Clinical trial results:
A randomized patient-and-physician blinded, placebo-controlled, 24-week study to assess the safety, tolerability and efficacy of LMB763 in patients with diabetic nephropathy

Summary

EudraCT number	2018-002491-40
Trial protocol	DE
Global end of trial date	03 May 2021

Results information

Result version number	v1 (current)
This version publication date	13 May 2022
First version publication date	13 May 2022

Trial information

Trial identification

Sponsor protocol code	CLMB763X2202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03804879
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharmaceuticals AG, 41 + 1 862 778 8300, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharmaceuticals AG, 41 + 1 862 778 8300, Novartis.email@Novartis.com

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	03 May 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 May 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the effect of nidufexor to placebo on albuminuria in patients with diabetic nephropathy already receiving treatment with ACEI or ARB.

To assess the safety and tolerability of nidufexor.

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	17 December 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 24
Country: Number of subjects enrolled	Czechia: 3
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Jordan: 10
Country: Number of subjects enrolled	Lebanon: 5
Country: Number of subjects enrolled	Turkey: 22
Country: Number of subjects enrolled	United States: 13
Worldwide total number of subjects	83
EEA total number of subjects	9

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)	50
From 65 to 84 years	33
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from 18 sites in 7 countries

Pre-assignment

Screening details:

Participants underwent a Screening period of up to 30 days which included screening and baseline assessments

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	LMB763

Arm description:

50 mg LMB763 (two LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.

Arm type	Experimental
Investigational medicinal product name	Nidufexor
Investigational medicinal product code	LMB763
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

50 mg LMB763 (two LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.

Arm title	Placebo

Arm description:

Placebo was orally administered once daily for 24 weeks in addition to SoC.

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

Dosage and administration details:

Placebo was orally administered once daily for 24 weeks in addition to SoC.

Number of subjects in period 1	LMB763	Placebo
Started	41	42
Pharmacokinetics (PK) analysis set	41	0 [1]
Pharmacodynamics (PD) analysis set	41	41
Completed	25	29
Not completed	16	13
Consent withdrawn by subject	3	1
Adverse event, non-fatal	3	-
Study Terminated By Sponsor	10	12

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Correct, for that analysis set placebo group is not entered

Baseline characteristics

Reporting groups	
Reporting group title	LMB763
Reporting group description:	
50 mg LMB763 (two LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.	
Reporting group title	Placebo
Reporting group description:	
Placebo was orally administered once daily for 24 weeks in addition to SoC.	

Reporting group values	LMB763	Placebo	Total
Number of subjects	41	42	83
Age categorical			
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)	26	24	50
From 65-84 years	15	18	33
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	60.8	61.6	
standard deviation	± 8.95	± 8.36	-
Sex: Female, Male			
Units: Participants			
Female	13	10	23
Male	28	32	60
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	1
White	41	41	82
More than one race	0	0	0
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	LMB763
Reporting group description:	
50 mg LMB763 (two LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.	
Reporting group title	Placebo
Reporting group description:	
Placebo was orally administered once daily for 24 weeks in addition to SoC.	

Primary: Ratio to baseline in urinary albumin to creatinine ratio (UACR)

End point title	Ratio to baseline in urinary albumin to creatinine ratio

End point description:

UACR is a ratio between albumin and creatinine, and it estimates 24-hour urine albumin excretion.

UACR (mg/mmol) = urine albumin [mg/L] / urine creatinine [mmol/L]. UACR was analyzed on a log-scale fitting a repeated measures mixed model including treatment and visit as fixed effects and log of baseline as continuous covariate. Baseline is the last measurement prior to treatment administration. No methods for imputation of missing data were used. Values reported were back-transformed to original scale. A lower score in the ratio to baseline indicates improvement.

End point type	Primary

End point timeframe:

Baseline and days 14, 29, 57, 85, 113, 141 and 169

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: Correct, for that analysis set placebo group is not entered

End point values	LMB763	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: Ratio to baseline				
least squares mean (confidence interval 80%)				
Day 14 (n=39, 42)	0.90 (0.79 to 1.02)	1.06 (0.94 to 1.20)		
Day 29 (n=37, 39)	0.83 (0.75 to 0.93)	1.00 (0.90 to 1.12)		
Day 57 (n=34, 35)	0.85 (0.76 to 0.94)	1.05 (0.95 to 1.17)		
Day 85 (n=29, 35)	0.84 (0.72 to 0.97)	1.07 (0.93 to 1.23)		
Day 113 (n=26, 30)	0.87 (0.73 to 1.04)	1.07 (0.90 to 1.26)		
Day 141 (n=23, 27)	0.84 (0.71 to 1.01)	1.15 (0.98 to 1.35)		
Day 169 (n=26, 30)	0.74 (0.61 to 0.89)	0.92 (0.78 to 1.10)		

Statistical analyses

No statistical analyses for this end point

Primary: Ratio to baseline in 24 hour urinary albumin at week 24 (day 169)

End point title	Ratio to baseline in 24 hour urinary albumin at week 24 (day 169)[2]

End point description:

Albuminuria describes the existence of albumin in the urine and the gold-standard to assess albuminuria is 24-hour urinary albumin excretion (milligram/24 hours). An analysis of covariance (ANCOVA) with treatment as the classification factor and log-transformed baseline as the covariate was conducted for log-transformed ratio to baseline 24-hour urinary albumin excretion. Baseline is the last measurement prior to treatment administration. No methods for imputation of missing data were used. Values reported were back-transformed to original scale. A lower score in the ratio to baseline indicates improvement.

End point type	Primary

End point timeframe:

Baseline and day 169

Notes:

[2] - 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: Correct, for that analysis set placebo group is not entered

End point values	LMB763	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	21		
Units: Ratio to baseline				
least squares mean (confidence interval 80%)	0.58 (0.45 to 0.74)	0.91 (0.72 to 1.14)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)[3]

End point description:

Number of participants with AEs and SAEs including significant changes from baseline in vital signs, electrocardiograms and laboratory values qualifying and reported as AEs. The number of participants in each category is reported in the table.

End point type	Primary

End point timeframe:

From the start of treatment to 28 days after end of treatment, assessed up to maximum duration of 197 days

Notes:

[3] - 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: Correct, for that analysis set placebo group is not entered

End point values	LMB763	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: Participants				
AEs	29	25		
SAEs	2	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Ratio to Baseline in Estimated glomerular filtration rate (eGFR)

End point title	Ratio to Baseline in Estimated glomerular filtration rate (eGFR)

End point description:

Estimate Glomerular Filtration Rate (GFR) calculates estimated GFR (eGFR) from serum creatinine levels to assess kidney function. eGFR (milliliter/minute) was analyzed on a log-scale fitting a repeated measures mixed model including treatment and visit as fixed effects and log of baseline as continuous covariate. Baseline is the last measurement prior to treatment administration. No methods for imputation of missing data were used. Values reported were back-transformed to original scale. A higher score in the ratio to baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline and days 14, 29, 57, 85, 113, 141 and 169

End point values	LMB763	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	41		
Units: Ratio to baseline				
least squares mean (confidence interval 80%)				
Day 14 (n=38, 41)	0.95 (0.93 to 0.98)	0.96 (0.94 to 0.99)		
Day 29 (n=36, 37)	0.94 (0.91 to 0.97)	0.94 (0.91 to 0.97)		
Day 57 (n=32, 32)	0.98 (0.95 to 1.02)	0.96 (0.93 to 1.00)		
Day 85 (n=28, 32)	0.97 (0.93 to 1.01)	0.94 (0.90 to 0.97)		
Day 113 (n=26, 23)	0.96 (0.92 to 0.99)	0.94 (0.91 to 0.98)		
Day 141 (n=22, 23)	0.98 (0.95 to 1.02)	0.93 (0.90 to 0.96)		
Day 169 (n=21, 25)	0.93 (0.89 to 0.97)	0.93 (0.90 to 0.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Peak Observed Concentration (Cmax) of LMB763

End point title	Maximum Peak Observed Concentration (Cmax) of LMB763[4]

End point description:

Pharmacokinetic (PK) parameters were calculated based on LMB763 blood concentrations determined by a validated liquid chromatography and tandem mass spectrometry (LC-MS/MS) method. Cmax was determined using non-compartmental methods. No methods for imputation of missing data were used.

End point type	Secondary

End point timeframe:

pre-dose and 1, 2, 4 and 6 hours after LMB763 administration on Day 1 and Day 14

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Correct, for that analysis set placebo group is not entered

End point values	LMB763			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Nanogram/milliliter				
arithmetic mean (standard deviation)				
Day 1 (n=41) Day 14 (n=37)	1090 (± 665) 1300 (± 691)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Blood Concentrations (Tmax) of LMB763

End point title	Time to Reach Maximum Blood Concentrations (Tmax) of LMB763[5]

End point description:

Pharmacokinetic (PK) parameters were calculated based on LMB763 blood concentrations determined by a validated liquid chromatography and tandem mass spectrometry (LC-MS/MS) method. Tmax was determined using non-compartmental methods. No methods for imputation of missing data were used.

End point type	Secondary

End point timeframe:

pre-dose and 1, 2, 4 and 6 hours after LMB763 administration on Day 1 and Day 14

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Correct, for that analysis set placebo group is not entered

End point values	LMB763			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Hour				
median (full range (min-max))				
Day 1 (n=41)	3.25 (0.75 to 6)			

Day 14 (n=37)	2 (0 to 6)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Area Under the Blood Concentration-time Curve From Time Zero to the Last Quantifiable Concentration (AUClast) of LMB763[6]

End point description:

Pharmacokinetic (PK) parameters were calculated based on LMB763 blood concentrations determined by a validated liquid chromatography and tandem mass spectrometry (LC-MS/MS) method. AUClast was determined using non-compartmental methods. No methods for imputation of missing data were used.

End point type	Secondary

End point timeframe:

pre-dose and 1, 2, 4 and 6 hours after LMB763 administration on Day 1 and Day 14

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Correct, for that analysis set placebo group is not entered

End point values	LMB763			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Hour*nanogram/milliliter				
arithmetic mean (standard deviation)				
Day 1	3710 (± 2510)			
Day 14	4850 (± 2910)			

Statistical analyses

No statistical analyses for this end point

Secondary: Ratio to baseline in Free water clearance

End point title	Ratio to baseline in Free water clearance

End point description:

The free water clearance (mL/min) was calculated using the following formula: (Total Volume (mL) / Elapsed Date & Time (min)) * (1-24 hr Urine Osmolality (mOsmol/kg)/ Serum Osmolality (mOsmol/kg))

The result of free water clearance was rounded to one decimal place prior to statistical analysis. An analysis of covariance (ANCOVA) with treatment as the classification factor and log-transformed baseline as the covariate was conducted for log-transformed ratio to baseline free water clearance. Baseline is the last measurement prior to treatment administration. No methods for imputation of missing data were used. Values reported were back-transformed to original scale. A higher score in the ratio to baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline and day 169

End point values	LMB763	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	11		
Units: Ratio to baseline				
least squares mean (confidence interval 80%)	0.97 (0.86 to 1.10)	0.97 (0.88 to 1.08)		

Statistical analyses

No statistical analyses for this end point

Secondary: Ratio to baseline in Lipoprotein A

End point title	Ratio to baseline in Lipoprotein A

End point description:

Lipoprotein A (gram/liter) is a component of the lipid profile which is a panel of blood tests used to find abnormalities in lipids. Ratio to baseline in Lipoprotein A was analyzed on a log-scale fitting a repeated measures mixed model including treatment and visit as fixed effects and log of baseline as continuous covariate. Baseline is the last measurement prior to treatment administration. No methods for imputation of missing data were used. Values reported were back-transformed to original scale. A lower score in the ratio to baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline and days 85 and 169

End point values	LMB763	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	41		
Units: Ratio to baseline				
least squares mean (confidence interval 80%)				
Day 85 (n=19, 24)	0.72 (0.67 to 0.77)	0.95 (0.90 to 1.01)		
Day 169 (n=12, 19)	0.75 (0.66 to 0.85)	0.89 (0.81 to 0.99)		

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:

Change from baseline in weight was analyzed on a log-scale fitting a repeated measures mixed model including treatment and visit as fixed effects and log of baseline as continuous covariate. Baseline is the last measurement prior to treatment administration. No methods for imputation of missing data were used. Values reported were back-transformed to original scale. A negative score in the percent change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline and days 14, 29, 57, 85, 113, 141 and 169

End point values	LMB763	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	41		
Units: Percent change from baseline				
least squares mean (confidence interval 80%)				
Day 14 (n=39, 41)	-0.08 (-0.45 to 0.29)	-0.13 (-0.50 to 0.23)		
Day 29 (n=37, 38)	-0.57 (-0.99 to -0.14)	-0.03 (-0.45 to 0.39)		
Day 57 (n=34, 34)	-0.69 (-1.35 to -0.04)	-0.24 (-0.90 to 0.41)		
Day 85 (n=29, 34)	-0.41 (-1.21 to 0.38)	0.08 (-0.70 to 0.86)		
Day 113 (n=25, 29)	-0.51 (-1.42 to 0.40)	0.21 (-0.67 to 1.09)		
Day 141 (n=23, 26)	-0.80 (-1.69 to 0.09)	0.43 (-0.44 to 1.29)		
Day 169 (n=22, 28)	-0.61 (-1.60 to 0.39)	0.55 (-0.38 to 1.47)		

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:

BMI was determined by height and weight measurements: Body weight (kg)/ [Height (m)]^2. Change from baseline in BMI was analyzed on a log-scale fitting a repeated measures mixed model including treatment and visit as fixed effects and log of baseline as continuous covariate. Baseline is the last measurement prior to treatment administration. No methods for imputation of missing data were used. Values reported were back-transformed to original scale. A negative score in the percent change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline and days 14, 29, 57, 85, 113, 141 and 169

End point values	LMB763	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	41		
Units: Percent change from baseline				
least squares mean (confidence interval 80%)				
Day 14 (n=39, 41)	-0.01 (-0.12 to 0.10)	-0.05 (-0.16 to 0.06)		
Day 29 (n=37, 38)	-0.19 (-0.32 to -0.05)	-0.02 (-0.15 to 0.12)		
Day 57 (n=34, 34)	-0.23 (-0.44 to -0.02)	-0.07 (-0.28 to 0.14)		
Day 85 (n=29, 34)	-0.13 (-0.40 to 0.13)	0.03 (-0.22 to 0.29)		
Day 113 (n=25, 29)	-0.18 (-0.47 to 0.12)	0.07 (-0.21 to 0.35)		
Day 141 (n=23, 26)	-0.31 (-0.60 to -0.01)	0.16 (-0.12 to 0.45)		
Day 169 (n=22, 28)	-0.29 (-0.61 to 0.04)	0.16 (-0.15 to 0.47)		

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:

Waist-to-hip ratio was derived using waist circumference and hip circumference, which was measured at the greatest protrusion of the buttocks. Change from baseline in waist-to-hip ratio was analyzed on a log-scale fitting a repeated measures mixed model including treatment and visit as fixed effects and log of baseline as continuous covariate. Baseline is the last measurement prior to treatment administration. No methods for imputation of missing data were used. Values reported were back-transformed to original scale. A negative score in the change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline and days 14, 29, 57, 85, 113, 141 and 169

End point values	LMB763	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	41		
Units: Ratio				
least squares mean (confidence interval 80%)				
Day 14 (n=39, 41)	-0.00 (-0.01 to 0.00)	-0.00 (-0.01 to 0.00)		

Day 29 (n=37, 37)	-0.00 (-0.01 to 0.00)	0.00 (-0.00 to 0.01)		
Day 57 (n=34, 34)	-0.00 (-0.01 to 0.00)	0.00 (-0.01 to 0.01)		
Day 85 (n=29, 34)	-0.00 (-0.01 to 0.00)	0.01 (-0.00 to 0.01)		
Day 113 (n=25, 29)	-0.00 (-0.01 to 0.01)	0.01 (0.00 to 0.02)		
Day 141 (n=24, 26)	-0.00 (-0.01 to 0.01)	0.02 (0.01 to 0.03)		
Day 169 (n=22, 28)	-0.00 (-0.01 to 0.01)	-0.00 (-0.01 to 0.00)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment-emergent adverse events	
Adverse event reporting additional description:	
Any sign or symptom that occurs during the study treatment plus the 28 days post treatment	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	LMB763 50 mg
Reporting group description:	
LMB763 50 mg	
Reporting group title	Total
Reporting group description:	
Total	
Reporting group title	Placebo
Reporting group description:	
Placebo	

Serious adverse events	LMB763 50 mg	Total	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 41 (4.88%)	4 / 83 (4.82%)	2 / 42 (4.76%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal disorder			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Erysipelas			

subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypervolaemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
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 50 mg	Total	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 41 (68.29%)	51 / 83 (61.45%)	23 / 42 (54.76%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 41 (4.88%)	4 / 83 (4.82%)	2 / 42 (4.76%)
occurrences (all)	2	4	2
Hypotension			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 41 (2.44%)	2 / 83 (2.41%)	1 / 42 (2.38%)
occurrences (all)	1	2	1
Fatigue			
subjects affected / exposed	2 / 41 (4.88%)	2 / 83 (2.41%)	0 / 42 (0.00%)
occurrences (all)	2	2	0

Oedema peripheral			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Pain			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Reproductive system and breast disorders			
Pruritus genital			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Asthma			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Oropharyngeal pain			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Blood bicarbonate decreased			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Blood creatinine increased			

subjects affected / exposed	4 / 41 (9.76%)	7 / 83 (8.43%)	3 / 42 (7.14%)
occurrences (all)	4	7	3
Blood fibrinogen increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Blood glucose increased			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Blood pressure increased			
subjects affected / exposed	0 / 41 (0.00%)	2 / 83 (2.41%)	2 / 42 (4.76%)
occurrences (all)	0	2	2
Blood uric acid increased			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Serum ferritin decreased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Ultrasound scan abnormal			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Urine albumin/creatinine ratio increased			
subjects affected / exposed	0 / 41 (0.00%)	3 / 83 (3.61%)	3 / 42 (7.14%)
occurrences (all)	0	4	4
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Injury			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Postoperative wound complication			

subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Rib fracture			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Scratch			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	3	3	0
Soft tissue injury			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	5	5
Bradycardia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
Cerebral artery stenosis			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Headache			
subjects affected / exposed	2 / 41 (4.88%)	4 / 83 (4.82%)	2 / 42 (4.76%)
occurrences (all)	4	7	3
Neuropathy peripheral			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Sciatica			
subjects affected / exposed	1 / 41 (2.44%)	2 / 83 (2.41%)	1 / 42 (2.38%)
occurrences (all)	1	2	1
Somnolence			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	2	2
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 41 (2.44%)	2 / 83 (2.41%)	1 / 42 (2.38%)
occurrences (all)	1	3	2
Iron deficiency anaemia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Nephrogenic anaemia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Abdominal pain upper			
subjects affected / exposed	2 / 41 (4.88%)	3 / 83 (3.61%)	1 / 42 (2.38%)
occurrences (all)	2	4	2
Colitis			
subjects affected / exposed	1 / 41 (2.44%)	2 / 83 (2.41%)	1 / 42 (2.38%)
occurrences (all)	1	3	2
Constipation			
subjects affected / exposed	2 / 41 (4.88%)	3 / 83 (3.61%)	1 / 42 (2.38%)
occurrences (all)	2	3	1
Diarrhoea			
subjects affected / exposed	2 / 41 (4.88%)	2 / 83 (2.41%)	0 / 42 (0.00%)
occurrences (all)	2	2	0
Dry mouth			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Flatulence			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Gastritis			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Gastrooesophageal reflux disease			

subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Hyperchlorhydria			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Vomiting			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Pruritus			
subjects affected / exposed	13 / 41 (31.71%)	19 / 83 (22.89%)	6 / 42 (14.29%)
occurrences (all)	17	25	8
Urticaria			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Chronic kidney disease			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Dysuria			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Renal colic			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Endocrine disorders			

Hypothyroidism			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 41 (2.44%)	2 / 83 (2.41%)	1 / 42 (2.38%)
occurrences (all)	1	2	1
Back pain			
subjects affected / exposed	3 / 41 (7.32%)	5 / 83 (6.02%)	2 / 42 (4.76%)
occurrences (all)	3	7	4
Myalgia			
subjects affected / exposed	2 / 41 (4.88%)	2 / 83 (2.41%)	0 / 42 (0.00%)
occurrences (all)	6	6	0
Pain in extremity			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
Abdominal wall abscess			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Acarodermatitis			
subjects affected / exposed	1 / 41 (2.44%)	2 / 83 (2.41%)	1 / 42 (2.38%)
occurrences (all)	1	2	1
Adenoviral conjunctivitis			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Bronchitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Cystitis			
subjects affected / exposed	0 / 41 (0.00%)	2 / 83 (2.41%)	2 / 42 (4.76%)
occurrences (all)	0	4	4
Erysipelas			
subjects affected / exposed	1 / 41 (2.44%)	2 / 83 (2.41%)	1 / 42 (2.38%)
occurrences (all)	1	2	1
Gastroenteritis			

subjects affected / exposed	2 / 41 (4.88%)	3 / 83 (3.61%)	1 / 42 (2.38%)
occurrences (all)	3	4	1
Influenza			
subjects affected / exposed	1 / 41 (2.44%)	2 / 83 (2.41%)	1 / 42 (2.38%)
occurrences (all)	1	2	1
Nasopharyngitis			
subjects affected / exposed	1 / 41 (2.44%)	3 / 83 (3.61%)	2 / 42 (4.76%)
occurrences (all)	1	3	2
Sinusitis			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Soft tissue infection			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	2 / 41 (4.88%)	3 / 83 (3.61%)	1 / 42 (2.38%)
occurrences (all)	3	4	1
Urinary tract infection bacterial			
subjects affected / exposed	1 / 41 (2.44%)	2 / 83 (2.41%)	1 / 42 (2.38%)
occurrences (all)	1	2	1
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 41 (0.00%)	2 / 83 (2.41%)	2 / 42 (4.76%)
occurrences (all)	0	2	2
Hyperglycaemia			
subjects affected / exposed	3 / 41 (7.32%)	5 / 83 (6.02%)	2 / 42 (4.76%)
occurrences (all)	3	6	3
Hyperkalaemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 83 (1.20%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Hypokalaemia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Iron deficiency			
subjects affected / exposed	1 / 41 (2.44%)	1 / 83 (1.20%)	0 / 42 (0.00%)
occurrences (all)	1	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 December 2018	The purpose of this amendment was to address non-hold comments in the study-may-proceed letter from FDA.
20 March 2019	The purpose of this amendment was to address requests and comments raised by the German Health Authority during the review of the original Clinical Trial Application for this study.
27 October 2020	The purpose of this amendment was to incorporate brief changes based on investigator feedback.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported