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	66	66	67
standard deviation	± 9.2	± 9.1	± 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

	4) for Dyskinesia Impairment and Disability Assessed by Unified Dyskinesia Rating Scale (UDysRS) at the End of Treatment Period (Day 28)

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

No statistical analyses for this end point

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 (± 9.617)	3.96 (± 11.866)	2.34 (± 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	This amendment included the following changes: • 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