NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Not applicable

Trial Indication(s)

Diabetic nephropathy

Protocol Number

CLMB763X2202

Protocol Title

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

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase 2

Study Start/End Dates

Study Start Date: December 2018 (Actual)
Primary Completion Date: May 2021 (Actual)
Study Completion Date: May 2021 (Actual)

Reason for Termination

Decision was made to terminate study early as data fulfilled the strategic purpose of the study

Study Design/Methodology

This study was a non-confirmatory, multicenter, patient- and investigator-blinded, randomized, and placebo-controlled, proof-of-concept trial assessing nidufexor vs. placebo in patients receiving standard of care (optimal tolerated doses of ARB or ACEI) for diabetic nephropathy due to type 2 diabetes. Patients were randomized in a 1:1 ratio to receive nidufexor 50 mg or placebo. The study consisted of a 30-day (Day -30 to Day-1) Screening Period, followed by a 24-week Treatment Period (Days 1 through 168). End of Study (EOS) assessments occurred on Day 169.

Centers

18 centers in 7 countries: United States(5), Lebanon(2), Germany(3), Czech Republic(1), Jordan(1), Argentina(3), Turkey(3)

Objectives:

Primary

- Ratio to baseline in urinary albumin to creatinine ratio (UACR)
- Ratio to baseline in 24 hour urinary albumin at week 24 (day 169)
- Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)

Secondary

- Ratio to Baseline in Estimated glomerular filtration rate (eGFR)
- Maximum Peak Observed Concentration (Cmax) of LMB763
- Time to Reach Maximum Blood Concentrations (Tmax) of LMB763
- Area Under the Blood Concentration-time Curve From Time Zero to the Last Quantifiable Concentration (AUClast) of LMB763
- Ratio to baseline in Free water clearance
- Ratio to baseline in Lipoprotein A
- Change from baseline in weight
- Change from baseline in body mass index (BMI)

- Change from baseline in waist-to-hip ratio

Test Product (s), Dose(s), and Mode(s) of Administration

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

Statistical Methods

A Mixed Model for Repeated Measures (MMRM) analysis was performed for log-transformed ratio to baseline UACR. Similarly, 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 urine albumin excretion. Log-transformed ratio to baseline for eGFR, free water clearance and Lp(a)) as well as % change from baseline in weight and change from baseline in BMI and WTH ratio were analyzed using the same MMRM. Nidufexor plasma concentration data were listed by patient and visit/sampling time point. Summary statistics included mean (arithmetic and geometric), SD, CV (arithmetic and geometric), median, minimum and maximum.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Male/female patients, 18-75 years
- Written informed consent
- Diagnosis of Type 2 diabetes mellitus, with diagnosis made at least 6 months prior to screening
- Diabetic nephropathy as evidenced by Urine albumin-Cr ratio (UACR) ≥300 mg/g Cr at screening while receiving a dose of angiotensin converting enzyme inhibitor or angiotensin receptor blocker that is the standard of care as judged by the study doctor.

Exclusion Criteria:

- History of type 1 diabetes mellitus
- Severe renal impairment manifesting as serum creatinine eGFR < 30 mL/min/1.73 m^2 at screening
- Pregnant or nursing (lactating) women
- Women of child-bearing potential, unless they are using basic methods of contraception during dosing of study treatment
- Uncontrolled diabetes mellitus at screening

- History or current diagnosis of ECG abnormalities prior to first study dose
- History of kidney disease other than diabetic nephropathy at screening
- Uncontrolled hypertension at screening
- Use of prohibited medications, including but not limited to GLP-1 agonists and SGLT2 inhibitors.

Participant Flow Table

Overall Study

	LMB763	Placebo	Total
Arm/Group Description	50 mg LMB763 (two LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.	Placebo was orally administered once daily for 24 weeks in addition to SoC.	
Started	41	42	83
Pharmacokinetics (PK) analysis set	41	0	41
Pharmacodynamics (PD) analysis set	41	41	82
Completed	25	29	54
Not Completed	16	13	29
Adverse Event	3	0	3
Study Terminated By Sponsor	10	12	22
Withdrawal by Subject	3	1	4

Baseline Characteristics

	LMB763	Placebo	Total
Arm/Group Description	50 mg LMB763 (two LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.	Placebo was orally administered once daily for 24 weeks in addition to SoC.	
Number of Participants [units: participants]	41	42	83
Age Continuous (units: Years) Mean ± Standard Deviation			
	60.8±8.95	61.6±8.36	61.2±8.61
Sex: Female, Male (units: Participants) Count of Participants (Not Applicable)			
Female	13	10	23
Male	28	32	60
Race (NIH/OMB) (units: Participants) Count of Participants (Not Applicable)			
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

Primary Outcome Result(s)

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

(Time Frame: Baseline and days 14, 29, 57, 85, 113, 141 and 169)

	LMB763	Placebo
Arm/Group Description	50 mg LMB763 (two LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.	Placebo was orally administered once daily for 24 weeks in addition to SoC.
Number of Participants Analyzed [units: participants]	41	42
Ratio to baseline in urinary albumin to creatinine ratio (UACR) (units: Ratio to baseline) Least Squares Mean (80% Confidence Interval)		

Day 14	0.90 (0.79 to 1.02)	1.06 (0.94 to 1.20)
Day 29	0.83 (0.75 to 0.93)	1.00 (0.90 to 1.12)
Day 57	0.85 (0.76 to 0.94)	1.05 (0.95 to 1.17)
Day 85	0.84 (0.72 to 0.97)	1.07 (0.93 to 1.23)
Day 113	0.87 (0.73 to 1.04)	1.07 (0.90 to 1.26)
Day 141	0.84 (0.71 to 1.01)	1.15 (0.98 to 1.35)
Day 169	0.74 (0.61 to 0.89)	0.92 (0.78 to 1.10)

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

(Time Frame: Baseline and day 169)

	LMB763	Placebo
Arm/Group Description	50 mg LMB763 (two LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.	Placebo was orally administered once daily for 24 weeks in addition to SoC.
Number of Participants Analyzed [units: participants]	17	21
Ratio to baseline in 24 hour urinary albumin at		

week 24 (day 169) (units: Ratio to baseline) Least Squares Mean (80% Confidence Interval)		
Day 169	0.58 (0.45 to 0.74)	0.91 (0.72 to 1.14)

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

(Time Frame: From the start of treatment to 28 days after end of treatment, assessed up to maximum duration of 197 days)

	LMB763	**Placebo**
Arm/Group Description	50 mg LMB763 (two LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.	Placebo was orally administered once daily for 24 weeks in addition to SoC.
Number of Participants Analyzed [units: participants]	41	42
Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs) (units: Participants) Count of Participants (Not Applicable)		
AEs	29 (70.73%)	25 (59.52%)
SAEs	2 (4.88%)	2 (4.76%)

Secondary Outcome Result(s)

Ratio to Baseline in Estimated glomerular filtration rate (eGFR)

(Time Frame: Baseline and days 14, 29, 57, 85, 113, 141 and 169)

	LMB763	Placebo
Arm/Group Description	50 mg LMB763 (two LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.	Placebo was orally administered once daily for 24 weeks in addition to SoC.
Number of Participants Analyzed [units: participants]	41	41
Ratio to Baseline in Estimated glomerular filtration rate (eGFR) (units: Ratio to baseline) Least Squares Mean (80% Confidence Interval)		
Day 14	0.95 (0.93 to 0.98)	0.96 (0.94 to 0.99)
Day 29	0.94 (0.91 to 0.97)	0.94 (0.91 to 0.97)
Day 57	0.98 (0.95 to 1.02)	0.96 (0.93 to 1.00)
Day 85	0.97 (0.93 to 1.01)	0.94 (0.90 to 0.97)
Day 113	0.96 (0.92 to 0.99)	0.94 (0.91 to 0.98)
Day 141	0.98 (0.95 to 1.02)	0.93 (0.90 to 0.96)

Day 169	0.93 (0.89 to 0.97)	0.93 (0.90 to 0.97)

Maximum Peak Observed Concentration (Cmax) of LMB763

(Time Frame: pre-dose and 1, 2, 4 and 6 hours after LMB763 administration on Day 1 and Day 14)

	LMB763
Arm/Group Description	50 mg LMB763 (two LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.
Number of Participants Analyzed [units: participants]	41
Maximum Peak Observed Concentration (Cmax) of LMB763 (units: Nanogram/milliliter) Mean ± Standard Deviation	
Day 1	1090 ± 665
Day 14	1300 ± 691

Time to Reach Maximum Blood Concentrations (Tmax) of LMB763

(Time Frame: pre-dose and 1, 2, 4 and 6 hours after LMB763 administration on Day 1 and Day 14)

	LMB763
Arm/Group Description	50 mg LMB763 (two LMB763 25

	mg capsules) were orally administered once daily for 24 weeks in addition to SoC.
Number of Participants Analyzed [units: participants]	41
Time to Reach Maximum Blood Concentrations (Tmax) of LMB763 (units: Hour) Median (Full Range)	
Day 1	3.25 (0.75 to 6)
Day 14	2 (0 to 6)

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

(Time Frame: pre-dose and 1, 2, 4 and 6 hours after LMB763 administration on Day 1 and Day 14)

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

Number of Participants Analyzed [units: participants]	41
Area Under the Blood Concentration-time Curve From Time Zero to the Last Quantifiable Concentration (AUClast) of LMB763 (units: Hour*nanogram/milliliter) Mean ± Standard Deviation	
Day 1	3710 ± 2510
Day 14	4850 ± 2910

Ratio to baseline in Free water clearance

(Time Frame: Baseline and day 169)

	LMB763	**Placebo**
Arm/Group Description	50 mg LMB763 (two LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.	Placebo was orally administered once daily for 24 weeks in addition to SoC.
Number of Participants Analyzed [units: participants]	8	11
Ratio to baseline in Free water clearance (units: Ratio to baseline) Least Squares Mean (80% Confidence Interval)		

Day 169	0.97 (0.86 to 1.10)	0.97 (0.88 to 1.08)

Ratio to baseline in Lipoprotein A

(Time Frame: Baseline and days 85 and 169)

	LMB763	Placebo
Arm/Group Description	50 mg LMB763 (two LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.	Placebo was orally administered once daily for 24 weeks in addition to SoC.
Number of Participants Analyzed [units: participants]	41	41
Ratio to baseline in Lipoprotein A (units: Ratio to baseline) Least Squares Mean (80% Confidence Interval)		
Day 85	0.72 (0.67 to 0.77)	0.95 (0.90 to 1.01)
Day 169	0.75 (0.66 to 0.85)	0.89 (0.81 to 0.99)

Change from baseline in weight

(Time Frame: Baseline and days 14, 29, 57, 85, 113, 141 and 169)

	LMB763	Placebo
Arm/Group Description	50 mg LMB763 (two	Placebo was orally

	LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.	administered once daily for 24 weeks in addition to SoC.
Number of Participants Analyzed [units: participants]	41	41
Change from baseline in weight (units: Percent change from baseline) Least Squares Mean (80% Confidence Interval)		
Day 14	-0.08 (-0.45 to 0.29)	-0.13 (-0.50 to 0.23)
Day 29	-0.57 (-0.99 to -0.14)	-0.03 (-0.45 to 0.39)
Day 57	-0.69 (-1.35 to -0.04)	-0.24 (-0.90 to 0.41)
Day 85	-0.41 (-1.21 to 0.38)	0.08 (-0.70 to 0.86)
Day 113	-0.51 (-1.42 to 0.40)	0.21 (-0.67 to 1.09)
Day 141	-0.80 (-1.69 to 0.09)	0.43 (-0.44 to 1.29)
Day 169	-0.61 (-1.60 to 0.39)	0.55 (-0.38 to 1.47)

Change from baseline in body mass index (BMI)

(Time Frame: Baseline and days 14, 29, 57, 85, 113, 141 and 169)

	LMB763	Placebo
Arm/Group Description	50 mg LMB763 (two LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.	Placebo was orally administered once daily for 24 weeks in addition to SoC.
Number of Participants Analyzed [units: participants]	41	41
Change from baseline in body mass index (BMI) (units: Percent change from baseline) Least Squares Mean (80% Confidence Interval)		
Day 14	-0.01 (-0.12 to 0.10)	-0.05 (-0.16 to 0.06)
Day 29	-0.19 (-0.32 to -0.05)	-0.02 (-0.15 to 0.12)
Day 57	-0.23 (-0.44 to -0.02)	-0.07 (-0.28 to 0.14)
Day 85	-0.13 (-0.40 to 0.13)	0.03 (-0.22 to 0.29)
Day 113	-0.18 (-0.47 to 0.12)	0.07 (-0.21 to 0.35)
Day 141	-0.31 (-0.60 to -0.01)	0.16 (-0.12 to 0.45)
Day 169	-0.29 (-0.61 to 0.04)	0.16 (-0.15 to 0.47)

Change from baseline in waist-to-hip ratio

(Time Frame: Baseline and days 14, 29, 57, 85, 113, 141 and 169)

	LMB763	Placebo
Arm/Group Description	50 mg LMB763 (two LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.	Placebo was orally administered once daily for 24 weeks in addition to SoC.
Number of Participants Analyzed [units: participants]	41	41
Change from baseline in waist-to-hip ratio (units: Ratio) Least Squares Mean (80% Confidence Interval)		
Day 14	-0.00 (-0.01 to 0.00)	-0.00 (-0.01 to 0.00)
Day 29	-0.00 (-0.01 to 0.00)	0.00 (-0.00 to 0.01)
Day 57	-0.00 (-0.01 to 0.00)	0.00 (-0.01 to 0.01)
Day 85	-0.00 (-0.01 to 0.00)	0.01 (-0.00 to 0.01)
Day 113	-0.00 (-0.01 to 0.01)	0.01 (0.00 to 0.02)
Day 141	-0.00 (-0.01 to 0.01)	0.02 (0.01 to 0.03)

Day 169	-0.00 (-0.01 to 0.01)	-0.00 (-0.01 to 0.00)

Safety Results

All-Cause Mortality

	LMB763 N = 41	Placebo N = 42	Total N = 83
Arm/Group Description	50 mg LMB763 (two LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.	Placebo was orally administered once daily for 24 weeks in addition to SoC.	Total
Total participants affected	0 (0.00%)	0 (0.00%)	0 (0.00%)

Serious Adverse Events by System Organ Class

Time Frame	Adverse events were reported from the start of treatment to 28 days after end of treatment, assessed up to maximum duration of 197 days
Additional Description	Any sign or symptom that occurs during the study treatment plus the 28 days post treatment
Source Vocabulary for Table Default	MedDRA (24.0)

Assessment Type for Table Default	Systematic Assessment

	LMB763 N = 41	**Placebo N = 42**	**Total N = 83**
Arm/Group Description	50 mg LMB763 (two LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.	Placebo was orally administered once daily for 24 weeks in addition to SoC.	Total
Total participants affected	2 (4.88%)	2 (4.76%)	4 (4.82%)
Infections and infestations			
Erysipelas	1 (2.44%)	0 (0.00%)	1 (1.20%)
Metabolism and nutrition disorders			
Hyperglycaemia	1 (2.44%)	0 (0.00%)	1 (1.20%)
Hypervolaemia	0 (0.00%)	1 (2.38%)	1 (1.20%)
Renal and urinary disorders			
Acute kidney injury*	1 (2.44%)	0 (0.00%)	1 (1.20%)
Renal disorder	0 (0.00%)	1 (2.38%)	1 (1.20%)
Skin and subcutaneous tissue disorders			
Dermatitis atopic	1 (2.44%)	0 (0.00%)	1 (1.20%)

* Non-systematic Assessment

Other Adverse Events by System Organ Class

Time Frame	Adverse events were reported from the start of treatment to 28 days after end of treatment, assessed up to maximum duration of 197 days
Additional Description	Any sign or symptom that occurs during the study treatment plus the 28 days post treatment
Source Vocabulary for Table Default	MedDRA (24.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	0%

	LMB763 N = 41	**Placebo N = 42**	**Total N = 83**
Arm/Group Description	50 mg LMB763 (two LMB763 25 mg capsules) were orally administered once daily for 24 weeks in addition to SoC.	Placebo was orally administered once daily for 24 weeks in addition to SoC.	Total
Total participants affected	28 (68.29%)	23 (54.76%)	51 (61.45%)
Blood and lymphatic system disorders			
Anaemia	1 (2.44%)	1 (2.38%)	2 (2.41%)
Iron deficiency anaemia	1 (2.44%)	0 (0.00%)	1 (1.20%)
Nephrogenic anaemia	1 (2.44%)	0 (0.00%)	1 (1.20%)

Cardiac disorders			
Angina pectoris	0 (0.00%)	1 (2.38%)	1 (1.20%)
Bradycardia	1 (2.44%)	0 (0.00%)	1 (1.20%)
Endocrine disorders			
Hypothyroidism	1 (2.44%)	0 (0.00%)	1 (1.20%)
Gastrointestinal disorders			
Abdominal pain	0 (0.00%)	1 (2.38%)	1 (1.20%)
Abdominal pain upper	2 (4.88%)	1 (2.38%)	3 (3.61%)
Colitis	1 (2.44%)	1 (2.38%)	2 (2.41%)
Constipation	2 (4.88%)	1 (2.38%)	3 (3.61%)
Diarrhoea	2 (4.88%)	0 (0.00%)	2 (2.41%)
Dry mouth	0 (0.00%)	1 (2.38%)	1 (1.20%)
Flatulence	1 (2.44%)	0 (0.00%)	1 (1.20%)
Gastritis	1 (2.44%)	0 (0.00%)	1 (1.20%)
Gastrooesophageal reflux disease	1 (2.44%)	0 (0.00%)	1 (1.20%)
Hyperchlorhydria	1 (2.44%)	0 (0.00%)	1 (1.20%)
Vomiting	1 (2.44%)	0 (0.00%)	1 (1.20%)
General disorders and administration site conditions			
Asthenia	1 (2.44%)	1 (2.38%)	2 (2.41%)
Fatigue	2 (4.88%)	0 (0.00%)	2 (2.41%)
Oedema peripheral	1 (2.44%)	0 (0.00%)	1 (1.20%)
Pain	1 (2.44%)	0 (0.00%)	1 (1.20%)

Infections and infestations			
Abdominal wall abscess	1 (2.44%)	0 (0.00%)	1 (1.20%)
Acarodermatitis	1 (2.44%)	1 (2.38%)	2 (2.41%)
Adenoviral conjunctivitis	1 (2.44%)	0 (0.00%)	1 (1.20%)
Bronchitis	0 (0.00%)	1 (2.38%)	1 (1.20%)
Cystitis	0 (0.00%)	2 (4.76%)	2 (2.41%)
Erysipelas	1 (2.44%)	1 (2.38%)	2 (2.41%)
Gastroenteritis	2 (4.88%)	1 (2.38%)	3 (3.61%)
Influenza	1 (2.44%)	1 (2.38%)	2 (2.41%)
Nasopharyngitis	1 (2.44%)	2 (4.76%)	3 (3.61%)
Sinusitis	1 (2.44%)	0 (0.00%)	1 (1.20%)
Soft tissue infection	0 (0.00%)	1 (2.38%)	1 (1.20%)
Urinary tract infection	2 (4.88%)	1 (2.38%)	3 (3.61%)
Urinary tract infection bacterial	1 (2.44%)	1 (2.38%)	2 (2.41%)
Injury, poisoning and procedural complications			
Arthropod bite	1 (2.44%)	0 (0.00%)	1 (1.20%)
Injury	0 (0.00%)	1 (2.38%)	1 (1.20%)
Postoperative wound complication	0 (0.00%)	1 (2.38%)	1 (1.20%)
Rib fracture	0 (0.00%)	1 (2.38%)	1 (1.20%)
Scratch	1 (2.44%)	0 (0.00%)	1 (1.20%)
Soft tissue injury	0 (0.00%)	1 (2.38%)	1 (1.20%)
Investigations			

Aspartate aminotransferase increased	1 (2.44%)	0 (0.00%)	1 (1.20%)
Blood bicarbonate decreased	1 (2.44%)	0 (0.00%)	1 (1.20%)
Blood creatine phosphokinase increased	1 (2.44%)	0 (0.00%)	1 (1.20%)
Blood creatinine increased	4 (9.76%)	3 (7.14%)	7 (8.43%)
Blood fibrinogen increased	0 (0.00%)	1 (2.38%)	1 (1.20%)
Blood glucose increased	1 (2.44%)	0 (0.00%)	1 (1.20%)
Blood pressure increased	0 (0.00%)	2 (4.76%)	2 (2.41%)
Blood uric acid increased	1 (2.44%)	0 (0.00%)	1 (1.20%)
Glycosylated haemoglobin increased	0 (0.00%)	1 (2.38%)	1 (1.20%)
Serum ferritin decreased	0 (0.00%)	1 (2.38%)	1 (1.20%)
Ultrasound scan abnormal	1 (2.44%)	0 (0.00%)	1 (1.20%)
Urine albumin/creatinine ratio increased	0 (0.00%)	3 (7.14%)	3 (3.61%)
Metabolism and nutrition disorders			
Diabetes mellitus	0 (0.00%)	2 (4.76%)	2 (2.41%)
Hyperglycaemia	3 (7.32%)	2 (4.76%)	5 (6.02%)
Hyperkalaemia	0 (0.00%)	1 (2.38%)	1 (1.20%)
Hypokalaemia	1 (2.44%)	0 (0.00%)	1 (1.20%)

Iron deficiency	1 (2.44%)	0 (0.00%)	1 (1.20%)
Musculoskeletal and connective tissue disorders			
Arthralgia	1 (2.44%)	1 (2.38%)	2 (2.41%)
Back pain	3 (7.32%)	2 (4.76%)	5 (6.02%)
Myalgia	2 (4.88%)	0 (0.00%)	2 (2.41%)
Pain in extremity	1 (2.44%)	0 (0.00%)	1 (1.20%)
Nervous system disorders			
Cerebral artery stenosis	1 (2.44%)	0 (0.00%)	1 (1.20%)
Headache	2 (4.88%)	2 (4.76%)	4 (4.82%)
Neuropathy peripheral	0 (0.00%)	1 (2.38%)	1 (1.20%)
Sciatica	1 (2.44%)	1 (2.38%)	2 (2.41%)
Somnolence	0 (0.00%)	1 (2.38%)	1 (1.20%)
Psychiatric disorders			
Insomnia	1 (2.44%)	0 (0.00%)	1 (1.20%)
Renal and urinary disorders			
Acute kidney injury	0 (0.00%)	1 (2.38%)	2 (2.41%)
Chronic kidney disease	0 (0.00%)	1 (2.38%)	1 (1.20%)
Dysuria	0 (0.00%)	1 (2.38%)	1 (1.20%)
Renal colic	0 (0.00%)	1 (2.38%)	1 (1.20%)
Reproductive system and breast disorders			
Pruritus genital	0 (0.00%)	1 (2.38%)	1 (1.20%)

Respiratory, thoracic and mediastinal disorders			
Asthma	1 (2.44%)	0 (0.00%)	1 (1.20%)
Chronic obstructive pulmonary disease	1 (2.44%)	0 (0.00%)	1 (1.20%)
Oropharyngeal pain	1 (2.44%)	0 (0.00%)	1 (1.20%)
Skin and subcutaneous tissue disorders			
Dry skin	1 (2.44%)	0 (0.00%)	1 (1.20%)
Hyperhidrosis	0 (0.00%)	1 (2.38%)	1 (1.20%)
Pruritus	13 (31.71%)	6 (14.29%)	19 (22.89%)
Urticaria	1 (2.44%)	0 (0.00%)	1 (1.20%)
Vascular disorders			
Hypertension	2 (4.88%)	2 (4.76%)	4 (4.82%)
Hypotension	1 (2.44%)	0 (0.00%)	1 (1.20%)
Peripheral arterial occlusive disease	1 (2.44%)	0 (0.00%)	1 (1.20%)

Other Relevant Findings

Not applicable.

Conclusion:

Nidufexor was efficacious and generally well tolerated for a period of 24 weeks in patients with diabetic nephropathy with an acceptable safety profile and no new safety signals identified. Nidufexor reduced albuminuria as demonstrated by

reduction in UACR and 24h urinary albumin excretion. Data from this study support further development of nidufexor in the treatment of patients of diabetic nephropathy.

Date of Clinical Trial Report

01-March-2022