient of variation)				
Change in week 12 (n=10,11,10,5)	1.63 ($\pm$ 45.19)	-5.8 ($\pm$ 66.1)	43.94 ($\pm$ 52.66)	-19.36 ($\pm$ 42.82)
change in week 24 (n=10,10,9,5)	-14.59 ($\pm$ 52.33)	-36.19 ($\pm$ 64.8)	32.54 ($\pm$ 87.83)	-26.05 ($\pm$ 31.5)
change in week 52 (n=9,8,9,5)	16.46 ($\pm$ 29.27)	-30.03 ($\pm$ 78.52)	92.15 ($\pm$ 60.21)	-9.2 ($\pm$ 43.34)

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline in Cholesterol levels up to 52 weeks

End point title	Changes from baseline in Cholesterol levels up to 52 weeks
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End point description:

Blood samples were collected for a fasting lipid panel, including cholesterol level. Lipid measurements were collected after a 12 hour (overnight) fast. For patients from LCQ908 arm of study CLCQ908A2212, baseline was the assessment obtained at Week 0 of current study. For patients from study CLCQ908B2302, baseline is defined as the average of values taken Day -3 and Week 0 (randomization) in study CLCQ908B2302. The geometric mean for the percentage (%) change is calculated from back-transforming the mean of the log transformed ratio to baseline values: $(\exp(\text{mean of the log-transformed ratio to baseline values}) - 1) \times 100$. Full analysis set (FAS) – All subjects in the extension study who were in FAS in either study LCQ908A2212 or LCQ908B2302. At each time point post-baseline, only patients with a value at both baseline and the post-dose time point are included.

End point type	Secondary
End point timeframe:	
Baseline, Week 12, 24 and 52	

End point values	Placebo of pradi­gastat (LCQ908) regimen	20 mg pradi­gastat (LCQ908) regimen	40 mg pradi­gastat (LCQ908) regimen	pradi­gastat (LCQ9908) regimen- from study A2212
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	10	5
Units: percentage change				
geometric mean (geometric coefficient of variation)				
Change in week 12 (n=10,11,10,5)	-5.58 (± 36.38)	-4.76 (± 36.26)	18.76 (± 31.54)	-10.42 (± 24.68)
change in week 24 (n=10,10,9,5)	-10.54 (± 27.87)	-21.54 (± 24.98)	7.45 (± 37.28)	-13.87 (± 25.64)
change in week 52 (n=9,8,9,5)	5.75 (± 17.51)	-13.76 (± 36.1)	40.95 (± 34.1)	-6.84 (± 22.55)

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline in HDL and Non HDL cholesterol levels up to 52 weeks

End point title	Changes from baseline in HDL and Non HDL cholesterol levels up to 52 weeks
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End point description:

Blood samples were collected for a fasting lipid panel, including HDL and non HDL cholesterol level. Lipid measurements were collected after a 12 hour (overnight) fast. For patients from LCQ908 arm of study CLCQ908A2212, baseline was the assessment obtained at Week 0 of current study. For patients from study CLCQ908B2302, baseline is defined as the average of values taken Day -3 and Week 0 (randomization) in study CLCQ908B2302. The geometric mean for the percentage (%) change is calculated from back-transforming the mean of the log transformed ratio to baseline values: $(\exp(\text{mean of the log-transformed ratio to baseline values}) - 1) \times 100$. Full analysis set (FAS) – All subjects in the extension study who were in FAS in either study LCQ908A2212 or LCQ908B2302. At each time point post-baseline, only patients with a value at both baseline and the post-dose time point are included.

End point type	Secondary
End point timeframe:	
Baseline, Week 12, 24 and 52	

End point values	Placebo of pradi­gastat (LCQ908) regimen	20 mg pradi­gastat (LCQ908) regimen	40 mg pradi­gastat (LCQ908) regimen	pradi­gastat (LCQ9908) regimen- from study A2212
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	10	5
Units: percentage change				
geometric mean (geometric coefficient of variation)				
HDL: Change in week 12 (n=10,11,10,5)	-14.13 (± 30.08)	3.37 (± 24.75)	-5.99 (± 22.19)	-7.09 (± 27.11)
Non HDL: change in week 12 (n=10,11,10,5)	-5.37 (± 39.61)	-7.72 (± 42.4)	20.7 (± 34.18)	-10.57 (± 26.16)

HDL: change in week 24 (n=10,10,9,5)	-7.11 (± 19.41)	-1.83 (± 31.36)	6.67 (± 22.19)	-15.6 (± 37.69)
Non HDL: change in week 24 (n=10,10,9,5)	-11.29 (± 29.53)	-25.22 (± 31.49)	7.17 (± 40.5)	-14.01 (± 28.04)
HDL: change in week 52 (n=9,8,9,5)	-10.85 (± 19.78)	8.11 (± 29.35)	-7.33 (± 27.63)	-21.41 (± 22.91)
Non HDL: change in week 52 (n=9,8,9,5)	8.06 (± 21.42)	-17.68 (± 42.65)	45.25 (± 37.45)	-6.09 (± 24.59)

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline in glycerol levels up to 52 weeks

End point title	Changes from baseline in glycerol levels up to 52 weeks
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End point description:

Blood samples were collected for a fasting lipid panel, including glycerol level. Lipid measurements were collected after a 12 hour (overnight) fast. For patients from LCQ908 arm of study CLCQ908A2212, baseline was the assessment obtained at Week 0 of current study. For patients from study CLCQ908B2302, baseline is defined as the average of values taken Day -3 and Week 0 (randomization) in study CLCQ908B2302. The geometric mean for the percentage (%) change is calculated from back-transforming the mean of the log transformed ratio to baseline values: $(\exp(\text{mean of the log-transformed ratio to baseline values}) - 1) \times 100$. Full analysis set (FAS) – All subjects in the extension study who were in FAS in either study LCQ908A2212 or LCQ908B2302. At each time point post-baseline, only patients with a value at both baseline and the post-dose time point are included.

End point type	Secondary
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End point timeframe:

Baseline, Week 12, 24 and 52

End point values	Placebo of pradigastat (LCQ908) regimen	20 mg pradigastat (LCQ908) regimen	40 mg pradigastat (LCQ908) regimen	pradigastat (LCQ9908) regimen- from study A2212
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	10	5
Units: percentage change				
geometric mean (geometric coefficient of variation)				
Change in week 12 (n=10,11,10,5)	-26.56 (± 72.88)	-15.5 (± 73.33)	0.68 (± 75.4)	-46.83 (± 105.58)
change in week 24 (n=10,10,9,5)	-40 (± 67.28)	-46.97 (± 62.46)	-36.26 (± 133.58)	-56.99 (± 96.06)
change in week 52 (n=9,8,9,5)	-38.15 (± 70.1)	-31.96 (± 64.76)	-28.52 (± 101.85)	-37.02 (± 81.67)

Statistical analyses

Secondary: Changes from baseline in free fatty acid levels up to 52 weeks

End point title	Changes from baseline in free fatty acid levels up to 52 weeks
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End point description:

Blood samples were collected for a fasting lipid panel, including free fatty acid level. Lipid measurements were collected after a 12 hour (overnight) fast. For patients from LCQ908 arm of study CLCQ908A2212, baseline was the assessment obtained at Week 0 of current study. For patients from study CLCQ908B2302, baseline is defined as the average of values taken Day -3 and Week 0 (randomization) in study CLCQ908B2302. The geometric mean for the percentage (%) change is calculated from back-transforming the mean of the log transformed ratio to baseline values: $(\exp(\text{mean of the log-transformed ratio to baseline values}) - 1) \times 100$. Full analysis set (FAS) – All subjects in the extension study who were in FAS in either study LCQ908A2212 or LCQ908B2302. At each time point post-baseline, only patients with a value at both baseline and the post-dose time point are included.

End point type	Secondary
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End point timeframe:

Baseline, Week 12, 24 and 52

End point values	Placebo of pradigastat (LCQ908) regimen	20 mg pradigastat (LCQ908) regimen	40 mg pradigastat (LCQ908) regimen	pradigastat (LCQ9908) regimen- from study A2212
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	10	5
Units: percentage change				
geometric mean (geometric coefficient of variation)				
Change in week 12 (n=10,11,10,5)	-23.11 (± 53.05)	-17.85 (± 62.48)	53.09 (± 44.83)	-46.58 (± 128.38)
change in week 24 (n=10,10,9,5)	-20.35 (± 80.16)	-30.44 (± 62.01)	36.18 (± 64.97)	-42.74 (± 108.73)
change in week 52 (n=9,8,9,5)	-16.99 (± 43.34)	-7.69 (± 54.21)	79.15 (± 49.37)	-18.29 (± 104.77)

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline in Apolipoprotein A1 levels up to 52 weeks

End point title	Changes from baseline in Apolipoprotein A1 levels up to 52 weeks
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End point description:

Fasting blood samples were collected by direct venipuncture or an indwelling cannula to evaluate the drug effect on lipoprotein biomarkers such as Apolipoprotein A1. For patients from LCQ908 arm of study CLCQ908A2212, baseline was the assessment obtained at Week 0 of current study. For patients from study CLCQ908B2302, baseline is defined as the average of values taken Day -3 and Week 0 (randomization) in study CLCQ908B2302. The geometric mean for the percentage (%) change is calculated from back-transforming the mean of the log transformed ratio to baseline values: $(\exp(\text{mean of the log-transformed ratio to baseline values}) - 1) \times 100$. Full analysis set (FAS) – All subjects in the extension study who were in FAS in either study LCQ908A2212 or LCQ908B2302. At each time point post-baseline, only patients with a value at both baseline and the post-dose time point are included.

End point type	Secondary
End point timeframe:	
Baseline, Week 12, 24 and 52	

End point values	Placebo of pradigastat (LCQ908) regimen	20 mg pradigastat (LCQ908) regimen	40 mg pradigastat (LCQ908) regimen	pradigastat (LCQ9908) regimen- from study A2212
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	10	5
Units: percentage change				
geometric mean (geometric coefficient of variation)				
Change in week 12 (n=11,11,10,5)	-3.24 (± 23.82)	2.55 (± 15.09)	6.58 (± 17.04)	2.95 (± 33.54)
change in week 24 (n=10,10,10,5)	4.8 (± 14.16)	1.41 (± 17.45)	5.57 (± 25.69)	5.11 (± 28.49)
change in week 52 (n=10,8,9,5)	4.51 (± 19.21)	10.01 (± 16.28)	4.43 (± 19.34)	-0.82 (± 16.79)

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline in Apolipoprotein B-48 levels up to 52 weeks

End point title	Changes from baseline in Apolipoprotein B-48 levels up to 52 weeks
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End point description:

Fasting blood samples were collected by direct venipuncture or an indwelling cannula to evaluate the drug effect on lipoprotein biomarkers such as Apolipoprotein B-48. For patients from LCQ908 arm of study CLCQ908A2212, baseline was the assessment obtained at Week 0 of current study. For patients from study CLCQ908B2302, baseline is defined as the average of values taken Day -3 and Week 0 (randomization) in study CLCQ908B2302. The geometric mean for the percentage (%) change is calculated from back-transforming the mean of the log transformed ratio to baseline values: $(\exp(\text{mean of the log-transformed ratio to baseline values}) - 1) \times 100$. Full analysis set (FAS) – All subjects in the extension study who were in FAS in either study LCQ908A2212 or LCQ908B2302. At each time point post-baseline, only patients with a value at both baseline and the post-dose time point are included.

End point type	Secondary
End point timeframe:	
Baseline, Week 12, 24 and 52	

End point values	Placebo of pradi­gastat (LCQ908) regimen	20 mg pradi­gastat (LCQ908) regimen	40 mg pradi­gastat (LCQ908) regimen	pradi­gastat (LCQ9908) regimen- from study A2212
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	10	5
Units: percentage change				
geometric mean (geometric coefficient of variation)				
Change in week 12 (n=11,11,10,5)	-4.03 (± 79.87)	33.24 (± 79.2)	109.67 (± 52.5)	-30.03 (± 61.78)
change in week 24 (n=10,10,10,5)	9.13 (± 30.79)	-10.23 (± 58.91)	105.52 (± 71.45)	-35.04 (± 31.11)
change in week 52 (n=10,8,9,5)	56.25 (± 57.65)	-22.63 (± 107.21)	135.33 (± 71.11)	27.75 (± 57.77)

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline in Apolipoprotein B-100 levels up to 52 weeks

End point title	Changes from baseline in Apolipoprotein B-100 levels up to 52 weeks
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End point description:

Fasting blood samples were collected by direct venipuncture or an indwelling cannula to evaluate the drug effect on lipoprotein biomarkers such as Apolipoprotein B-100. For patients from LCQ908 arm of study CLCQ908A2212, baseline was the assessment obtained at Week 0 of current study. For patients from study CLCQ908B2302, baseline is defined as the average of values taken Day -3 and Week 0 (randomization) in study CLCQ908B2302. The geometric mean for the percentage (%) change is calculated from back-transforming the mean of the log transformed ratio to baseline values: $(\exp(\text{mean of the log-transformed ratio to baseline values}) - 1) \times 100$. Full analysis set (FAS) – All subjects in the extension study who were in FAS in either study LCQ908A2212 or LCQ908B2302. At each time point post-baseline, only patients with a value at both baseline and the post-dose time point are included.

End point type	Secondary
End point timeframe:	
Baseline, Week 12, 24 and 52	

End point values	Placebo of pradi­gastat (LCQ908) regimen	20 mg pradi­gastat (LCQ908) regimen	40 mg pradi­gastat (LCQ908) regimen	pradi­gastat (LCQ9908) regimen- from study A2212
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	10	5
Units: percentage change				
geometric mean (geometric coefficient of variation)				
Change in week 12 (n=9,11,9,5)	-15.75 (± 41.5)	15.1 (± 58.53)	-8.34 (± 32.73)	3.33 (± 32.46)
change in week 24 (n=10,9,10,5)	-2.75 (± 63.1)	21.33 (± 38.76)	-18.28 (± 52.94)	11.68 (± 43.73)
change in week 52 (n=10,7,9,5)	-12.52 (± 44.16)	25.39 (± 36.77)	-10.73 (± 37.2)	10.02 (± 39.08)

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 are reported in this record from First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

Part B - 40 mg pradigastat (LCQ908) regimen had no adverse event (serious or other).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Part A-placebo of pradigastat (LCQ908) regimen
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Reporting group description:

Part A: Patients who were randomized to placebo in study CLCQ908B2302/NCT01514461. In current study, patients initiated at 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained.

Reporting group title	Part A-20mg pradigastat (LCQ908) regimen
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Reporting group description:

Part A: Patients who were randomized to LCQ908 20 mg in study CLCQ908B2302/NCT01514461. In current study, patients initiated at LCQ908 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained.

Reporting group title	Part A-40mg pradigastat (LCQ908) regimen
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Reporting group description:

Part A: Patients who were randomized to LCQ908 40 mg in study CLCQ908B2302/NCT01514461. In current study, patients initiated at LCQ908 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained.

Reporting group title	Part A: pradigastat (LCQ908) regimen- from study A2212
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Reporting group description:

Part A: Patients who were randomized to LCQ908 in study CLCQ908A2212/NCT01146522. In current study, patients initiated at LCQ908 10 mg/day. After at least 8 weeks of treatment with a dose, optional up-titration to the next possible dose was allowed. One down titration allowed from the highest dose attained.

Reporting group title	Part B-placebo of pradigastat (LCQ908) regimen
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Reporting group description:

Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.

Reporting group title	Part B-20mg pradigastat (LCQ908) regimen
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Reporting group description:

Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10 mg to 40 mg) at the investigators discretion and based on individual patients' tolerance and safety profile.

Reporting group title	Part B- pradigastat (LCQ908) regimen- from study A2212
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Reporting group description:

Part B: Patients who consented to take part in the Part B continued their treatment at the same dose as they took when they completed Part A. LCQ908 treatment could be titrated (within the dose range 10

Serious adverse events	Part A-placebo of pradigastat (LCQ908) regimen	Part A-20mg pradigastat (LCQ908) regimen	Part A-40mg pradigastat (LCQ908) regimen
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 11 (9.09%)	6 / 12 (50.00%)	2 / 10 (20.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
CORONARY ARTERY STENOSIS			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (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
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (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
Gastrointestinal disorders			
PANCREATITIS			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (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
PANCREATITIS ACUTE			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
GASTROENTERITIS			

subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (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
POSTOPERATIVE WOUND INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (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
DIABETES MELLITUS INADEQUATE CONTROL			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (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
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (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
MALNUTRITION			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part A: pradigastat (LCQ908) regimen- from study A2212	Part B-placebo of pradigastat (LCQ908) regimen	Part B-20mg pradigastat (LCQ908) regimen
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
ASPARTATE AMINOTRANSFERASE INCREASED			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
CORONARY ARTERY STENOSIS			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
PANCREATITIS			
subjects affected / exposed	2 / 5 (40.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS ACUTE			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
GASTROENTERITIS			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POSTOPERATIVE WOUND INFECTION			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DEHYDRATION			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETES MELLITUS INADEQUATE CONTROL			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MALNUTRITION			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part B- pradigastat (LCQ908) regimen- from study A2212		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
CORONARY ARTERY STENOSIS			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
ANAEMIA			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
PANCREATITIS			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PANCREATITIS ACUTE			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
GASTROENTERITIS			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
POSTOPERATIVE WOUND INFECTION			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DIABETES MELLITUS INADEQUATE CONTROL			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

MALNUTRITION			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part A-placebo of pradigastat (LCQ908) regimen	Part A-20mg pradigastat (LCQ908) regimen	Part A-40mg pradigastat (LCQ908) regimen
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)	12 / 12 (100.00%)	10 / 10 (100.00%)
Vascular disorders			
AORTIC ANEURYSM			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HOT FLUSH			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HYPERTENSION			
subjects affected / exposed	0 / 11 (0.00%)	2 / 12 (16.67%)	1 / 10 (10.00%)
occurrences (all)	0	2	1
General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
THIRST			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
VESSEL PUNCTURE SITE INDURATION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			

DYSMENORRHOEA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
ERECTILE DYSFUNCTION			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
PREMATURE MENOPAUSE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
DYSPNOEA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
PHARYNGEAL INFLAMMATION			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
PNEUMOTHORAX			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
RHINORRHOEA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
AGITATION			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
DEPRESSED MOOD			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
INSOMNIA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
STRESS			

subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0
Investigations			
CARDIAC MURMUR			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
CAROTID BRUIT			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
WEIGHT DECREASED			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
FALL			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
FIBULA FRACTURE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
LIGAMENT RUPTURE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
MUSCLE STRAIN			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
POST PROCEDURAL INFLAMMATION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
WOUND			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			

ABNORMAL PALMAR/PLANTAR CREASES subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0
Cardiac disorders CARDIAC FAILURE subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0
Nervous system disorders APHONIA subjects affected / exposed occurrences (all) DIZZINESS subjects affected / exposed occurrences (all) HEADACHE subjects affected / exposed occurrences (all) MIGRAINE subjects affected / exposed occurrences (all) PARAESTHESIA subjects affected / exposed occurrences (all) RESTLESS LEGS SYNDROME subjects affected / exposed occurrences (all) SCIATICA subjects affected / exposed occurrences (all) SYNCOPE subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 1 / 11 (9.09%) 1	0 / 12 (0.00%) 0 1 / 12 (8.33%) 1 2 / 12 (16.67%) 2 1 / 12 (8.33%) 1 0 / 12 (0.00%) 0 1 / 12 (8.33%) 1 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0	0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 2 / 10 (20.00%) 2 0 / 10 (0.00%) 0 1 / 10 (10.00%) 1 0 / 10 (0.00%) 0 2 / 10 (20.00%) 2 0 / 10 (0.00%) 0
Blood and lymphatic system disorders ANAEMIA subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0

Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
VERTIGO POSITIONAL			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	1 / 11 (9.09%)	2 / 12 (16.67%)	1 / 10 (10.00%)
occurrences (all)	1	2	1
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN			
subjects affected / exposed	2 / 11 (18.18%)	1 / 12 (8.33%)	1 / 10 (10.00%)
occurrences (all)	5	2	7
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
CONSTIPATION			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
DIARRHOEA			
subjects affected / exposed	8 / 11 (72.73%)	11 / 12 (91.67%)	5 / 10 (50.00%)
occurrences (all)	50	41	9
DYSPEPSIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
FAECAL INCONTINENCE			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
FOOD POISONING			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
GASTRITIS			

subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
NAUSEA			
subjects affected / exposed	2 / 11 (18.18%)	4 / 12 (33.33%)	3 / 10 (30.00%)
occurrences (all)	3	5	3
PANCREATITIS			
subjects affected / exposed	0 / 11 (0.00%)	2 / 12 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	6	0
PANCREATITIS ACUTE			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
STEATORRHOEA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
TONGUE CYST			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	1 / 11 (9.09%)	2 / 12 (16.67%)	1 / 10 (10.00%)
occurrences (all)	2	3	1
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
PSORIASIS			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
RASH			
subjects affected / exposed	0 / 11 (0.00%)	2 / 12 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
XANTHOMA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			

BACK PAIN			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	2 / 10 (20.00%)
occurrences (all)	1	1	2
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
MYALGIA			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
NECK PAIN			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
OSTEOARTHRITIS			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
ROTATOR CUFF SYNDROME			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
SYNOVIAL CYST			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
TENDONITIS			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
CYSTITIS			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
GASTROENTERITIS			

subjects affected / exposed	1 / 11 (9.09%)	2 / 12 (16.67%)	0 / 10 (0.00%)
occurrences (all)	1	3	0
INFLUENZA			
subjects affected / exposed	6 / 11 (54.55%)	2 / 12 (16.67%)	2 / 10 (20.00%)
occurrences (all)	7	2	2
LUNG INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
NASOPHARYNGITIS			
subjects affected / exposed	4 / 11 (36.36%)	4 / 12 (33.33%)	0 / 10 (0.00%)
occurrences (all)	5	4	0
PNEUMONIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
POST PROCEDURAL INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
SINUSITIS			
subjects affected / exposed	1 / 11 (9.09%)	2 / 12 (16.67%)	1 / 10 (10.00%)
occurrences (all)	1	2	1
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	2
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
VAGINAL INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
VULVOVAGINAL MYCOTIC INFECTION			

subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
GOUT			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
HYPOKALAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
VITAMIN B COMPLEX DEFICIENCY			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
VITAMIN D DEFICIENCY			
subjects affected / exposed	0 / 11 (0.00%)	2 / 12 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	Part A: pradigastat (LCQ908) regimen- from study A2212	Part B-placebo of pradigastat (LCQ908) regimen	Part B-20mg pradigastat (LCQ908) regimen
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	4 / 5 (80.00%)	3 / 6 (50.00%)
Vascular disorders			
AORTIC ANEURYSM			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
HOT FLUSH			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
HYPERTENSION			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			

FATIGUE			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
THIRST			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
VESSEL PUNCTURE SITE INDURATION			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
DYSMENORRHOEA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
ERECTILE DYSFUNCTION			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PREMATURE MENOPAUSE			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
DYSPNOEA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PHARYNGEAL INFLAMMATION			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PNEUMOTHORAX			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

RHINORRHOEA subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Psychiatric disorders AGITATION subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
DEPRESSED MOOD subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
INSOMNIA subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
STRESS subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1
Investigations CARDIAC MURMUR subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
CAROTID BRUIT subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
WEIGHT DECREASED subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Injury, poisoning and procedural complications CONTUSION subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
FALL subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
FIBULA FRACTURE subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0

LIGAMENT RUPTURE subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
MUSCLE STRAIN subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
POST PROCEDURAL INFLAMMATION subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
WOUND subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Congenital, familial and genetic disorders ABNORMAL PALMAR/PLANTAR CREASES subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Cardiac disorders CARDIAC FAILURE subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Nervous system disorders APHONIA subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1
DIZZINESS subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 3	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1
HEADACHE subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
MIGRAINE subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0
PARAESTHESIA subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0

RESTLESS LEGS SYNDROME subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
SCIATICA subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
SYNCOPE subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Blood and lymphatic system disorders ANAEMIA subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Ear and labyrinth disorders EAR PAIN subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
VERTIGO POSITIONAL subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Gastrointestinal disorders ABDOMINAL DISCOMFORT subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
ABDOMINAL DISTENSION subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
ABDOMINAL PAIN subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1
ABDOMINAL PAIN UPPER subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
CONSTIPATION subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
DIARRHOEA			

subjects affected / exposed	4 / 5 (80.00%)	2 / 5 (40.00%)	1 / 6 (16.67%)
occurrences (all)	13	4	1
DYSPEPSIA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
FAECAL INCONTINENCE			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
FOOD POISONING			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
GASTRITIS			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	2 / 5 (40.00%)	2 / 5 (40.00%)	2 / 6 (33.33%)
occurrences (all)	3	2	3
PANCREATITIS			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
PANCREATITIS ACUTE			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
STEATORRHOEA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
TONGUE CYST			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
VOMITING			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

PSORIASIS			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
RASH			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
XANTHOMA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
MYALGIA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
NECK PAIN			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
OSTEOARTHRITIS			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
ROTATOR CUFF SYNDROME			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
SYNOVIAL CYST			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
TENDONITIS			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Infections and infestations			
BRONCHITIS			
subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
CYSTITIS			
subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
GASTROENTERITIS			
subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
INFLUENZA			
subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
LUNG INFECTION			
subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
NASOPHARYNGITIS			
subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	2 / 5 (40.00%) 2	1 / 6 (16.67%) 2
PNEUMONIA			
subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
POST PROCEDURAL INFECTION			
subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
SINUSITIS			
subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0
UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
VAGINAL INFECTION			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
VULVOVAGINAL MYCOTIC INFECTION			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
GOUT			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
HYPOKALAEMIA			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
VITAMIN B COMPLEX DEFICIENCY			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
VITAMIN D DEFICIENCY			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part B- pradigastat (LCQ908) regimen- from study A2212		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)		
Vascular disorders			

AORTIC ANEURYSM subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
HOT FLUSH subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
HYPERTENSION subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
General disorders and administration site conditions FATIGUE subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
NON-CARDIAC CHEST PAIN subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
THIRST subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
VESSEL PUNCTURE SITE INDURATION subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Reproductive system and breast disorders DYSMENORRHOEA subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
ERECTILE DYSFUNCTION subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
PREMATURE MENOPAUSE subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Respiratory, thoracic and mediastinal disorders			

COUGH			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
DYSPNOEA			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
PHARYNGEAL INFLAMMATION			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
PNEUMOTHORAX			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
RHINORRHOEA			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
AGITATION			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
DEPRESSED MOOD			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
INSOMNIA			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
STRESS			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Investigations			
CARDIAC MURMUR			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
CAROTID BRUIT			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
WEIGHT DECREASED			

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Injury, poisoning and procedural complications CONTUSION subjects affected / exposed occurrences (all) FALL subjects affected / exposed occurrences (all) FIBULA FRACTURE subjects affected / exposed occurrences (all) LIGAMENT RUPTURE subjects affected / exposed occurrences (all) MUSCLE STRAIN subjects affected / exposed occurrences (all) POST PROCEDURAL INFLAMMATION subjects affected / exposed occurrences (all) WOUND subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0		
Congenital, familial and genetic disorders ABNORMAL PALMAR/PLANTAR CREASES subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Cardiac disorders CARDIAC FAILURE subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Nervous system disorders APHONIA			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
DIZZINESS			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
HEADACHE			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
MIGRAINE			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
PARAESTHESIA			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
RESTLESS LEGS SYNDROME			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
SCIATICA			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
SYNCOPE			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
VERTIGO POSITIONAL			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			

ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
ABDOMINAL PAIN			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	2		
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
CONSTIPATION			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
DIARRHOEA			
subjects affected / exposed	3 / 4 (75.00%)		
occurrences (all)	18		
DYSPEPSIA			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
FAECAL INCONTINENCE			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
FOOD POISONING			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
GASTRITIS			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
NAUSEA			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
PANCREATITIS			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

PANCREATITIS ACUTE subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
STEATORRHOEA subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
TONGUE CYST subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
VOMITING subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Skin and subcutaneous tissue disorders ALOPECIA subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
PSORIASIS subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
RASH subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
XANTHOMA subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Musculoskeletal and connective tissue disorders BACK PAIN subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
MUSCULOSKELETAL PAIN subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
MYALGIA subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
NECK PAIN			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
OSTEOARTHRITIS			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
ROTATOR CUFF SYNDROME			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
SYNOVIAL CYST			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
TENDONITIS			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
CYSTITIS			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
GASTROENTERITIS			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
INFLUENZA			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
LUNG INFECTION			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
NASOPHARYNGITIS			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

PNEUMONIA	subjects affected / exposed	0 / 4 (0.00%)		
	occurrences (all)	0		
POST PROCEDURAL INFECTION	subjects affected / exposed	0 / 4 (0.00%)		
	occurrences (all)	0		
RESPIRATORY TRACT INFECTION	subjects affected / exposed	0 / 4 (0.00%)		
	occurrences (all)	0		
SINUSITIS	subjects affected / exposed	0 / 4 (0.00%)		
	occurrences (all)	0		
UPPER RESPIRATORY TRACT INFECTION	subjects affected / exposed	0 / 4 (0.00%)		
	occurrences (all)	0		
URINARY TRACT INFECTION	subjects affected / exposed	0 / 4 (0.00%)		
	occurrences (all)	0		
VAGINAL INFECTION	subjects affected / exposed	0 / 4 (0.00%)		
	occurrences (all)	0		
VULVOVAGINAL MYCOTIC INFECTION	subjects affected / exposed	0 / 4 (0.00%)		
	occurrences (all)	0		
Metabolism and nutrition disorders				
DECREASED APPETITE	subjects affected / exposed	0 / 4 (0.00%)		
	occurrences (all)	0		
GOUT	subjects affected / exposed	0 / 4 (0.00%)		
	occurrences (all)	0		
HYPOGLYCAEMIA	subjects affected / exposed	0 / 4 (0.00%)		
	occurrences (all)	0		
HYPOKALAEMIA				

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
VITAMIN B COMPLEX DEFICIENCY			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
VITAMIN D DEFICIENCY			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 April 2014	Amendment was issued 25 months after study start was introduced to extend the trial duration of CLCQ908B2305 from 52 weeks to 130 weeks to allow the patients in LCQ908B2305 to continue their treatment with pradigastat after they completed the original 52 week study. Following amendment 2, the original 52 week duration became Part A of LCQ908B2305 and the 78 week extension became Part B, together, the total duration of LCQ908B2305 was 130 weeks. In addition, as a part of this amendment, a change was made to allow additional interim analyses during this extended trial as needed for evaluation of efficacy and safety of pradigastat. All changes made to the protocol in amendment 2 had no impact on patient safety, the scientific validity of the trial or overall study objectives. Patients were re-consented with a revised informed consent form for the additional study Part B, as per this amendment.
24 February 2015	Amendment was issued almost 3 years after study start was introduced to implement the sponsor's decision to end the CLCQ908B2305 extension trial (Part B) at the same time as the last patient in Part A completed 52 weeks. The findings from the December 2014 interim analysis suggested that the size of benefit that was anticipated from continued participation of patients in the 18 month extension trial (Part B) no longer supported trial extension beyond Part A.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

As the anticipated benefit from the continued participation of patients in 18 month extension (Part B) was not supported by results of the December 2014 interim analysis, Novartis decided to terminate the Part B to be effective as of May 31, 2015.

Notes: