



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 |
|-----------------------|--------------|

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 |
|------------------|------------------------------------|

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 |
|------------------|------------------------------------|

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 |
|------------------|---|

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 |
|------------------|------------------------------------|

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 |
|------------------|------------------------------------|

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 (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 |
|-----------------------|--|

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] |
|-----------------|---|

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 |
|----------------|---------|

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 |
|-----------------|---|

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 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) | 1.63 (± 45.19) | -5.8 (± 66.1) | 43.94 (± 52.66) | -19.36 (± 42.82) |
| change in week 24 (n=10,10,9,5) | -14.59 (± 52.33) | -36.19 (± 64.8) | 32.54 (± 87.83) | -26.05 (± 31.5) |
| change in week 52 (n=9,8,9,5) | 16.46 (± 29.27) | -30.03 (± 78.52) | 92.15 (± 60.21) | -9.2 (± 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 |
|-----------------|--|

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 |
|-----------------|--|

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 |
|-----------------|---|

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(mean of the log-transformed ratio to baseline values) - 1)*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) | -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 |
|-----------------|--|

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 |
|----------------|-----------|

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 |
|-----------------|--|

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 |
|-----------------|--|

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 |
|-----------------|---|

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 |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 18.0 |

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Part A-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.

| | |
|-----------------------|--|
| Reporting group title | Part A-20mg 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.

| | |
|-----------------------|--|
| Reporting group title | Part A-40mg 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.

| | |
|-----------------------|--|
| Reporting group title | Part A: pradigastat (LCQ908) 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.

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

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 |
|-----------------------|--|

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 |
|-----------------------|--|

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 occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 12 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| GOUT | | | |
| subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 12 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| HYPOGLYCAEMIA | | | |
| subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 12 (8.33%) 1 | 0 / 10 (0.00%) 0 |
| HYPOKALAEMIA | | | |
| subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 12 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| VITAMIN B COMPLEX DEFICIENCY | | | |
| subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 12 (8.33%) 1 | 0 / 10 (0.00%) 0 |
| VITAMIN D DEFICIENCY | | | |
| subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 2 / 12 (16.67%) 2 | 0 / 10 (0.00%) 0 |

| Non-serious adverse events | Part A: pradiastat (LCQ908) regimen- from study A2212 | Part B-placebo of pradiastat (LCQ908) regimen | Part B-20mg pradiastat (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 occurrences (all) | 1 / 5 (20.00%) 1 | 0 / 5 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| HOT FLUSH | | | |
| subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 5 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| HYPERTENSION | | | |
| subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 6 (0.00%) 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 | 0 / 5 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| BRONCHITIS | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CYSTITIS | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INFLUENZA | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LUNG INFECTION | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 2 / 5 (40.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 2 | 2 |
| PNEUMONIA | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| POST PROCEDURAL INFECTION | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SINUSITIS | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 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 | <p>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.</p> <p>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.</p> |
| 24 February 2015 | <p>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.</p> |

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: