Clinical trial results:
A Phase 2, Double-blind, Randomized, Placebo-controlled, Parallel-group Study to Evaluate the Efficacy and Safety of LX9211 in the Treatment of Postherpetic Neuralgia (RELIEF-PHN1)

Summary

EudraCT number	2020-004639-26
Trial protocol	CZ PL
Global end of trial date	28 December 2022

Results information

Result version number	v1 (current)
This version publication date	06 January 2024
First version publication date	06 January 2024

Trial information

Trial identification

Sponsor protocol code	LX9211.1-202-PHN

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04662281
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Lexicon Pharmaceuticals, Inc.
Sponsor organisation address	2445 Technology Forest Blvd, The Woodlands, TX, United States, 77381-5261
Public contact	Vice President, Clinical Operations, Lexicon Pharmaceuticals, +1 281-863-3000, clinicaloperations@lexpharma.com
Scientific contact	Head of LX9211 Clinical Development, Lexicon Pharmaceuticals, +1 281-863-3000, clinicaloperations@lexpharma.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	28 December 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy of LX9211 in reducing pain related to postherpetic neuralgia (PHN).

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 December 2020
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	Poland: 7
Country: Number of subjects enrolled	Czechia: 4
Country: Number of subjects enrolled	United States: 68
Worldwide total number of subjects	79
EEA total number of subjects	11

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	35
From 65 to 84 years	44
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects took part in the study at multiple investigative sites in Poland, Czechia, and the United States from 10 December 2020 to 28 December 2022.

Pre-assignment

Screening details:

Following a 2-week single blind Placebo Run-in period, a total of 79 subjects were randomised and treated in the study, with 41 subjects receiving a placebo and 38 subjects receiving LX9211.

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, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Following a 2-week Single-blind Placebo Run-in period, subjects received a single loading dose of matching-placebo to LX9211 tablet, orally, on Day 1 and maintenance doses, orally, once daily from Day 2 to Week 6.

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

Dosage and administration details:

LX9211-matching -placebo tablet was administered, orally as specified in the respective arm.

Arm title	LX9211

Arm description:

Following a 2-week Single-blind Placebo Run-in period, subjects received a single loading dose of 200 milligrams (mg) tablet, orally, on Day 1 and maintenance doses of 20 mg, orally, once daily from Day 2 to Week 6.

Arm type	Experimental
Investigational medicinal product name	LX9211
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

LX9211 tablet was administered, orally as specified in the respective arm.

Number of subjects in period 1	Placebo	LX9211
Started	41	38
Completed	34	21
Not completed	7	17
Subject Choice	1	2
Reason Not Specified	1	2
Adverse event	4	13
Lack of efficacy	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Following a 2-week Single-blind Placebo Run-in period, subjects received a single loading dose of matching-placebo to LX9211 tablet, orally, on Day 1 and maintenance doses, orally, once daily from Day 2 to Week 6.	
Reporting group title	LX9211
Reporting group description:	
Following a 2-week Single-blind Placebo Run-in period, subjects received a single loading dose of 200 milligrams (mg) tablet, orally, on Day 1 and maintenance doses of 20 mg, orally, once daily from Day 2 to Week 6.	

Reporting group values	Placebo	LX9211	Total
Number of subjects	41	38	79
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	63.6	65.4	
standard deviation	± 12.5	± 11.7	-
Gender categorical Units: Subjects			
Female	24	23	47
Male	17	15	32
Ethnicity Units: Subjects			
Hispanic or Latino	12	11	23
Not Hispanic or Latino	29	27	56
Race Units: Subjects			
Black or African American	2	0	2
White	39	37	76
Unknown or Not Reported	0	1	1

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Following a 2-week Single-blind Placebo Run-in period, subjects received a single loading dose of matching-placebo to LX9211 tablet, orally, on Day 1 and maintenance doses, orally, once daily from Day 2 to Week 6.

Reporting group title	LX9211

Reporting group description:

Following a 2-week Single-blind Placebo Run-in period, subjects received a single loading dose of 200 milligrams (mg) tablet, orally, on Day 1 and maintenance doses of 20 mg, orally, once daily from Day 2 to Week 6.

Primary: Change from Baseline (Week 2 of the Run-in period) in Average Daily Pain Score (ADPS)

End point title	Change from Baseline (Week 2 of the Run-in period) in Average Daily Pain Score (ADPS)

End point description:

ADPS is based on question 5 of Zoster Brief Pain Inventory (ZBPI) and assessed on an 11-point numerical rating scale where, 0 (no pain) to 10 (pain as
bad as you can imagine). Higher ADPS scores indicated a worse outcome. The mITT population included all randomised subjects who had taken at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Baseline (Week 2 of the Run-in period) to Week 6

End point values	Placebo	LX9211		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36[1]	22[2]		
Units: score on a scale				
least squares mean (standard error)	-1.62 (± 0.360)	-2.42 (± 0.397)		

Notes:

[1] - Number of subjects analysed signifies subjects who were evaluable for this endpoint.

[2] - Number of subjects analysed signifies subjects who were evaluable for this endpoint.

Statistical analyses

Statistical analysis title	Placebo Vs LX9211

Statistical analysis description:

The Mixed Model Repeated Measures (MMRM) model was used to assess the difference between LX9211 and placebo in the primary endpoint and it included fixed effects of treatment, week, treatment-by-week interaction, the randomization stratum of Baseline pain severity (moderate, severe), and the Baseline ADPS score as a covariate.

Comparison groups	LX9211 v Placebo

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
Method	MMRM
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.82
upper limit	0.21

Secondary: Change from Baseline in Pain Interfering With Sleep based on Question 9F of the ZBPI at Week 6

End point title	Change from Baseline in Pain Interfering With Sleep based on Question 9F of the ZBPI at Week 6

End point description:

Pain interfering with sleep is based on Question 9F of the ZBPI "Indicate the one number that describes how, in the past 24-hours shingles pain has interfered with your: Sleep; 0 = does not interfere to 10 = Completely interferes. Higher the number more the worsening of sleep due to pain interference. The mITT population included all randomised subjects who had taken at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline to Week 6

End point values	Placebo	LX9211		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35[3]	22[4]		
Units: score on a scale				
least squares mean (standard error)	-1.43 (± 0.323)	-2.04 (± 0.364)		

Notes:

[3] - Number of subjects analysed signifies subjects who were evaluable for this endpoint.

[4] - Number of subjects analysed signifies subjects who were evaluable for this endpoint.

Statistical analyses

Statistical analysis title	Placebo Vs LX9211

Statistical analysis description:

The MMRM model included fixed effects of treatment, week, treatment-by-week interaction, the randomisation stratum of Baseline pain severity (moderate, severe), and the Baseline ADPS score as a covariate.

Comparison groups	Placebo v LX9211

Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.181
Method	MMRM
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.53
upper limit	0.29

Secondary: Percentage of Subjects with ≥30% Reduction in Pain Intensity in ADPS From Baseline at Week 6

End point title	Percentage of Subjects with ≥30% Reduction in Pain Intensity in ADPS From Baseline at Week 6

End point description:

ADPS is based on question 5 of Zoster Brief Pain Inventory (ZBPI) and assessed on an 11-point numerical rating scale where, 0 = No Pain to 10 = pain as bad as you can imagine. Higher ADPS scores indicated a worse outcome. The mITT population included all randomised subjects who had taken at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline to Week 6

End point values	Placebo	LX9211		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	38		
Units: percentage of subjects				
number (not applicable)	34.1	42.1		

Statistical analyses

Statistical analysis title	Placebo Vs LX9211

Statistical analysis description:

Cochran-Mantel-Haenszel (CMH) test stratified by the different levels of the randomization stratification factors of Baseline severity score (moderate, severe) was used.

Comparison groups	Placebo v LX9211

Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.504
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.42
upper limit	29.34

Secondary: Percentage of Subjects with ≥50% Reduction in Pain Intensity in ADPS From Baseline at Week 6

End point title	Percentage of Subjects with ≥50% Reduction in Pain Intensity in ADPS From Baseline at Week 6

End point description:

ADPS is based on question 5 of ZBPI and assessed on an 11-point numerical rating scale where, 0 = No Pain to 10 = pain as bad as you can imagine. Higher ADPS scores indicated a worse outcome. The mITT population included all randomised subjects who had taken at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline to Week 6

End point values	Placebo	LX9211		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	38		
Units: percentage of subjects				
number (not applicable)	19.5	23.7		

Statistical analyses

Statistical analysis title	Placebo Vs LX9211

Statistical analysis description:

CMH test stratified by the different levels of the randomisation stratification factors of Baseline severity score (moderate, severe) was used.

Comparison groups	Placebo v LX9211
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.671
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	4.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.99
upper limit	22.33

Secondary: Change from Baseline in Interference in General Activity, Mood, Walking Ability, Normal Work, Relations With Other People, Sleep, and Enjoyment of Life Interference Based on the Questions 9A-G of the ZBPI

End point title	Change from Baseline in Interference in General Activity, Mood, Walking Ability, Normal Work, Relations With Other People, Sleep, and Enjoyment of Life Interference Based on the Questions 9A-G of the ZBPI

End point description:

The ZBPI, a 9-item questionnaire assesses the severity of pain and its impact on functioning in subjects with PHN. The categories based on questions 9A-G of the ZBPI that were analyzed are general activity, mood, walking ability, normal work (includes both outside the home and housework) relations with other people, sleep, and enjoyment of life: 0 no interference - 10 complete interference. Higher ZBPI score indicates a worse outcome. The mITT population included all randomised subjects who had taken at least 1 dose of study drug. Here, 'n' signifies the number of subjects analysed at a given timepoint in this endpoint

End point type	Secondary

End point timeframe:

Baseline to Week 6

End point values	Placebo	LX9211		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	38		
Units: score on a scale				
least squares mean (standard error)				
General Activity, Change at Week 6 (n= 29, 26)	-0.52 (± 0.392)	-1.75 (± 0.417)		
Mood, Change at Week 6 (n= 29, 26)	-1.52 (± 0.407)	-2.36 (± 0.435)		
Walking Ability, Change at Week 6 (n= 29, 26)	-0.28 (± 0.373)	-0.72 (± 0.391)		
Normal Work, Change at Week 6 (n= 29, 26)	-0.61 (± 0.383)	-1.28 (± 0.397)		
Relations With Other People (n= 29, 26)	-0.89 (± 0.381)	-1.27 (± 0.400)		
Relations with Sleep, Change at Week 6 (n= 29, 26)	-1.61 (± 0.370)	-1.66 (± 0.382)		
Enjoyment of Life, Change at Week 6 (n= 29, 26)	-1.13 (± 0.405)	-1.93 (± 0.435)		

Statistical analyses

Statistical analysis title	Placebo Vs LX9211

Statistical analysis description:

General Activity: The change from baseline to Week 6 in general activity was analysed using the MMRM model. The MMRM model included fixed effects of treatment, week, treatment-by-week interaction, the randomisation stratum of Baseline pain severity (moderate, severe), and the Baseline ADPS score as a covariate.

Comparison groups	LX9211 v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.024
Method	MMRM
Parameter estimate	Difference in Least Squares Means
Point estimate	-1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	-0.17

Statistical analysis title	Placebo Vs LX9211

Statistical analysis description:

Mood: The change from baseline to Week 6 in mood was analysed using the MMRM model. The MMRM model included fixed effects of treatment, week, treatment-by-week interaction, the randomisation stratum of Baseline pain severity (moderate, severe), and the Baseline ADPS score as a covariate.

Comparison groups	Placebo v LX9211
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.138
Method	MMRM
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.95
upper limit	0.27

Statistical analysis title	Placebo Vs LX9211

Statistical analysis description:

Walking Ability: The change from baseline to Week 6 in walking ability was analysed using the MMRM model. The MMRM model included fixed effects of treatment, week, treatment-by-week interaction, the randomisation stratum of Baseline pain severity (moderate, severe), and the Baseline ADPS score as a covariate.

Comparison groups	Placebo v LX9211

Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.397
Method	MMRM
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.45
upper limit	0.58

Statistical analysis title	Placebo Vs LX9211

Statistical analysis description:

Normal Work: The change from baseline to Week 6 in normal work was analysed using the MMRM model. The MMRM model included fixed effects of treatment, week, treatment-by-week interaction, the randomisation stratum of Baseline pain severity (moderate, severe), and the Baseline ADPS score as a covariate.

Comparison groups	Placebo v LX9211
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.192
Method	MMRM
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.69
upper limit	0.34

Statistical analysis title	Placebo Vs LX9211

Statistical analysis description:

Relations With Other People: The change from baseline to Week 6 in relation with other people was analysed using the MMRM model. The MMRM model included fixed effects of treatment, week, treatment-by-week interaction, the randomisation stratum of Baseline pain severity (moderate, severe), and the Baseline ADPS score as a covariate.

Comparison groups	Placebo v LX9211
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.463
Method	MMRM
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.38

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.41
upper limit	0.65

Statistical analysis title	Placebo Vs LX9211

Statistical analysis description:

Sleep: The change from baseline to Week 6 in relations with sleep was analysed using the MMRM model. The MMRM model included fixed effects of treatment, week, treatment-by-week interaction, the randomisation stratum of Baseline pain severity (moderate, severe), and the Baseline ADPS score as a covariate.

Comparison groups	Placebo v LX9211
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.908
Method	MMRM
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.05
upper limit	0.93

Statistical analysis title	Placebo Vs LX9211

Statistical analysis description:

Enjoyment of Life: The change from baseline to Week 6 in enjoyment of life was analysed using the MMRM model. The MMRM model included fixed effects of treatment, week, treatment-by-week interaction, the randomisation stratum of Baseline pain severity (moderate, severe), and the Baseline ADPS score as a covariate.

Comparison groups	Placebo v LX9211
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.158
Method	MMRM
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0.31

Secondary: Percentage of Subjects Discontinuing Treatment due to Lack of Efficacy Defined as Increase in ADPS from Baseline of ≥30% Based on Question 5 of the ZBPI

End point title	Percentage of Subjects Discontinuing Treatment due to Lack of Efficacy Defined as Increase in ADPS from Baseline of ≥30% Based on Question 5 of the ZBPI

End point description:

ADPS is based on question 5 of ZBPI and assessed on an 11-point numerical rating scale where, 0 = No Pain to 10 = pain as bad as you can imagine.

End point type	Secondary

End point timeframe:

Baseline to Week 6

End point values	Placebo	LX9211		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[5]	0[6]		
Units: percentage of subjects				
number (not applicable)				

Notes:

[5] - Data for the outcome measure was not analysed due to change in planned analyses.

[6] - Data for the outcome measure was not analysed due to change in planned analyses.

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Impression of Change (PGIC) at Week 6

End point title	Patient Global Impression of Change (PGIC) at Week 6

End point description:

PGIC is assessed on a 7-point rating scale where 1= very much improved to 7 = very much worse. Higher scores indicate worse outcomes. The mITT population included all randomised subjects who had taken at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline to Week 6

End point values	Placebo	LX9211		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36[7]	27[8]		
Units: score on a scale				
least squares mean (standard error)	3.06 (± 0.222)	2.65 (± 0.265)		

Notes:

[7] - Number of subjects analysed signifies subjects who were evaluable for this endpoint.

[8] - Number of subjects analysed signifies subjects who were evaluable for this endpoint.

Statistical analyses

Statistical analysis title	Placebo Vs LX9211

Statistical analysis description:

Analysis of variance (ANOVA) model was used with treatment and randomisation stratum of Baseline pain severity (moderate, severe) as independent variables.

Comparison groups	Placebo v LX9211
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.192
Method	ANOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.05
upper limit	0.22

Secondary: Time to Loss of Efficacy From Week 6 to Week 11 Among Subjects Achieving ≥30% Reduction in Pain Intensity in ADPS Based on Question 5 of the ZBPI.

End point title	Time to Loss of Efficacy From Week 6 to Week 11 Among Subjects Achieving ≥30% Reduction in Pain Intensity in ADPS Based on Question 5 of the ZBPI.

End point description:

ADPS is based on question 5 of ZBPI and assessed on an 11-point numerical rating scale where, 0 = No Pain to 10 = pain as bad as you can imagine.

End point type	Secondary

End point timeframe:

Week 6 to Week 11

End point values	Placebo	LX9211		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[9]	0[10]		
Units: years				
arithmetic mean (standard deviation)	()	()		

Notes:

[9] - Data for the outcome measure was not analysed due to change in planned analyses.

[10] - Data for the outcome measure was not analysed due to change in planned analyses.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs)

End point description:

Adverse Events (AEs) are defined as any sign, symptom, or diagnosis/disease that is unfavorable or unintended, that is new, or if pre-existing, worsens in subjects administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. Treatment-emergent AEs are defined as any AEs reported after the first dose of double-blind study medication on study Day 1. The safety population included those subjects who took at least 1 dose of study drug during the Double-blind Treatment period.

End point type	Secondary

End point timeframe:

From informed consent to the end of safety follow-up (up to 15 weeks)

End point values	Placebo	LX9211		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	38		
Units: subjects				
number (not applicable)	13	24		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From informed consent to the end of safety follow-up (up to 15 weeks)

Adverse event reporting additional description:

The data is reported for subjects in the Double-blind Treatment Period and Single-blind Placebo Safety Follow-up Treatment Period. The safety population included those subjects who took at least 1 dose of study drug during the Double-blind Treatment period. Adverse events reported occurred at a frequency >=5% in any treatment group.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Placebo (Double-blind Treatment Period)

Reporting group description:

Following a 2-week Single-blind Placebo Run-in period, subjects received a single loading dose of matching-placebo to LX9211 tablet, orally, on Day 1 and maintenance doses, orally, once daily from Day 2 to Week 6.

Reporting group title	LX9211 (Double-blind Treatment Period)

Reporting group description:

Following a 2-week Single-blind Placebo Run-in period, subjects received a single loading dose of 200 mg tablet, orally, on Day 1 and maintenance doses of 20 mg, orally, once daily from Day 2 to Week 6.

Reporting group title	Placebo (Single-blind Placebo Safety Follow-up Period)

Reporting group description:

Following completion of the 6-week double-blind Treatment Period, all subjects entered the 5-week single-blind Placebo Safety Follow-up Period and received a daily dose of matching placebo to LX9211 tablet, orally.

Reporting group title	LX9211 (Single-blind Placebo Safety Follow-up Period)

Reporting group description:

Following completion of the 6-week double-blind Treatment Period, all subjects entered the 5-week single-blind Placebo Safety Follow-up Period and received a daily dose of LX9211 tablet, orally.

Serious adverse events	Placebo (Double-blind Treatment Period)	LX9211 (Double-blind Treatment Period)	Placebo (Single-blind Placebo Safety Follow-up Period)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 41 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	LX9211 (Single-blind Placebo Safety Follow-up Period)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 31 (0.00%)		
number of deaths (all causes)	0		

number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Placebo (Double-blind Treatment Period)	LX9211 (Double-blind Treatment Period)	Placebo (Single-blind Placebo Safety Follow-up Period)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 41 (7.32%)	21 / 38 (55.26%)	2 / 38 (5.26%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 41 (4.88%)	11 / 38 (28.95%)	0 / 38 (0.00%)
occurrences (all)	2	11	0
Headache			
subjects affected / exposed	2 / 41 (4.88%)	4 / 38 (10.53%)	0 / 38 (0.00%)
occurrences (all)	3	6	0
Balance disorder			
subjects affected / exposed	0 / 41 (0.00%)	2 / 38 (5.26%)	0 / 38 (0.00%)
occurrences (all)	0	2	0
Somnolence			
subjects affected / exposed	0 / 41 (0.00%)	2 / 38 (5.26%)	0 / 38 (0.00%)
occurrences (all)	0	2	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 41 (0.00%)	2 / 38 (5.26%)	0 / 38 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Constipatiopn			
subjects affected / exposed	0 / 41 (0.00%)	4 / 38 (10.53%)	0 / 38 (0.00%)
occurrences (all)	0	4	0
Diarrhea			
subjects affected / exposed	3 / 41 (7.32%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	3	0	0
Nausea			
subjects affected / exposed	0 / 41 (0.00%)	3 / 38 (7.89%)	0 / 38 (0.00%)
occurrences (all)	0	3	0

Dry mouth			
subjects affected / exposed	0 / 41 (0.00%)	2 / 38 (5.26%)	0 / 38 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 41 (4.88%)	3 / 38 (7.89%)	2 / 38 (5.26%)
occurrences (all)	2	3	2

Non-serious adverse events	LX9211 (Single-blind Placebo Safety Follow-up Period)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 31 (3.23%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Balance disorder			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Constipatiopn			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Diarrhea			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Nausea			

subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Dry mouth			
subjects affected / exposed	0 / 31 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 October 2020	• EudraCT Number was provided as unique study reference for participating European Sites • Study Drug Administration: Run-in period Tables was removed as all patients during this time point were to be administered study placebo only • Futility assessment was not needed as interim efficacy analysis provided needed statistical data • Global protocol alignment with regard to patients being able to consume a light meal prior to study visits to ensure that patient's weight was collected despite having had consumed food • Safety Physician contact information was updated as new person was performing this role • Appendix A: Clarification to table footer (i) to better outline which pregnancy test types (serum/urine) were collected during time points (Screening and Day 1 [Baseline]) • Appendix A: Clarification to table footer (k) performed to better outline the collection time points of Cp2hr, biomarker/target engagement, and cytokine and chemokine blood samples
03 March 2021	• To streamline brand and dose, only the acetaminophen provided by the Sponsor as a rescue medicine was to be used during the course of the study. It was noted that the use of personally acquired acetaminophen was prohibited. • To avoid confusion, the text in the protocol was globally aligned regarding the permitted time frame for brief use of opioid medication for the management of non-PHN acute pain prior to the Screening Visit. • Use of NSAIDs for the specific treatment of PHN pain was excluded. • The Sponsor was responsible for deciding if Verified Clinical Trials were established in specific countries. • The Safety Physician contact information was updated as new person performing this role.
15 October 2021	• Modified plans for interim analysis and their implications • The exclusion of patients with facial PHN were eligible for participation if trigeminal neuralgia was excluded as a cause • Changed the physical address of Lexicon Pharmaceuticals, Inc.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported