



Clinical trial results:

A Multi-centre, Double-blind, Randomised, Placebo-controlled, Parallel-arm Phase IIa Trial to Evaluate the Efficacy, Safety and Tolerability of 28-Day Oral Treatment with PXT002331 (Foliglurax) in Reducing Motor Complications of Levodopa Therapy in Subjects with Parkinson's Disease Experiencing End-of-dose Wearing Off and Levodopa-Induced Dyskinesia (AMBLED)

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2017-000135-14 |
| Trial protocol | AT DE GB ES IT |
| Global end of trial date | 02 March 2020 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 26 February 2021 |
| First version publication date | 26 February 2021 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | PXT-CL17-001 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|------------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03162874 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | H.Lundbeck A/S: 18023A |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Prexton Therapeutics BV |
| Sponsor organisation address | Kloosterstraat 9, Oss, Netherlands, 5349 AB |
| Public contact | Lundbeck Clinical Trials, H. Lundbeck A/S, +45 36301311, LundbeckClinicalTrials@lundbeck.com |
| Scientific contact | Lundbeck Clinical Trials, H. Lundbeck A/S, +45 36301311, LundbeckClinicalTrials@lundbeck.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 | 02 March 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 19 February 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 02 March 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to assess the efficacy of 2 doses of foliglurax as an adjunct to levodopa in the reduction of OFF time in participants with Parkinson's Disease (PD).

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki (2013) and International Council for Harmonisation (ICH) Good Clinical Practice (1996).

Background therapy:

Participants continued to take their usual levodopa treatment, as well as permitted anti-Parkinsonian drugs (if any), from their own prescribed supply throughout the study. Participants were treated with a stable regimen of their levodopa-containing therapy and any permitted anti-Parkinsonian drugs during the study according to their usual regimen.

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 25 May 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Spain: 24 |
| Country: Number of subjects enrolled | United Kingdom: 26 |
| Country: Number of subjects enrolled | Austria: 3 |
| Country: Number of subjects enrolled | France: 33 |
| Country: Number of subjects enrolled | Germany: 32 |
| Country: Number of subjects enrolled | Italy: 39 |
| Worldwide total number of subjects | 157 |
| EEA total number of subjects | 157 |

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) | 62 |
| From 65 to 84 years | 95 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants who met all the inclusion criteria and none of the exclusion criteria were enrolled.

Participants were randomised in 1:1:1 ratio to 3 treatment groups: Foliglurax 10 mg twice daily (BID), Foliglurax 30 mg BID, or Placebo BID.

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 |

Arms

| | |
|------------------------------|----------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Foliglurax 10 mg BID |

Arm description:

Participants received 10 milligrams (mg) foliglurax capsules orally BID on Days 1 to 27, and a final single dose on the morning of Day 28.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Foliglurax |
| Investigational medicinal product code | PXT002331 |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Foliglurax was administered per dose and schedule specified in the arm description.

| | |
|------------------|----------------------|
| Arm title | Foliglurax 30 mg BID |
|------------------|----------------------|

Arm description:

Participants received 30 mg foliglurax capsules orally BID on Days 1 to 27, and a final single dose on the morning of Day 28.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Foliglurax |
| Investigational medicinal product code | PXT002331 |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Foliglurax was administered per dose and schedule specified in the arm description.

| | |
|------------------|-------------|
| Arm title | Placebo BID |
|------------------|-------------|

Arm description:

Participants received placebo matched to foliglurax capsules orally BID on Days 1 to 27, and a final single dose on the morning of Day 28.

| | |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

| | |
|--|---------------|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | PXT002331 |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo matched to foliglurax was administered per schedule specified in the arm description.

| Number of subjects in period 1 | Foliglurax 10 mg BID | Foliglurax 30 mg BID | Placebo BID |
|--|-------------------------|-------------------------|-------------|
| Started | 53 | 52 | 52 |
| Received at least 1 dose of study drug | 53 | 52 | 52 |
| Completed | 45 | 48 | 46 |
| Not completed | 8 | 4 | 6 |
| Consent withdrawn by subject | 1 | 2 | 2 |
| Adverse event, non-fatal | 5 | 2 | 1 |
| Other than specified | - | - | 1 |
| Protocol deviation | 2 | - | 2 |

Baseline characteristics

Reporting groups

| | |
|--|----------------------|
| Reporting group title | Foliglurax 10 mg BID |
| Reporting group description: Participants received 10 milligrams (mg) foliglurax capsules orally BID on Days 1 to 27, and a final single dose on the morning of Day 28. | |
| Reporting group title | Foliglurax 30 mg BID |
| Reporting group description: Participants received 30 mg foliglurax capsules orally BID on Days 1 to 27, and a final single dose on the morning of Day 28. | |
| Reporting group title | Placebo BID |
| Reporting group description: Participants received placebo matched to foliglurax capsules orally BID on Days 1 to 27, and a final single dose on the morning of Day 28. | |

| Reporting group values | Foliglurax 10 mg BID | Foliglurax 30 mg BID | Placebo BID |
|------------------------------------|----------------------|----------------------|-------------|
| Number of subjects | 53 | 52 | 52 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|-------------|-------------|-------------|
| Age continuous Units: years arithmetic mean standard deviation | 66 ± 9.2 | 66 ± 9.1 | 67 ± 8.9 |
| Gender categorical Units: Subjects | | | |
| Female | 21 | 28 | 24 |
| Male | 32 | 24 | 28 |

| Reporting group values | Total | | |
|------------------------------------|-------|--|--|
| Number of subjects | 157 | | |
| Age categorical Units: Subjects | | | |

| | | | |
|---|----|--|--|
| Age continuous Units: years arithmetic mean standard deviation | - | | |
| Gender categorical Units: Subjects | | | |
| Female | 73 | | |
| Male | 84 | | |

End points

End points reporting groups

| | |
|--|----------------------|
| Reporting group title | Foliglurax 10 mg BID |
| Reporting group description: Participants received 10 milligrams (mg) foliglurax capsules orally BID on Days 1 to 27, and a final single dose on the morning of Day 28. | |
| Reporting group title | Foliglurax 30 mg BID |
| Reporting group description: Participants received 30 mg foliglurax capsules orally BID on Days 1 to 27, and a final single dose on the morning of Day 28. | |
| Reporting group title | Placebo BID |
| Reporting group description: Participants received placebo matched to foliglurax capsules orally BID on Days 1 to 27, and a final single dose on the morning of Day 28. | |

Primary: Change From Baseline in the Daily Awake OFF Time Based on Participant Hauser Diary Entries at the End of Treatment Period (Day 28)

| | |
|--|--|
| End point title | Change From Baseline in the Daily Awake OFF Time Based on Participant Hauser Diary Entries at the End of Treatment Period (Day 28) |
| End point description: Participants completed a 3-day Hauser diary with waking status (time OFF) every 30 minutes while awake before the Baseline and Day 28 Visits. The Hauser diary was completed by the participant during 3 consecutive days immediately preceding each scheduled site visit. An "OFF state" was defined as the time when medication was not providing benefit with respect to mobility, slowness and stiffness. OFF episodes might be heralded by nonmotor symptoms (for example, pain, anxiety) prior to the appearance of motor symptoms. Efficacy Full Analysis Set (FAS) included all participants who received at least 1 dose of foliglurax or placebo and had a valid baseline assessment and at least 1 valid postbaseline assessment (either at Day 14 or 28) of the primary efficacy variable (that is, Hauser daily awake OFF time). Here, 'n' signifies participants analysed for this endpoint at specified timepoints. | |
| End point type | Primary |
| End point timeframe: Baseline, Day 28 | |

| End point values | Foliglurax 10 mg BID | Foliglurax 30 mg BID | Placebo BID | |
|--------------------------------------|----------------------|----------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 50 | 49 | |
| Units: hours | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 50, 50, 49) | 5.05 (± 2.245) | 4.88 (± 2.127) | 4.74 (± 2.079) | |
| Change at Day 28 (n = 45, 47, 46) | -0.43 (± 2.028) | -0.70 (± 2.200) | -0.31 (± 1.718) | |

Statistical analyses

| | |
|---|------------------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Statistical analysis description: | |
| Analysis was performed using a restricted maximum likelihood-based mixed model for repeated measures (MMRM) approach. The model included terms for treatment (10 mg Foliglurax BID, 30 mg Foliglurax BID and placebo BID), day (Day 28), day-by-treatment and site as fixed factors and the baseline OFF time score and its interaction with day as covariates. | |
| Comparison groups | Foliglurax 10 mg BID v Placebo BID |
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2639 ^[1] |
| Method | Mixed models analysis |
| Parameter estimate | Least Square (LS) Mean Difference |
| Point estimate | -0.27 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -0.96 |
| upper limit | 0.43 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.419 |

Notes:

[1] - Testing was performed at a 5% 1-sided level without adjustment for multiplicity.

| | |
|---|------------------------------------|
| Statistical analysis title | Statistical analysis 2 |
| Statistical analysis description: | |
| Analysis was performed using a restricted maximum likelihood-based MMRM approach. The model included terms for treatment (10 mg Foliglurax BID, 30 mg Foliglurax BID and placebo BID), day (Day 28), day-by-treatment and site as fixed factors and the baseline OFF time score and its interaction with day as covariates. | |
| Comparison groups | Foliglurax 30 mg BID v Placebo BID |
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.1455 ^[2] |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.44 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -1.12 |
| upper limit | 0.25 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.412 |

Notes:

[2] - Testing was performed at a 5% 1-sided level without adjustment for multiplicity.

Secondary: Change From Baseline in the Total Objective Score (Parts 3 and 4) for Dyskinesia Impairment and Disability Assessed by Unified Dyskinesia Rating Scale (UDysRS) at the End of Treatment Period (Day 28)

| | |
|-----------------|--|
| End point title | Change From Baseline in the Total Objective Score (Parts 3 and |
|-----------------|--|

End point description:

UDysRS Part 3 contains 7 questions about objective evaluation of dyskinesia impairment (dyskinesia severity, anatomic distribution, and type); and Part 4 contains 4 questions regarding dyskinesia disability based on Part 3 activities. Each question was scored with respect to severity, which was rated on a scale where 0 = normal, 1 = slight, 2 = mild, 3 = moderate and 4 = severe. The scores for the 2 Parts combined ranged from 0-44; with a higher score representing more severe dyskinesia. Efficacy FAS included all participants who received at least 1 dose of foliglurax or placebo and had a valid baseline assessment and at least 1 valid postbaseline assessment (either at Day 14 or 28) of the primary efficacy variable (that is, Hauser daily awake OFF time). Here, 'n' signifies participants analysed for this endpoint at specified timepoints.

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

End point timeframe:

Baseline, Day 28

| End point values | Foliglurax 10 mg BID | Foliglurax 30 mg BID | Placebo BID | |
|--------------------------------------|----------------------|----------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 50 | 49 | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 50, 50, 49) | 17.76 (± 5.049) | 17.08 (± 5.010) | 18.37 (± 6.870) | |
| Change at Day 28 (n = 47, 48, 46) | -3.06 (± 6.281) | -3.21 (± 5.608) | -3.07 (± 6.187) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in UDysRS Score at the End of Treatment Period (Day 28)

| | |
|-----------------|--|
| End point title | Change From Baseline in UDysRS Score at the End of Treatment Period (Day 28) |
|-----------------|--|

End point description:

UDysRS is a tool used to assess dyskinesia in PD. Part 1 contains 11 questions about ON time dyskinesia and the impact of ON-dyskinesia on experiences of daily living. Part 2 contains 4 questions about OFF-dystonia rating. Part 3 contains 7 questions about objective evaluation of dyskinesia impairment and Part 4 contains 4 questions regarding dyskinesia disability. Each question was scored with respect to severity, which was rated on a scale where 0 = normal, 1 = slight, 2 = mild, 3 = moderate and 4 = severe. UDysRS total score was obtained by summing the item scores, ranging from 0 to 104 with higher scores indicating more disability. Efficacy FAS included all participants who received at least 1 dose of foliglurax or placebo and had a valid baseline assessment and at least 1 valid postbaseline assessment (either at Day 14 or 28) of primary efficacy variable (that is, Hauser daily awake OFF time). Here, 'n' signifies participants analysed for this endpoint at specified timepoints.

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

End point timeframe:

Baseline, Day 28

| End point values | Foliglurax 10 mg BID | Foliglurax 30 mg BID | Placebo BID | |
|--------------------------------------|----------------------|----------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 50 | 49 | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 50, 50, 49) | 42.98 (± 11.996) | 41.80 (± 8.683) | 43.06 (± 13.204) | |
| Change at Day 28 (n = 47, 48, 46) | -8.32 (± 10.933) | -8.46 (± 10.433) | -7.80 (± 9.923) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving a Clinically Significant Reduction in OFF Time (at Least 1 Hour as Defined by Hauser et al.) From Baseline to End of Treatment Period (Day 28) Based on Participant Hauser Diary Entries

| | |
|-----------------|---|
| End point title | Percentage of Participants Achieving a Clinically Significant Reduction in OFF Time (at Least 1 Hour as Defined by Hauser et al.) From Baseline to End of Treatment Period (Day 28) Based on Participant Hauser Diary Entries |
|-----------------|---|

End point description:

Participants completed a 3-day Hauser diary with waking status (time OFF) every 30 minutes while awake before the Baseline and Day 28 Visits. The Hauser diary was completed by the participant during 3 consecutive days immediately preceding each scheduled site visit. An "OFF state" was defined as the time when medication was not providing benefit with respect to mobility, slowness and stiffness. OFF episodes might be heralded by nonmotor symptoms (for example, pain, anxiety) prior to the appearance of motor symptoms. Efficacy FAS included all participants who received at least 1 dose of foliglurax or placebo and had a valid baseline assessment and at least 1 valid postbaseline assessment (either at Day 14 or 28) of the primary efficacy variable (that is, Hauser daily awake OFF time). Here, 'Number of participants analysed' signifies participants analysed for this endpoint.

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

End point timeframe:

Baseline, Day 28

| End point values | Foliglurax 10 mg BID | Foliglurax 30 mg BID | Placebo BID | |
|-----------------------------------|----------------------|----------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 45 | 47 | 46 | |
| Units: percentage of participants | | | | |
| number (not applicable) | 31.1 | 44.7 | 30.4 | |

Statistical analyses

Secondary: Change From Baseline in the Percentage of Daily Awake OFF Time Based on Participant Hauser Diary Entries at the End of Treatment Period (Day 28)

| | |
|-----------------|--|
| End point title | Change From Baseline in the Percentage of Daily Awake OFF Time Based on Participant Hauser Diary Entries at the End of Treatment Period (Day 28) |
|-----------------|--|

End point description:

Participants completed a 3-day Hauser diary with waking status (time OFF) every 30 minutes while awake before the Baseline and Day 28 Visits. The Hauser diary was completed by the participant during 3 consecutive days immediately preceding each scheduled site visit. An "OFF state" was defined as the time when medication was not providing benefit with respect to mobility, slowness and stiffness. OFF episodes might be heralded by nonmotor symptoms (for example, pain, anxiety) prior to the appearance of motor symptoms. Efficacy FAS included all participants who received at least 1 dose of foliglurax or placebo and had a valid baseline assessment and at least 1 valid postbaseline assessment (either at Day 14 or 28) of the primary efficacy variable (that is, Hauser daily awake OFF time). Here, 'n' signifies participants analysed for this endpoint at specified timepoints.

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

End point timeframe:

Baseline, Day 28

| End point values | Foliglurax 10 mg BID | Foliglurax 30 mg BID | Placebo BID | |
|---|----------------------|----------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 50 | 49 | |
| Units: percentage of daily awake OFF time | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 50, 50, 49) | 21.04 (± 9.353) | 20.33 (± 8.861) | 19.77 (± 8.661) | |
| Change at Day 28 (n = 45, 47, 46) | -1.79 (± 8.450) | -2.90 (± 9.169) | -1.30 (± 7.158) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Daily Awake ON Time Without Troublesome Dyskinesia Based on Participant Hauser Diary Entries at the End of Treatment Period (Day 28)

| | |
|-----------------|--|
| End point title | Change From Baseline in the Daily Awake ON Time Without Troublesome Dyskinesia Based on Participant Hauser Diary Entries at the End of Treatment Period (Day 28) |
|-----------------|--|

End point description:

Participants completed a 3-day Hauser diary with waking status (time ON without troublesome dyskinesia) every 30 minutes while awake before the Baseline and Day 28 Visits. The Hauser diary was completed by the participant during 3 consecutive days immediately preceding each scheduled site visit. An "ON state" was defined as the time when medication was providing benefit with respect to mobility, slowness and stiffness, and might or might not be providing complete alleviation of all PD symptoms. Daily awake ON time without troublesome dyskinesia was defined as ON time without dyskinesia plus ON time with nontroublesome dyskinesia. Efficacy FAS included all participants who received at least 1 dose of foliglurax or placebo and had a valid baseline assessment and at least 1 valid postbaseline assessment (either at Day 14 or 28) of the primary efficacy variable (that is, Hauser daily awake OFF

time). Here, 'n' signifies participants analysed for this endpoint at specified timepoints.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Day 28 | |

| End point values | Foliglurax 10 mg BID | Foliglurax 30 mg BID | Placebo BID | |
|--------------------------------------|----------------------|----------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 50 | 49 | |
| Units: hours | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 50, 50, 49) | 8.75 (± 2.474) | 8.83 (± 2.654) | 8.77 (± 2.792) | |
| Change at Day 28 (n = 45, 47, 46) | 1.05 (± 2.308) | 0.95 (± 2.848) | 0.56 (± 2.519) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Percentage of Daily Awake ON Time Without Troublesome Dyskinesia Based on Participant Hauser Diary Entries at the End of Treatment Period (Day 28)

| | |
|-----------------|--|
| End point title | Change From Baseline in the Percentage of Daily Awake ON Time Without Troublesome Dyskinesia Based on Participant Hauser Diary Entries at the End of Treatment Period (Day 28) |
|-----------------|--|

End point description:

Participants completed a 3-day Hauser diary with waking status (time ON without troublesome dyskinesia) every 30 minutes while awake before the Baseline and Day 28 Visits. The Hauser diary was completed by the participant during 3 consecutive days immediately preceding each scheduled site visit. An "ON state" was defined as the time when medication was providing benefit with respect to mobility, slowness and stiffness, and might or might not be providing complete alleviation of all PD symptoms. Daily awake ON time without troublesome dyskinesia was defined as ON time without dyskinesia plus ON time with nontroublesome dyskinesia. Efficacy FAS included all participants who received at least 1 dose of foliglurax or placebo and had a valid baseline assessment and at least 1 valid postbaseline assessment (either at Day 14 or 28) of the primary efficacy variable (that is, Hauser daily awake OFF time). Here, 'n' signifies participants analysed for this endpoint at specified timepoints.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Day 28 | |

| End point values | Foliglurax 10 mg BID | Foliglurax 30 mg BID | Placebo BID | |
|--|----------------------|----------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 50 | 49 | |
| Units: percentage of daily awake ON time | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n = 50, 50, 49) | 36.46 (± 10.308) | 36.79 (± 11.058) | 36.55 (± 11.632) | |

| | | | | |
|-----------------------------------|---------------------|----------------------|----------------------|--|
| Change at Day 28 (n = 45, 47, 46) | 4.38 (\pm 9.617) | 3.96 (\pm 11.866) | 2.34 (\pm 10.495) | |
|-----------------------------------|---------------------|----------------------|----------------------|--|

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First dose up to follow-up (up to Day 42)

Adverse event reporting additional description:

Safety set included all eligible participants who received at least 1 dose of foliglurax or placebo.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------------------|
| Reporting group title | Foliglurax 10 mg BID |
|-----------------------|----------------------|

Reporting group description:

Participants received 10 mg foliglurax capsules orally BID on Days 1 to 27, and a final single dose on the morning of Day 28.

| | |
|-----------------------|----------------------|
| Reporting group title | Foliglurax 30 mg BID |
|-----------------------|----------------------|

Reporting group description:

Participants received 30 mg foliglurax capsules orally BID on Days 1 to 27, and a final single dose on the morning of Day 28.

| | |
|-----------------------|-------------|
| Reporting group title | Placebo BID |
|-----------------------|-------------|

Reporting group description:

Participants received placebo matched to foliglurax capsules orally BID on Days 1 to 27, and a final single dose on the morning of Day 28.

| Serious adverse events | Foliglurax 10 mg BID | Foliglurax 30 mg BID | Placebo BID |
|---|----------------------|----------------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 53 (5.66%) | 1 / 52 (1.92%) | 3 / 52 (5.77%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Tendon injury | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wrist fracture | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| On and off phenomenon | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 53 (1.89%) | 1 / 52 (1.92%) | 0 / 52 (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 colic | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Muscle rigidity | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Viral labyrinthitis | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | Foliglurax 10 mg BID | Foliglurax 30 mg BID | Placebo BID |
|--|-------------------------|-------------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 53 (22.64%) | 14 / 52 (26.92%) | 10 / 52 (19.23%) |
| Investigations | | | |
| Protein urine present | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 3 / 52 (5.77%) | 1 / 52 (1.92%) |
| occurrences (all) | 1 | 3 | 1 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 4 / 53 (7.55%) | 3 / 52 (5.77%) | 0 / 52 (0.00%) |
| occurrences (all) | 4 | 3 | 0 |
| Nervous system disorders | | | |
| Dyskinesia | | | |

| | | | |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 3 / 53 (5.66%) | 3 / 52 (5.77%) | 4 / 52 (7.69%) |
| occurrences (all) | 3 | 3 | 4 |
| Headache | | | |
| subjects affected / exposed | 3 / 53 (5.66%) | 2 / 52 (3.85%) | 1 / 52 (1.92%) |
| occurrences (all) | 3 | 2 | 1 |
| On and off phenomenon | | | |
| subjects affected / exposed | 2 / 53 (3.77%) | 5 / 52 (9.62%) | 6 / 52 (11.54%) |
| occurrences (all) | 2 | 5 | 6 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 31 October 2018 | <p>This amendment included the following changes:</p> <ul style="list-style-type: none">• Change in contract research organisation (CRO) medical monitor;• Clarified secondary efficacy outcome endpoints;• Clarified that there were multiple scores in the Hospital Anxiety and Depression Scale (HADS);• Moved Columbia-Suicide Severity Rating Scale (C-SSRS) and Scale for Assessment of Positive Symptoms for Parkinson's Disease Psychosis (SAPS-PD) to Safety and Tolerability Assessments;• Corrected the baseline QTcF as the average from the Screening Visit 1 and clarified that the time window for UDysRS assessments was defined during the Screening Visit 2;• Corrected exclusion criterion to include human immunodeficiency virus (HIV)-1 or -2 antibodies instead of both HIV-1 and -2 antibodies;• Added flexibility to exclusion criterion to clarify that participant rescreening was permitted, as this criterion was not intended to apply to screen failures;• Clarified that electrocardiograms (ECGs) should be performed before vital signs measurements and switched assessment text accordingly;• Clarified that follicle-stimulating hormone (FSH) testing was only to be performed at screening;• Corrected clinical laboratory units as per the central laboratory;• Updated the blood volume for foliglurax pharmacokinetic (PK) as a smaller volume could be used;• Revised the efficacy FAS and efficacy per protocol set (PPS) to better meet regulatory expectations and changed populations to sets;• Revised the primary efficacy analysis model to better meet regulatory expectations and modified the primary efficacy analyses so it was based on the efficacy FAS but was also to be repeated on the efficacy PPS;• Added a blinded interim PK analysis to support formulation development;• Clarified that serious adverse events (SAEs) were reported via electronic case report form (eCRF) and paper SAE report;• Clarified multiple items in the schedule of activities. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported