



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 standard deviation | 63.6 ± 12.5 | 65.4 ± 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 $\geq 30\%$ Reduction in Pain Intensity in ADPS From Baseline at Week 6

| | |
|------------------------|---|
| End point title | Percentage of Subjects with $\geq 30\%$ 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 $\geq 50\%$ Reduction in Pain Intensity in ADPS From Baseline at Week 6

| | |
|---|---|
| End point title | Percentage of Subjects with $\geq 50\%$ 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

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

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|--|-----------------------------------|
| 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 $\geq 30\%$ 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 $\geq 30\%$ 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 (\pm 0.222) | 2.65 (\pm 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 $\geq 5\%$ 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 | | | |
| Constipation | | | |
| 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 occurrences (all) | 0 / 41 (0.00%) 0 | 2 / 38 (5.26%) 2 | 0 / 38 (0.00%) 0 |
| Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all) | 2 / 41 (4.88%) 2 | 3 / 38 (7.89%) 3 | 2 / 38 (5.26%) 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 occurrences (all) Headache subjects affected / exposed occurrences (all) Balance disorder subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 0 / 31 (0.00%) 0 0 / 31 (0.00%) 0 0 / 31 (0.00%) 0 | | |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhea subjects affected / exposed occurrences (all) Nausea | 0 / 31 (0.00%) 0 0 / 31 (0.00%) 0 | | |

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 23 October 2020 | <ul style="list-style-type: none">• 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 | <ul style="list-style-type: none">• 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 | <ul style="list-style-type: none">• 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