# Clinical trial results:
# A Randomized, Patient and Investigator Blinded, Placebo Controlled, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics and Efficacy of LMB763 in Patients With Non-alcoholic Steatohepatitis (NASH)

## Summary

| | |
|---|---|
| EudraCT number | 2016-002833-31 |
| Trial protocol | GB |
| Global end of trial date | 04 March 2019 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 09 October 2019 |
| First version publication date | 09 October 2019 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | CLMB763X2201 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02913105 |
| 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 Pharmaceuticals AG, +41 613241111, |
| Scientific contact | Clinical Disclosure Office, Novartis Pharmaceuticals 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 | 04 March 2019 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 04 March 2019 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

- To determine the safety and tolerability of LMB763 during 12 weeks of treatment
- To determine the effect of LMB763 on circulating alanine aminotransferase (ALT) levels

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 | 24 October 2016 |
| 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 | Australia: 3 |
| Country: Number of subjects enrolled | Jordan: 15 |
| Country: Number of subjects enrolled | New Zealand: 21 |
| Country: Number of subjects enrolled | Switzerland: 7 |
| Country: Number of subjects enrolled | United States: 72 |
| Country: Number of subjects enrolled | United Kingdom: 3 |
| Worldwide total number of subjects | 121 |
| EEA total number of subjects | 3 |

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) | 110 |
| From 65 to 84 years | 11 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted in 25 centres across 6 countries.

### Pre-assignment

Screening details:

A total of 121 subjects were enrolled in the study, and included in the safety population. Placebo data have been pooled from placebo treated subjects from both cohorts (100 mg and 50 mg matching placebo).

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | LMB763 100 mg |

Arm description:

LMB763 100 mg capsules, orally, once daily for 12 weeks (84 days) under fasted conditions (no food or drink for at least 6 hours).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | LMB763 100 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

LMB763 100 mg capsules, orally, once daily for 12 weeks (84 days) under fasted conditions (no food or drink for at least 6 hours).

| | |
|---|---|
| **Arm title** | LMB763 50 mg |

Arm description:

LMB763 50 mg (2 x 25 mg) capsules, orally, once daily for 12 weeks (84 days) under fasted conditions (no food or drink for at least 6 hours).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | LMB763 50 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

LMB763 50 mg (2 x 25 mg) capsules, orally, once daily for 12 weeks (84 days) under fasted conditions (no food or drink for at least 6 hours).

| | |
|---|---|
| **Arm title** | Pooled Placebo |

Arm description:

LMB763 100 mg or 50 mg matching placebo capsules, orally, once daily for 12 weeks (84 days) under fasted conditions (no food or drink for at least 6 hours).

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Pooled Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

LMB763 100 mg or 50 mg matching placebo capsules, orally, once daily for 12 weeks (84 days) under fasted conditions (no food or drink for at least 6 hours)

| **Number of subjects in period 1** | LMB763 100 mg | LMB763 50 mg | Pooled Placebo |
|---|---|---|---|
| Started | 37 | 44 | 40 |
| Completed | 22 | 39 | 33 |
| Not completed | 15 | 5 | 7 |
| Physician decision | 1 | 1 | - |
| Adverse event, non-fatal | 11 | - | 4 |
| Reason Not Specified | 3 | 1 | 1 |
| Non-Compliance With Study Drug | - | - | 1 |
| Withdrawal by Subject | - | 3 | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | LMB763 100 mg |
| Reporting group description: | |
| LMB763 100 mg capsules, orally, once daily for 12 weeks (84 days) under fasted conditions (no food or drink for at least 6 hours). | |
| Reporting group title | LMB763 50 mg |
| Reporting group description: | |
| LMB763 50 mg (2 x 25 mg) capsules, orally, once daily for 12 weeks (84 days) under fasted conditions (no food or drink for at least 6 hours). | |
| Reporting group title | Pooled Placebo |
| Reporting group description: | |
| LMB763 100 mg or 50 mg matching placebo capsules, orally, once daily for 12 weeks (84 days) under fasted conditions (no food or drink for at least 6 hours). | |

| Reporting group values | LMB763 100 mg | LMB763 50 mg | Pooled Placebo |
|---|---|---|---|
| Number of subjects | 37 | 44 | 40 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 30 | 44 | 36 |
| From 65-84 years | 7 | 0 | 4 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 51.3 | 49.5 | 51.6 |
| standard deviation | ± 15.55 | ± 8.45 | ± 11.65 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 22 | 23 | 24 |
| Male | 15 | 21 | 16 |

| Reporting group values | Total | | |
|---|---|---|---|
| Number of subjects | 121 | | |
| Age categorical<br>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) | 110 | | |
| From 65-84 years | 11 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 69 | | |
| Male | 52 | | |

## End points

### End points reporting groups

| Reporting group title | LMB763 100 mg |
|---|---|

Reporting group description:

LMB763 100 mg capsules, orally, once daily for 12 weeks (84 days) under fasted conditions (no food or drink for at least 6 hours).

| Reporting group title | LMB763 50 mg |
|---|---|

Reporting group description:

LMB763 50 mg (2 x 25 mg) capsules, orally, once daily for 12 weeks (84 days) under fasted conditions (no food or drink for at least 6 hours).

| Reporting group title | Pooled Placebo |
|---|---|

Reporting group description:

LMB763 100 mg or 50 mg matching placebo capsules, orally, once daily for 12 weeks (84 days) under fasted conditions (no food or drink for at least 6 hours).

| Subject analysis set title | LMB763 100 mg |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Pharmacokinetic (PK) analysis set included all subjects with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and with no protocol deviations that impact on PK data.

| Subject analysis set title | LMB763 50 mg |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

PK analysis set included all subjects with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and with no protocol deviations that impact on PK data.

### Primary: Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

| End point title | Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)[1] |
|---|---|

End point description:

An AE is defined as any untoward medical occurrence in a clinical study subject, temporally associated with the use of a study treatment, whether or not considered related to the study treatment. An SAE is defined as any untoward medical occurrence that, at any dose that results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent disability/incapacity, is a congenital anomaly/birth defect or any other situation as per Medical or scientific judgment. Safety analysis set included all subjects that received at least one dose of study drug.

| End point type | Primary |
|---|---|

End point timeframe:

From date of first subject first treatment until Last Patient Last Visit (LPLV) (up to Day 112 (End of Study (EOS))

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: No statistical analysis was planned for this end point

| End point values | LMB763 100 mg | LMB763 50 mg | Pooled Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 37[2] | 44[3] | 40[4] | |
| Units: subjects | | | | |
| AEs | 35 | 37 | 33 | |
| SAEs | 2 | 3 | 0 | |

Notes:

[2] - Safety analysis set.

[3] - Safety analysis set.

[4] - Safety analysis set.

### Statistical analyses

No statistical analyses for this end point

## Primary: Change From Baseline in Alanine Aminotransferase (ALT) Levels

| End point title | Change From Baseline in Alanine Aminotransferase (ALT) Levels |
|---|---|

End point description:

ALT level assessment was one of the diagnostic parameters in Liver function test (LFT). Baseline was defined as the mean of ALT levels at baseline and pre-dose visits. Geometric Mean and Geometric Coefficient of Variation for change are based on log-transformed ratio to baseline (i.e., change from baseline in the log domain). Pharmacodynamic (PD) analysis set included all subjects with available PD data and no protocol deviations with relevant impact on PD data. 'n' represents the number of subjects in each category with a value at both Baseline and that time point.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline to Day 84 (Week 12)

| End point values | LMB763 100 mg | LMB763 50 mg | Pooled Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 37[5] | 44[6] | 40[7] | |
| Units: units per litre (U/L) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Baseline for Day 84 Analysis | 67.215 (± 30.8) | 48.114 (± 42.2) | 59.544 (± 39.5) | |
| Change from Baseline at Day 84 | 0.667 (± 33.8) | 0.702 (± 41.1) | 0.901 (± 25.5) | |

Notes:

[5] - PD analysis set: n = 24, 24

[6] - PD analysis set: n = 40, 40

[7] - PD analysis set: n = 33, 33

### Statistical analyses

| Statistical analysis title | LMB763 100 mg, LMB763 50 mg |
|---|---|
| Comparison groups | LMB763 100 mg v LMB763 50 mg |

| | |
|---|---|
| Number of subjects included in analysis | 81 |
| Analysis specification | Pre-specified |
| Analysis type | other[8] |
| P-value | = 0.7489 [9] |
| Method | ANCOVA |
| Parameter estimate | Geometric Mean Ratios |
| Point estimate | 0.97 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.83 |
| upper limit | 1.13 |

Notes:

[8] - Log transformed ratio to baseline was analyzed using a repeated measures model which included effects for treatment, visit, treatment by visit interaction, stratification factor (Body Mass Index (BMI) group), log-transformed baseline and log-transformed baseline by visit interaction. BMI was separated into two groups low BMI (Asian<30 and Non-Asian<35) and high BMI (Asian >=30 and Non-Asian>=35).

[9] - An unstructured variance-covariance structure was used.

| **Statistical analysis title** | LMB763 100 mg, Pooled Placebo |
|---|---|
| Comparison groups | LMB763 100 mg v Pooled Placebo |
| Number of subjects included in analysis | 77 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[10] |
| P-value | = 0.0005 [11] |
| Method | ANCOVA |
| Parameter estimate | Geometric Mean Ratios |
| Point estimate | 0.72 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.62 |
| upper limit | 0.84 |

Notes:

[10] - Log transformed ratio to baseline was analyzed using a repeated measures model which included effects for treatment, visit, treatment by visit interaction, stratification factor (BMI group), log-transformed baseline and log-transformed baseline by visit interaction. BMI was separated into two groups low BMI (Asian<30 and Non-Asian<35) and high BMI (Asian >=30 and Non-Asian>=35).

[11] - An unstructured variance-covariance structure was used.

| **Statistical analysis title** | LMB763 50 mg, Pooled Placebo |
|---|---|
| Comparison groups | LMB763 50 mg v Pooled Placebo |
| Number of subjects included in analysis | 84 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[12] |
| P-value | = 0.0005 [13] |
| Method | ANCOVA |
| Parameter estimate | Geometric Mean Ratios |
| Point estimate | 0.74 |

| Confidence interval | |
|---|---|
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.65 |
| upper limit | 0.85 |

Notes:

[12] - Log transformed ratio to baseline was analyzed using a repeated measures model which included effects for treatment, visit, treatment by visit interaction, stratification factor (BMI group), log-transformed baseline and log-transformed baseline by visit interaction. BMI was separated into two groups low BMI (Asian<30 and Non-Asian<35) and high BMI (Asian >=30 and Non-Asian>=35).

[13] - An unstructured variance-covariance structure was used.

## Secondary: Observed Maximum Plasma Concentration (Cmax) of LMB763

| End point title | Observed Maximum Plasma Concentration (Cmax) of LMB763 |
|---|---|

End point description:

PK analysis set included all subjects with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and with no protocol deviations that impact on PK data. 'n' represents the number of subjects in each category with a value at both Baseline and that time point.

| End point type | Secondary |
|---|---|

End point timeframe:

Days 1 and 42

| End point values | LMB763 100 mg | LMB763 50 mg | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 37[14] | 43[15] | | |
| Units: nanograms per millilitre (ng/mL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 | 3080 (± 1360) | 1290 (± 620) | | |
| Day 42 | 2230 (± 1190) | 1290 (± 690) | | |

Notes:

[14] - PK analysis set: n = 37, 23

[15] - PK analysis set: n = 43, 42

### Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Reach Maximum Concentration (Tmax) of LMB763

| End point title | Time to Reach Maximum Concentration (Tmax) of LMB763 |
|---|---|

End point description:

PK analysis set included all subjects with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and with no protocol deviations that impact on PK data. 'n' represents the number of subjects in each category with a value at both Baseline and that time point.

| End point type | Secondary |
|---|---|

End point timeframe:

Days 1 and 42

| End point values | LMB763 100 mg | LMB763 50 mg | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 37[16] | 43[17] | | |
| Units: hour (h) | | | | |
| median (full range (min-max)) | | | | |
| Day 1 | 2.00 (1.00 to 6.00) | 2.00 (1.00 to 6.08) | | |
| Day 42 | 2.03 (1.00 to 6.03) | 2.02 (1.00 to 6.00) | | |

Notes:

[16] - Pk analysis set: n = 37, 24

[17] - Pk analysis set: n = 43, 42

### Statistical analyses

No statistical analyses for this end point

## Secondary: Area Under Plasma Concentration-time Curve From Time Zero to Time of Last Quantifiable Concentration (AUClast) of LMB763

| End point title | Area Under Plasma Concentration-time Curve From Time Zero to Time of Last Quantifiable Concentration (AUClast) of LMB763 |
|---|---|

End point description:

PK analysis set included all subjects with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and with no protocol deviations that impact on PK data. 'n' represents the number of subjects in each category with a value at both Baseline and that time point.

| End point type | Secondary |
|---|---|

End point timeframe:

Days 1 and 42

| End point values | LMB763 100 mg | LMB763 50 mg | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 37[18] | 43[19] | | |
| Units: h*ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 | 11200 (± 4740) | 4360 (± 2350) | | |
| Day 42 | 8570 (± 4120) | 5180 (± 2870) | | |

Notes:

[18] - Pk analysis set: n = 37, 23

[19] - Pk analysis set: n = 42, 42

### Statistical analyses

No statistical analyses for this end point

## Secondary: Accumulation Ratio (Racc) of LMB763

| End point title | Accumulation Ratio (Racc) of LMB763 |
|---|---|

End point description:

PK analysis set included all subjects with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and with no protocol deviations that impact on PK data.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 42

| **End point values** | LMB763 100 mg | LMB763 50 mg | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 24[20] | 42[21] | | |
| Units: ratio | | | | |
| arithmetic mean (standard deviation) | 0.903 (± 0.472) | 1.31 (± 0.641) | | |

Notes:

[20] - PD analysis set.

[21] - PD analysis set.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Percentage of Liver Fat as Measured by Magnetic Resonance Imaging (MRI)

| End point title | Change From Baseline in Percentage of Liver Fat as Measured by Magnetic Resonance Imaging (MRI) |
|---|---|

End point description:

Subjects were to undergo MRI twice (Baseline and End of Treatment) during the course of the study to quantitate liver fat. Baseline was defined as the last available measurement prior to the first dose. Geometric Mean and Geometric Coefficient of Variation for change are based on log-transformed ratio to baseline (i.e., change from baseline in the log domain). PD analysis set included all subjects with available PD data and no protocol deviations with relevant impact on PD data. 'n' represents the number of subjects in each category with a value at both Baseline and that time point.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline to Day 84 (Week 12)

| **End point values** | LMB763 100 mg | LMB763 50 mg | Pooled Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 35[22] | 44[23] | 39[24] | |
| Units: percentage of liver fat | | | | |
| geometric mean (geometric coefficient of variation) | | | | |

| | | | | |
|---|---|---|---|---|
| Baseline for Day 84 Analysis | 18.751 (± 37.4) | 17.715 (± 42.6) | 17.476 (± 73.9) | |
| Change from Baseline at Day 84 | 0.648 (± 29.3) | 0.681 (± 38.6) | 0.962 (± 22.2) | |

Notes:

[22] - PD analysis set: n = 22, 22

[23] - PD analysis set: n = 41, 41

[24] - PD analysis set: n = 32, 32

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Weight

| End point title | Change From Baseline in Weight |
|---|---|

End point description:

Baseline was defined as the last available measurement prior to the first dose. PD analysis set included all subjects with available PD data and no protocol deviations with relevant impact on PD data. 'n' represents the number of subjects in each category with a value at both Baseline and that time point.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline to Days 28, 42, 56, 84 and 112 (EOS)

| End point values | LMB763 100 mg | LMB763 50 mg | Pooled Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 37[25] | 44[26] | 40[27] | |
| Units: kilogram (kg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline for Day 28 Analysis | 99.07 (± 22.560) | 97.82 (± 17.829) | 95.47 (± 22.921) | |
| Change from Baseline at Day 28 | -0.78 (± 1.591) | -0.71 (± 1.725) | -0.17 (± 1.516) | |
| Baseline for Day 42 Analysis | 96.89 (± 22.135) | 97.82 (± 17.829) | 95.30 (± 23.465) | |
| Change from Baseline at Day 42 | -1.04 (± 1.683) | -1.08 (± 2.335) | -0.24 (± 1.677) | |
| Baseline for Day 56 Analysis | 97.07 (± 22.555) | 97.86 (± 18.043) | 95.71 (± 23.244) | |
| Change from Baseline at Day 56 | -1.39 (± 1.970) | -1.39 (± 2.188) | -0.26 (± 1.777) | |
| Baseline for Day 84 Analysis | 97.34 (± 23.370) | 97.11 (± 17.905) | 95.91 (± 23.563) | |
| Change from Baseline at Day 84 | -1.47 (± 2.169) | -2.02 (± 3.451) | -0.21 (± 1.989) | |
| Baseline for Day 112 (EOS) Analysis | 98.74 (± 23.941) | 95.38 (± 14.810) | 95.85 (± 23.926) | |
| Change from Baseline at Day 112 (EOS) | -1.26 (± 3.014) | -1.66 (± 3.543) | 0.35 (± 2.125) | |

Notes:

[25] - PD analysis set. n = 30, 30, 27, 27, 26, 26, 24, 24, 22, 22

[26] - PD analysis set. n = 43, 43, 43, 43, 42, 42, 40, 40, 39, 39

[27] - PD analysis set. n = 37, 37, 34, 34, 35, 35, 34, 34, 33, 33

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Body Mass Index (BMI)

| End point title | Change From Baseline in Body Mass Index (BMI) |
|---|---|

End point description:

Baseline was defined as the last available measurement prior to the first dose at specified visit (day). PD analysis set included all subjects with available PD data and no protocol deviations with relevant impact on PD data. 'n' represents the number of subjects in each category with a value at both Baseline and that time point.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline to Days 28, 42, 56, 84 and 112 (EOS)

| **End point values** | LMB763 100 mg | LMB763 50 mg | Pooled Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 37[28] | 44[29] | 40[30] | |
| Units: kilograms per metre square (kg/m^2) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline for Day 28 Analysis | 34.81 (± 5.641) | 34.41 (± 5.270) | 34.93 (± 5.180) | |
| Change from Baseline at Day 28 | -0.29 (± 0.545) | -0.26 (± 0.638) | -0.05 (± 0.511) | |
| Baseline for Day 42 Analysis | 34.05 (± 5.162) | 34.41 (± 5.270) | 34.56 (± 5.233) | |
| Change from Baseline at Day 42 | -0.36 (± 0.591) | -0.40 (± 0.845) | -0.08 (± 0.572) | |
| Baseline for Day 56 Analysis | 34.12 (± 5.253) | 34.37 (± 5.327) | 34.75 (± 5.269) | |
| Change from Baseline at Day 56 | -0.50 (± 0.688) | -0.49 (± 0.799) | -0.10 (± 0.663) | |
| Baseline for Day 84 Analysis | 34.18 (± 5.467) | 34.04 (± 5.190) | 34.89 (± 5.275) | |
| Change from Baseline at Day 84 | -0.52 (± 0.764) | -0.72 (± 1.215) | -0.09 (± 0.718) | |
| Baseline for Day 112 (EOS) Analysis | 34.60 (± 5.522) | 33.82 (± 4.980) | 34.96 (± 5.342) | |
| Change from Baseline at Day 112 (EOS) | -0.45 (± 0.974) | -0.60 (± 1.276) | 0.12 (± 0.776) | |

Notes:

[28] - PD analysis set. n = 30, 30, 27, 27, 26, 26, 24, 24, 22, 22

[29] - PD analysis set. n = 43, 43, 43, 43, 42, 42, 40, 40, 39, 39

[30] - PD analysis set. n = 37, 37, 34, 34, 35, 35, 34, 34, 33, 33

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Waist to Hip Ratio

| End point title | Change From Baseline in Waist to Hip Ratio |
|---|---|

End point description:

Baseline was defined as the last available measurement prior to the first dose. PD analysis set included all subjects with available PD data and no protocol deviations with relevant impact on PD data. 'n' represents the number of subjects in each category with a value at both Baseline and that time point.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline to Days 28, 42, 56, 84 and 112 (EOS)

| **End point values** | LMB763 100 mg | LMB763 50 mg | Pooled Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 37[31] | 44[32] | 40[33] | |
| Units: ratio | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline for Day 28 Analysis | 0.96 (± 0.065) | 0.96 (± 0.055) | 0.95 (± 0.089) | |
| Change from Baseline at Day 28 | 0.00 (± 0.039) | 0.00 (± 0.034) | -0.00 (± 0.039) | |
| Baseline for Day 42 Analysis | 0.96 (± 0.061) | 0.95 (± 0.056) | 0.96 (± 0.086) | |
| Change from Baseline at Day 42 | 0.01 (± 0.077) | -0.00 (± 0.039) | 0.00 (± 0.036) | |
| Baseline for Day 56 Analysis | 0.96 (± 0.061) | 0.96 (± 0.054) | 0.96 (± 0.087) | |
| Change from Baseline at Day 56 | -0.00 (± 0.029) | -0.00 (± 0.033) | -0.01 (± 0.029) | |
| Baseline for Day 84 Analysis | 0.95 (± 0.063) | 0.96 (± 0.055) | 0.96 (± 0.087) | |
| Change from Baseline at Day 84 | 0.00 (± 0.043) | -0.01 (± 0.044) | 0.01 (± 0.046) | |
| Baseline for Day 112 (EOS) Analysis | 0.96 (± 0.059) | 0.96 (± 0.054) | 0.96 (± 0.087) | |
| Change from Baseline at Day 112 (EOS) | -0.00 (± 0.030) | 0.00 (± 0.050) | -0.00 (± 0.037) | |

Notes:

[31] - PD analysis set. n = 30, 30, 27, 27, 25, 25, 24, 24, 22, 22

[32] - PD analysis set. n = 43, 43, 40, 40, 42, 42, 40, 40, 39, 39

[33] - PD analysis set. n = 36, 36, 34, 34, 34, 34 , 34, 34, 33, 33

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From to Baseline in Liver Stiffness

| End point title | Change From to Baseline in Liver Stiffness |
|---|---|

End point description:

Fibroscan® was performed where available to assess liver stiffness. Baseline was defined as the last available measurement prior to the first dose. Geometric Mean and Geometric Coefficient of Variation for change are based on log-transformed ratio to baseline (i.e., change from baseline in the log domain). PD analysis set included all subjects with available PD data and no protocol deviations with relevant impact on PD data.'n' represents the number of subjects in each category with a value at both Baseline and that time point.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline to Day 84 (Week 12)

| End point values | LMB763 100 mg | LMB763 50 mg | Pooled Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 10[34] | 17[35] | 18[36] | |
| Units: kilopascal (kPa) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Baseline for Day 84 Analysis | 7.689 (± 71.1) | 6.082 (± 29.5) | 7.108 (± 52.5) | |
| Change from Baseline at Day 84 | 0.955 (± 35.3) | 1.053 (± 26.9) | 1.041 (± 38.6) | |

Notes:

[34] - PD analysis set: n = 7, 7

[35] - PD analysis set: n = 15, 15

[36] - PD analysis set: n = 16, 16

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Enhanced Liver Fibrosis (ELF) Test Panel

| End point title | Change From Baseline in Enhanced Liver Fibrosis (ELF) Test Panel |
|---|---|

End point description:

Enhanced liver fibrosis test (ELF) panel included hyaluronic acid (HA), tissue inhibitor of metalloproteinases (TIMP-1), and amino-terminal pro-peptide of procollagen type III (PIIINP) as markers of liver fibrosis. Baseline was defined as the last available measurement prior to the first dose. Geometric Mean and Geometric Coefficient of Variation for change are based on log-transformed ratio to baseline (i.e., change from baseline in the log domain). PD analysis set included all subjects with available PD data and no protocol deviations with relevant impact on PD data. 'n' represents the number of subjects in each category with a value at both Baseline and that time point.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline to Days 42 and 84

| End point values | LMB763 100 mg | LMB763 50 mg | Pooled Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 37[37] | 44[38] | 40[39] | |
| Units: ELF score | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Baseline for Day 42 Analysis | 9.063 (± 7.3) | 8.731 (± 8.2) | 9.212 (± 8.0) | |
| Change from Baseline at Day 42 | 1.005 (± 5.5) | 1.016 (± 5.8) | 1.009 (± 7.5) | |
| Baseline for Day 84 Analysis | 9.051 (± 7.7) | 8.739 (± 8.4) | 9.220 (± 7.8) | |
| Change from Baseline at Day 84 | 1.005 (± 5.9) | 1.030 (± 6.2) | 1.007 (± 6.3) | |

Notes:

[37] - PD analysis set. n = 26, 26, 24, 24

[38] - PD analysis set. n = 42, 42, 37, 37

[39] - PD analysis set. n = 33, 33, 33, 33

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Fibrosis Biomarker Test

| End point title | Change From Baseline in Fibrosis Biomarker Test |
|---|---|

End point description:

Fibrosis Biomarker test included hyaluronic acid (HA), amino-terminal pro-peptide of procollagen type III (PIIINP), and tissue inhibitor of metalloproteinases (TIMP-1) as markers of liver fibrosis. Baseline was defined as the last available measurement prior to the first dose. Geometric Mean and Geometric Coefficient of Variation for change are based on log-transformed ratio to baseline (i.e., change from baseline in the log domain). PD analysis set included all subjects with available PD data and no protocol deviations with relevant impact on PD data. 'n' represents the number of subjects in each category with a value at both Baseline and that time point.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline to Days 42 and 84

| End point values | LMB763 100 mg | LMB763 50 mg | Pooled Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 37[40] | 44[41] | 40[42] | |
| Units: micrograms per litre (ug/L) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| HA: Baseline for Day 42 Analysis | 33.646 (± 72.2) | 26.869 (± 75.4) | 39.282 (± 74.9) | |
| HA: Change from Baseline at Day 42 | 1.002 (± 49.5) | 1.133 (± 54.4) | 1.111 (± 77.0) | |
| HA: Baseline for Day 84 Analysis | 32.246 (± 72.9) | 27.320 (± 78.2) | 40.865 (± 79.5) | |
| HA: Change from Baseline at Day 84 | 1.023 (± 54.0) | 1.254 (± 51.4) | 1.071 (± 64.9) | |
| PIIINP: Baseline for Day 42 Analysis | 9.023 (± 31.3) | 7.850 (± 28.2) | 9.087 (± 35.5) | |
| PIIINP: Change from Baseline at Day 42 | 1.016 (± 22.8) | 1.071 (± 24.3) | 1.010 (± 26.4) | |
| PIIINP: Baseline for Day 84 Analysis | 9.263 (± 34.6) | 7.859 (± 27.4) | 8.934 (± 32.3) | |
| PIIINP: Change from Baseline at Day 84 | 1.003 (± 21.2) | 1.048 (± 26.9) | 1.004 (± 20.1) | |
| TIMP-1: Baseline for Day 42 Analysis | 242.99 (± 17.5) | 199.21 (± 78.4) | 254.37 (± 23.1) | |
| TIMP-1: Change from Baseline at Day 42 | 1.060 (± 14.6) | 1.017 (± 11.9) | 0.995 (± 13.3) | |
| TIMP-1: Baseline for Day 84 Analysis | 247.42 (± 18.8) | 193.32 (± 83.6) | 245.09 (± 20.5) | |
| TIMP-1: Change from Baseline at Day 84 | 1.073 (± 17.0) | 1.036 (± 10.4) | 1.000 (± 19.2) | |

Notes:

[40] - PD analysis set. n = 26, 26, 24, 24, 26, 26, 24, 24, 26, 26, 24,24

[41] - PD analysis set. n = 43, 43, 38, 38, 43, 43, 38, 38, 43, 43, 38, 38

[42] - PD analysis set. n = 33, 33, 33, 33, 33, 33, 33, 33, 33, 33, 33, 33

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Fasting Lipid Profile: Cholesterol (Chol) and Triglycerides (TG)

| End point title | Change From Baseline in Fasting Lipid Profile: Cholesterol (Chol) and Triglycerides (TG) |
|---|---|

End point description:

Lipid measurements were collected under fasted conditions. Baseline was defined as the last available measurement prior to the first dose. Geometric Mean and Geometric Coefficient of Variation for change are based on log-transformed ratio to baseline (i.e., change from baseline in the log domain). PD analysis set included all subjects with available PD data and no protocol deviations with relevant impact on PD data. 'n' represents the number of subjects in each category with a value at both Baseline and that time point.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline to Days 7, 14, 28, 42, 56, 84 and 112 (EOS)

| End point values | LMB763 100 mg | LMB763 50 mg | Pooled Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 37[43] | 44[44] | 40[45] | |
| Units: milligrams per decilitre (mg/dL) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Chol: Baseline for Day 7 Analysis | 184.85 (± 23.0) | 183.30 (± 22.1) | 188.97 (± 22.0) | |
| Chol: Change from Baseline at Day 7 | 0.957 (± 14.5) | 1.001 (± 9.0) | 1.002 (± 10.2) | |
| Chol: Baseline for Day 14 Analysis | 186.57 (± 23.1) | 183.30 (± 22.1) | 188.97 (± 22.0) | |
| Chol: Change from Baseline at Day 14 | 0.963 (± 17.0) | 1.037 (± 11.8) | 1.000 (± 10.4) | |
| Chol: Baseline for Day 28 Analysis | 188.09 (± 23.2) | 183.50 (± 22.3) | 190.44 (± 22.4) | |
| Chol: Change from Baseline at Day 28 | 0.952 (± 15.2) | 1.025 (± 14.6) | 1.007 (± 12.2) | |
| Chol: Baseline for Day 42 Analysis | 206.50 (± 18.3) | 182.59 (± 22.3) | 191.65 (± 21.1) | |
| Chol: Change from Baseline at Day 42 | 0.943 (± 17.2) | 1.001 (± 15.1) | 0.940 (± 14.2) | |
| Chol: Baseline for Day 56 Analysis | 192.25 (± 22.5) | 182.39 (± 22.5) | 190.33 (± 21.0) | |
| Chol: Change from Baseline at Day 56 | 0.963 (± 17.2) | 1.033 (± 16.1) | 1.002 (± 15.2) | |
| Chol: Baseline for Day 84 Analysis | 188.88 (± 22.0) | 181.63 (± 22.4) | 187.20 (± 23.6) | |
| Chol: Change from Baseline at Day 84 | 0.958 (± 17.9) | 1.037 (± 18.9) | 1.006 (± 13.5) | |
| Chol: Baseline for Day 112 (EOS) Analysis | 187.34 (± 22.8) | 181.47 (± 22.0) | 187.13 (± 23.1) | |

| | | | | |
|---|---|---|---|---|
| Chol: Change from Baseline at Day 112 (EOS) | 0.989 (± 13.6) | 1.039 (± 16.8) | 1.009 (± 13.2) | |
| TG: Baseline for Day 7 Analysis | 185.66 (± 55.0) | 198.88 (± 47.8) | 175.18 (± 58.7) | |
| TG: Change from Baseline at Day 7 | 0.876 (± 38.8) | 0.854 (± 25.8) | 1.020 (± 28.6) | |
| TG: Baseline for Day 14 Analysis | 178.22 (± 50.5) | 198.88 (± 47.8) | 175.18 (± 58.7) | |
| TG: Change from Baseline at Day 14 | 0.864 (± 36.2) | 0.881 (± 28.1) | 1.013 (± 35.9) | |
| TG: Baseline for Day 28 Analysis | 166.54 (± 45.0) | 201.00 (± 47.7) | 177.66 (± 60.6) | |
| TG: Change from Baseline at Day 28 | 0.968 (± 36.4) | 0.937 (± 37.0) | 0.971 (± 33.7) | |
| TG: Baseline for Day 42 Analysis | 181.97 (± 44.6) | 203.65 (± 47.4) | 174.48 (± 64.4) | |
| TG: Change from Baseline at Day 42 | 0.868 (± 34.5) | 0.872 (± 36.1) | 0.920 (± 35.2) | |
| TG: Baseline for Day 56 Analysis | 167.66 (± 47.5) | 202.64 (± 48.8) | 174.78 (± 60.6) | |
| TG: Change from Baseline at Day 56 | 0.932 (± 34.2) | 0.948 (± 38.9) | 0.965 (± 28.1) | |
| TG: Baseline for Day 84 Analysis | 163.71 (± 48.6) | 201.96 (± 49.5) | 184.99 (± 59.7) | |
| TG: Change from Baseline at Day 84 | 0.863 (± 43.8) | 0956 (± 45.8) | 0.947 (± 33.3) | |
| TG: Baseline for Day 112 (EOS) Analysis | 172.80 (± 46.1) | 203.55 (± 49.2) | 179.36 (± 62.5) | |
| TG: Change from Baseline at Day 112 (EOS) | 0.931 (± 38.5) | 1.003 (± 39.9) | 1.039 (± 39.0) | |

Notes:

[43] - PD analysis: n=36,
36,34,34,29,29,19,19,25,25,24,24,22,22,36,36,34,34,29,29,19,19,25,25,24,24,22,22
[44] - PD analysis: n=44,
44,44,44,43,43,42,42,41,41,40,40,39,39,44,44,44,44,43,43,42,42,41,41,40,40, 39,39
[45] - PD analysis: n=40,
40,40,40,37,37,30,30,33,33,32,32,33,33,40,40,40,40,37,37,30,30,33,33,32,32,33,33

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Fasting Lipid Profile: High-density Lipoprotein (HDL) and Low-density Lipoprotein (LDL) Cholesterol

| End point title | Change From Baseline in Fasting Lipid Profile: High-density Lipoprotein (HDL) and Low-density Lipoprotein (LDL) Cholesterol |
|---|---|

End point description:

Baseline was defined as the last available measurement prior to the first dose. Geometric Mean and Geometric Coefficient of Variation for change are based on log-transformed ratio to baseline (i.e., change from baseline in the log domain). PD analysis set included all subjects with available PD data and no protocol deviations with relevant impact on PD data. 'n' represents the number of subjects in each category with a value at both Baseline and that time point.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline to Days 7, 14, 28, 42, 56, 84 and 112 (EOS)

| End point values | LMB763 100 mg | LMB763 50 mg | Pooled Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 37[46] | 44[47] | 40[48] | |
| Units: millimole per litre (mmol/L) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| HDL: Baseline for Day 7 Analysis | 1.059 (± 30.0) | 1.014 (± 25.4) | 1.206 (± 28.2) | |
| HDL: Change from Baseline at Day 7 | 0.874 (± 15.0) | 0.969 (± 10.0) | 1.017 (± 12.7) | |
| HDL: Baseline for Day 14 Analysis | 1.093 (± 24.8) | 1.014 (± 25.4) | 1.206 (± 28.2) | |
| HDL: Change from Baseline at Day 14 | 0.876 (± 19.1) | 0.982 (± 13.4) | 0.979 (± 10.0) | |
| HDL: Baseline for Day 28 Analysis | 1.143 (± 23.8) | 1.014 (± 25.7) | 1.221 (± 28.9) | |
| HDL: Change from Baseline at Day 28 | 0.862 (± 14.1) | 0.952 (± 15.1) | 1.009 (± 14.7) | |
| HDL: Baseline for Day 42 Analysis | 1.172 (± 26.9) | 1.007 (± 25.7) | 1.212 (± 30.6) | |
| HDL: Change from Baseline at Day 42 | 0.888 (± 19.4) | 0.941 (± 15.5) | 1.005 (± 12.2) | |
| HDL: Baseline for Day 56 Analysis | 1.148 (± 25.5) | 1.008 (± 25.9) | 1.226 (± 29.1) | |
| HDL: Change from Baseline at Day 56 | 0.875 (± 17.0) | 0.956 (± 15.1) | 1.022 (± 13.9) | |
| HDL: Baseline for Day 84 Analysis | 1.158 (± 24.9) | 1.016 (± 26.6) | 1.219 (± 29.7) | |
| HDL: Change from Baseline at Day 84 | 0.891 (± 16.1) | 0.920 (± 19.9) | 1.031 (± 12.5) | |
| HDL: Baseline for Day 112 (EOS) Analysis | 1.115 (± 22.1) | 1.013 (± 26.1) | 1.218 (± 29.6) | |
| HDL: Change from Baseline at Day 112 (EOS) | 1.004 (± 14.5) | 1.037 (± 17.2) | 1.007 (± 11.5) | |
| LDL: Baseline for Day 7 Analysis | 2.647 (± 39.0) | 2.591 (± 40.6) | 2.628 (± 34.2) | |
| LDL: Change from Baseline at Day 7 | 1.009 (± 18.7) | 1.076 (± 20.2) | 0.977 (± 17.1) | |
| LDL: Baseline for Day 14 Analysis | 2.664 (± 39.8) | 2.591 (± 40.6) | 2.666 (± 34.3) | |
| LDL: Change from Baseline at Day 14 | 1.021 (± 23.6) | 1.125 (± 19.7) | 0.998 (± 14.3) | |
| LDL: Baseline for Day 28 Analysis | 2.612 (± 39.4) | 2.553 (± 40.7) | 2.614 (± 36.3) | |
| LDL: Change from Baseline at Day 28 | 0.996 (± 27.5) | 1.092 (± 23.0) | 1.017 (± 15.7) | |
| LDL: Baseline for Day 42 Analysis | 3.070 (± 28.7) | 2.559 (± 41.0) | 2.679 (± 35.1) | |
| LDL: Change from Baseline at Day 42 | 0.989 (± 29.9) | 1.079 (± 24.5) | 0.914 (± 21.1) | |
| LDL: Baseline for Day 56 Analysis | 2.841 (± 32.0) | 2.527 (± 42.0) | 2.621 (± 36.0) | |
| LDL: Change from Baseline at Day 56 | 1.011 (± 27.9) | 1.091 (± 24.8) | 0.991 (± 24.7) | |
| LDL: Baseline for Day 84 Analysis | 2.725 (± 30.8) | 2.528 (± 41.8) | 2.498 (± 36.8) | |
| LDL: Change from Baseline at Day 84 | 1.029 (± 22.5) | 1.107 (± 31.7) | 1.025 (± 22.2) | |
| LDL: Baseline for Day 112 (EOS) Analysis | 2.695 (± 31.6) | 2.418 (± 40.0) | 2.482 (± 36.2) | |
| LDL: Change from Baseline at Day 112 (EOS) | 1.010 (± 18.7) | 1.035 (± 34.1) | 1.026 (± 19.9) | |

Notes:

[46] - PD analysis: n=36,
36,34,34,29,29,19,19,24,24,24,24,22,22,34,34,33,33,29,29,19,19,24,24,24,24,22,22
[47] - PD analysis: n=44,
44,44,44,43,43,42,42,41,41,40,40,39,39,43,43,43,43,41,41,41,41,38,38,38,38,35,35
[48] - PD analysis: n=40,
40,40,40,37,37,30,30,33,33,32,32,33,33,37,37,35,35,36,36,28,28,32,32,29,29,29,29

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Visual Analog Scale (VAS) for Itching of Skin

| End point title | Change From Baseline in Visual Analog Scale (VAS) for Itching of Skin |
|---|---|

End point description:

A 10 cm VAS was used to assess the severity of subjects itch (ranging from 0 = no itch at all to 10 =

the worst imaginable itch). The score (distance from left) on the VAS was recorded by the subject marking with a line and used to test for an effect of LMB763 over placebo. Baseline was defined as the last available measurement prior to the first dose. A positive change from Baseline indicates improvement. PD analysis set included all subjects with available PD data and no protocol deviations with relevant impact on PD data. 'n' represents the number of subjects in each category with a value at both Baseline and that time point.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline to Day 84 (Week 12)

| **End point values** | LMB763 100 mg | LMB763 50 mg | Pooled Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 37[49] | 44[50] | 40[51] | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline for Day 84 Analysis | 8.87 (± 19.108) | 4.62 (± 10.356) | 9.68 (± 19.552) | |
| Change from Baseline at Day 84 | 9.35 (± 18.746) | 4.85 (± 21.798) | 2.03 (± 24.037) | |

Notes:

[49] - PD analysis set: n = 23, 23

[50] - PD analysis set: n = 39, 39

[51] - PD analysis set: n = 34, 34

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until LPLV (up to Day 112 (EOS)).

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 21.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | LMB763 100 mg |
| Reporting group description: | |
| LMB763 100 mg | |
| Reporting group title | LMB763 50 mg |
| Reporting group description: | |
| LMB763 50 mg | |
| Reporting group title | Pooled Placebo |
| Reporting group description: | |
| Pooled Placebo | |

| Serious adverse events | LMB763 100 mg | LMB763 50 mg | Pooled Placebo |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 3 / 44 (6.82%) | 0 / 40 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Benign small intestinal neoplasm | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (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 |
| Jaundice cholestatic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (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 |
| Infections and infestations | | | |
| Otitis media | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (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 |

Frequency threshold for reporting non-serious adverse events: 0 %

| **Non-serious adverse events** | LMB763 100 mg | LMB763 50 mg | Pooled Placebo |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 35 / 37 (94.59%) | 37 / 44 (84.09%) | 33 / 40 (82.50%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Benign breast neoplasm | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lipoma | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypertension | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 1 | 0 | 1 |
| Hypotension | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Discomfort | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Fatigue | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 2 / 44 (4.55%) | 4 / 40 (10.00%) |
| occurrences (all) | 2 | 2 | 4 |
| Feeling cold | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 4 / 37 (10.81%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Seasonal allergy | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Ovarian calcification | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory, thoracic and mediastinal | | | |

| | | | |
|---|---|---|---|
| disorders | | | |
| Bronchial hyperreactivity | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 2 / 44 (4.55%) | 2 / 40 (5.00%) |
| occurrences (all) | 4 | 3 | 2 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Paranasal sinus discomfort | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory tract congestion | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinus congestion | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sneezing | | | |

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| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 3 / 40 (7.50%) |
| occurrences (all) | 0 | 1 | 3 |
| Insomnia | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 2 / 44 (4.55%) | 0 / 40 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 2 / 44 (4.55%) | 4 / 40 (10.00%) |
| occurrences (all) | 1 | 2 | 4 |
| Albumin urine present | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Alpha-2 macroglobulin | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Alpha-2 macroglobulin increased | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Apolipoprotein A-I decreased | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 4 / 37 (10.81%) | 1 / 44 (2.27%) | 1 / 40 (2.50%) |
| occurrences (all) | 4 | 1 | 1 |
| Bacterial test positive | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Basophil count increased | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Blood alkaline phosphatase increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 37 (8.11%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood calcium decreased | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 3 / 40 (7.50%) |
| occurrences (all) | 0 | 0 | 3 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Blood glucose increased | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 1 / 44 (2.27%) | 2 / 40 (5.00%) |
| occurrences (all) | 1 | 1 | 2 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood urea increased | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood urine present | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Crystal urine present | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 2 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 1 | 0 | 1 |

| | | | |
|---|---|---|---|
| Electrocardiogram abnormal | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eosinophil count increased | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 2 / 40 (5.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Free fatty acids increased | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 2 / 40 (5.00%) |
| occurrences (all) | 1 | 0 | 2 |
| Glomerular filtration rate decreased | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Glycosylated haemoglobin increased | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Low density lipoprotein decreased | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Lymphocyte count increased | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 0 / 44 (0.00%) | 2 / 40 (5.00%) |
| occurrences (all) | 2 | 0 | 2 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 4 / 37 (10.81%) | 1 / 44 (2.27%) | 4 / 40 (10.00%) |
| occurrences (all) | 6 | 1 | 4 |
| Prothrombin time prolonged | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Transaminases increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urine albumin/creatinine ratio | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urine albumin/creatinine ratio increased | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 4 / 44 (9.09%) | 5 / 40 (12.50%) |
| occurrences (all) | 3 | 4 | 5 |
| Urine protein/creatinine ratio increased | | | |
| subjects affected / exposed | 7 / 37 (18.92%) | 8 / 44 (18.18%) | 3 / 40 (7.50%) |
| occurrences (all) | 10 | 8 | 3 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| White blood cells urine positive | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Injury, poisoning and procedural complications | | | |
| Arthropod bite | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Burns second degree | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Contusion | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 2 / 40 (5.00%) |
| occurrences (all) | 1 | 0 | 2 |
| Fall | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ligament sprain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 44 (4.55%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 2 | 1 |
| Muscle strain | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin abrasion | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Wrist fracture | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Nervous system disorders | | | |
| Diabetic neuropathy | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 3 / 44 (6.82%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 3 | 1 |
| Head discomfort | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Headache | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 7 / 44 (15.91%) | 8 / 40 (20.00%) |
| occurrences (all) | 3 | 8 | 9 |
| Lumbar radiculopathy | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Migraine | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 1 | 0 | 1 |
| Myasthenia gravis | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 3 / 44 (6.82%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 1 | 0 | 1 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood and lymphatic system disorders | | | |
| Eosinophilia | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Ear pain | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Motion sickness | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Vertigo | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Eye disorders | | | |
| Blepharitis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastrointestinal disorders | | | |

| | | | |
|---|---|---|---|
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 1 / 44 (2.27%) | 1 / 40 (2.50%) |
| occurrences (all) | 1 | 1 | 1 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 44 (4.55%) | 2 / 40 (5.00%) |
| occurrences (all) | 0 | 2 | 2 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 3 / 40 (7.50%) |
| occurrences (all) | 1 | 0 | 3 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 2 / 44 (4.55%) | 3 / 40 (7.50%) |
| occurrences (all) | 3 | 2 | 3 |
| Abnormal faeces | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 4 / 37 (10.81%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 4 / 37 (10.81%) | 4 / 44 (9.09%) | 4 / 40 (10.00%) |
| occurrences (all) | 6 | 4 | 7 |
| Dyspepsia | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 0 / 44 (0.00%) | 3 / 40 (7.50%) |
| occurrences (all) | 3 | 0 | 3 |
| Faeces pale | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---|---|---|
| Hyperchlorhydria | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 1 | 0 | 1 |
| Melaena | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 7 / 37 (18.92%) | 5 / 44 (11.36%) | 2 / 40 (5.00%) |
| occurrences (all) | 7 | 6 | 3 |
| Tongue pruritus | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 3 / 44 (6.82%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Hepatobiliary disorders | | | |
| Jaundice | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blister | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dermal cyst | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Ecchymosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 37 (2.70%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Erythema | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 1 | 0 | 1 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Petechiae | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Pruritus | | | |
| subjects affected / exposed | 20 / 37 (54.05%) | 13 / 44 (29.55%) | 6 / 40 (15.00%) |
| occurrences (all) | 28 | 14 | 6 |
| Pruritus generalised | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Psoriasis | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Rash erythematous | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Rash follicular | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Rash pruritic | | | |
| subjects affected / exposed | 4 / 37 (10.81%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Skin atrophy | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin mass | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal and urinary disorders | | | |
| Hydronephrosis | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Renal disorder | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 4 / 44 (9.09%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 4 | 1 |
| Urine abnormality | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Urine odour abnormal | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Back pain | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 3 / 44 (6.82%) | 1 / 40 (2.50%) |
| occurrences (all) | 1 | 3 | 1 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscle spasms | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 1 | 1 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 3 / 40 (7.50%) |
| occurrences (all) | 0 | 0 | 3 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 44 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 1 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 44 (4.55%) | 3 / 40 (7.50%) |
| occurrences (all) | 0 | 3 | 4 |
| Infections and infestations | | | |
| Atypical pneumonia | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 1 / 44 (2.27%) | 4 / 40 (10.00%) |
| occurrences (all) | 1 | 1 | 4 |
| Nail infection | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 2 / 44 (4.55%) | 3 / 40 (7.50%) |
| occurrences (all) | 2 | 2 | 3 |
| Oral herpes | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 44 (4.55%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 2 / 44 (4.55%) | 0 / 40 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Tinea infection | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 4 / 44 (9.09%) | 2 / 40 (5.00%) |
| occurrences (all) | 3 | 4 | 2 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 44 (4.55%) | 3 / 40 (7.50%) |
| occurrences (all) | 0 | 2 | 3 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 4 / 44 (9.09%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 4 | 2 |
| Viral myositis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Viral rhinitis | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Vulvovaginal candidiasis | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vulvovaginal mycotic infection | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Gout | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 44 (2.27%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 4 / 37 (10.81%) | 4 / 44 (9.09%) | 0 / 40 (0.00%) |
| occurrences (all) | 4 | 6 | 0 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 3 / 44 (6.82%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 0 / 44 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 2 / 44 (4.55%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 01 January 2017 | Amendment 1 was generated in response to requests from the Medicines and Healthcare Products Regulatory Agency (MHRA) to include an additional pregnancy test and add serum phosphate to the clinical chemistry panel in accordance with the recommended renal monitoring procedures in the Investigator Brochure. |
| 01 May 2017 | Based on US FDA feedback regarding the potent inhibitory effects of nidufexor on CYP2C8 (Ki = 0.0213 µM, IC50 = 0.41 µM), which suggested a potential for drug-drug interactions (DDI) to occur between CYP2C8 substrates and nidufexor, the protocol was amended to highlight the potential for DDI and emphasize the potential for nidufexor to increase exposure of drugs metabolized by CYP2C8, including repaglinide, pioglitazone and rosiglitazone, and those dependent on export by BCRP. For all these drugs careful attention was paid to the drug interaction sections of the prescribing information. |
| 01 October 2017 | Amendment v03 aimed to explore a reduced dose of nidufexor which was expected to have a pharmacological effect on biomarkers of disease activity, as well as to lower the ALT threshold required for inclusion based on emerging data on the NASH phenotype and requirements for Phase 2 studies, and feedback received from investigators. |

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.

The sponsor decided to terminate the study early, as data obtained were deemed sufficient to inform any potential future development steps; interim results showed that the 50 mg nidufexor dose was well tolerated with favourable efficacy.

Notes: