Clinical trial results:
A Randomized, Double-blind, Placebo-controlled Study to Assess the Safety, Tolerability and Preliminary Efficacy of NLX-112 versus Placebo in Levodopa-induced Dyskinesia in Parkinson's Disease

Summary

EudraCT number	2020-006053-22
Trial protocol	SE
Global end of trial date	18 January 2023

Results information

Result version number	v1 (current)
This version publication date	02 February 2024
First version publication date	02 February 2024

Trial information

Trial identification

Sponsor protocol code	NLX-112-DYS-101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05148884
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Neurolixis SAS
Sponsor organisation address	2 rue Georges Charpak, L'Arobase Le Causse Espace d'Entreprises, Labruguiere, France, FR-81290
Public contact	CEO, Neurolixis SAS, anewmantancredi@neurolixis.com
Scientific contact	CEO, Neurolixis SAS, anewmantancredi@neurolixis.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	18 January 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 January 2023
Global end of trial reached?	Yes
Global end of trial date	18 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of NLX-112, titrated up to a maximum of 2 mg/day, compared to placebo during eight weeks of daily treatment in PD patients with LID.

Protection of trial subjects:

The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and are compliant with the International Conference of Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) E6 (R2) guidance, the EU Clinical Trials Directive 2001/20/EC, and applicable local regulatory requirements. It was the responsibility of each Investigator or an authorized associate to give each potential study patient adequate verbal and written information before any study specific assessments were performed.

The information included the objectives and the procedures of the study as well as any risks or inconvenience involved. It was emphasized that participation in the study was voluntary and that the patient could withdraw from participation at any time and for any reason, without any prejudice. All patients were given the opportunity to ask questions about the study and were given sufficient time to consider participation before signing the Informed consent form (ICF). Before performing any study-related procedures, the ICF was signed and personally dated by the patient and the Investigator. A copy of the patient information including the signed ICF was provided to the patient. Documentation of the discussion and the date of informed consent were recorded in the source documentation and in the electronic case report form (eCRF).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 November 2021
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	Sweden: 27
Worldwide total number of subjects	27
EEA total number of subjects	27

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)	12
From 65 to 84 years	14
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Potential participants in the study were identified according to the routines of the clinical study sites. Patients were recruited at 5 clinical sites, with a planned average of 4 to 6 patients per site.

Pre-assignment

Screening details:

A total of 35 patients were screened and 27 were randomized and dosed in the study. Eighteen patients were allocated to treatment with NLX-112 and 9 were allocated to placebo. Twenty-three patients, 15 on NLX-112 and 8 on placebo, completed the study.

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

This was a double-blind study and the allocation of treatments was not disclosed until a clean file had been declared and the database had been locked. The IMP and the placebo were identical in appearance and taste.

Arms

Are arms mutually exclusive?	Yes
Arm title	NLX-112

Arm description:

Patients were randomized to receive either active treatment with NLX-112 or placebo. This arm represents the patients that received NLX-112.

Arm type	Experimental
Investigational medicinal product name	NLX-112
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients self-administered NLX-112 2 times each day, once in the morning and once in the evening, according to a dosing instruction sheet. Tablets were to be taken with approximately 240 mL water during a meal.

Arm title	Placebo

Arm description:

Patients were randomized to receive either active treatment with NLX-112 or placebo. This arm represents the patients that received placebo.

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:

Patients self-administered placebo 2 times each day, once in the morning and once in the evening, according to a dosing instruction sheet. Tablets were to be taken with approximately 240 mL water during a meal.

Number of subjects in period 1	NLX-112	Placebo
Started	18	9
Completed	15	8
Not completed	3	1
Consent withdrawn by subject	3	-
Deep brain stimulation operation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	NLX-112
Reporting group description:	
Patients were randomized to receive either active treatment with NLX-112 or placebo. This arm represents the patients that received NLX-112.	
Reporting group title	Placebo
Reporting group description:	
Patients were randomized to receive either active treatment with NLX-112 or placebo. This arm represents the patients that received placebo.	

Reporting group values	NLX-112	Placebo	Total
Number of subjects	18	9	27
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	8	4	12
From 65-84 years	9	5	14
85 years and over	1	0	1
Age continuous Units: years			
arithmetic mean	65.7	64.6	
standard deviation	± 9.7	± 6.3	-
Gender categorical Units: Subjects			
Female	8	4	12
Male	10	5	15

End points

End points reporting groups

Reporting group title	NLX-112
Reporting group description:	
Patients were randomized to receive either active treatment with NLX-112 or placebo. This arm represents the patients that received NLX-112.	
Reporting group title	Placebo
Reporting group description:	
Patients were randomized to receive either active treatment with NLX-112 or placebo. This arm represents the patients that received placebo.	

Primary: Frequency, intensity and seriousness of AEs

End point title	Frequency, intensity and seriousness of AEs[1]
End point description:	
Number of patients with Adverse events (AEs) divided into categories of severity/intensity (grade 1 to grade 5 following the common terminology criteria for AEs (CTCAE) v5.0) and assessed relationship to IMP (unlikely, possibly or probably related).	
End point type	Primary
End point timeframe:	
AEs (including SAEs) were collected from the start of IMP administration until the end-of-study visit.	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, the end-point is reported using descriptive statistics only.

End point values	NLX-112	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	9		
Units: Number of subjects				
Any AE	16	7		
Any SAE	0	1		
Congenital Anomaly or Birth Defect	0	0		
Persistent/Significant Disability/Incapacity	0	0		
Requires or Prolongs Hospitalization	0	1		
Is Life Threatening	0	0		
Other Medically Important Serious Event	0	0		
Any AE leading to withdrawal from study	1	0		
Any AE leading to death	0	0		
Causality - Unlikely Related	11	4		
Causality - Possibly Related	15	5		
Causality - Probably Related	3	3		
Action taken with study drug - Dose Not Changed	12	6		
Action taken with study drug - Dose Reduced	4	3		
Action taken with study drug - Drug Interrupted	0	1		
Action taken with study drug - Not Applicable	5	2		

Severity - Mild	14	7		
Severity - Moderate	10	4		
Severity - Severe	0	1		
Severity - Life-Threatening	0	0		
Severity - Death	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Clinically significant (CS) changes from baseline in electrocardiogram (ECG)

End point title	Clinically significant (CS) changes from baseline in electrocardiogram (ECG)[2]

End point description:

Number of patients with clinically significant changes from baseline in Electrocardiogram (Rate, PR interval, QRS duration, QT, QTcB, and QTcF). Any abnormalities were specified and documented as either clinically significant or not clinically significant.
All ECGs were interpreted as normal or abnormal, not clinically significant by the Investigator at screening, baseline (Visit 2) and all subsequent post-dose visits to the clinics. There were no clinically relevant changes from baseline, and no obvious differences between the treatment groups, either in terms of overall ECG evaluations or change from baseline in individual ECG parameters.

End point type	Primary

End point timeframe:

Visit 1 (Screening), Visit 2 (Baseline, Day 1), Visit 4 (Clinic Safety Visit, Day 14), Visit 5 (Clinic Safety Visit, Day 21), Visit 6 (Clinic Efficacy Visit, Day 28), Visit 7 (Clinic Efficacy Visit, Day 42) and Visit 9 (Follow-up Clinic Visit, Day 70).

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, the end-point is reported using descriptive statistics only.

End point values	NLX-112	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[3]	9[4]		
Units: Number of patients with CS changes	0	0		

Notes:

[3] - Full analysis set.

[4] - Full analysis set.

Statistical analyses

No statistical analyses for this end point

Primary: Clinically significant (CS) changes from baseline in vital signs

End point title	Clinically significant (CS) changes from baseline in vital signs[5]

End point description:

Number of patients with clinically significant changes from baseline in vital signs (Systolic blood pressure (mmHg), diastolic blood pressure (mmHg), Heart rate, respiratory rate, body temperature). Any vital signs outside the normal ranges at each site were judged as either not clinically significant or clinically significant.
There were no clinically relevant changes from baseline in mean vital signs parameters over time and no clinically relevant differences in any vital signs parameter between the active treatment group or the

placebo group as assessed by the Investigator. Eighteen of the 27 randomized patients, 12 on NLX-112 and 6 on placebo, had abnormal vital signs assessed as not clinically significant on one or more occasions during the study. Of these, 2 patients, both on NLX-112, had abnormal vital signs assessed as significant.

End point type	Primary

End point timeframe:

Visit 1 (Screening), Visit 2 (Baseline, Day 1), Visit 4 (Clinic Safety Visit, Day 14), Visit 5 (Clinic Safety Visit, Day 21), Visit 6 (Clinic Efficacy Visit, Day 28), Visit 7 (Clinic Efficacy Visit, Day 42) and Visit 9 (Follow-up Clinic Visit, Day 70).

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, the end-point is reported using descriptive statistics only.

End point values	NLX-112	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[6]	9[7]		
Units: Number of patients with CS changes	2	0		

Notes:

[6] - Full analysis set.

[7] - Full analysis set.

Statistical analyses

No statistical analyses for this end point

Primary: Clinically significant (CS) changes from baseline in safety laboratory parameters

End point title	Clinically significant (CS) changes from baseline in safety laboratory parameters[8]

End point description:

Number of patients with clinically significant changes from baseline in safety laboratory parameters. Any lab values outside the normal ranges were judged as not clinically significant or clinically significant. There were no clinically relevant changes from baseline in mean clinical chemistry, hematology, coagulation or urinalysis parameters over time and no clinically relevant differences in any laboratory parameter between the active treatment group or the placebo group as assessed by the Investigator. All 27 randomized patients had abnormal laboratory values on one or more occasions over the course of the study. A majority of the abnormal laboratory values were assessed as not clinically significant. No coagulation parameter was assessed as abnormal. Three patients had abnormal laboratory values assessed as clinically significant, which in 2 cases were reported as AEs (inflammatory marker increased and hyperglycemia, both assessed as unrelated to treatment with NLX-112).

End point type	Primary

End point timeframe:

Visit 1 (Screening), Visit 2 (Baseline, Day 1), Visit 4 (Clinic Safety Visit, Day 14), Visit 5 (Clinic Safety Visit, Day 21), Visit 6 (Clinic Efficacy Visit, Day 28), Visit 7 (Clinic Efficacy Visit, Day 42) and Visit 9 (Follow-up Clinic Visit, Day 70).

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, the end-point is reported using descriptive statistics only.

End point values	NLX-112	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[9]	9[10]		
Units: Number of patients with CS changes	2	1		

Notes:

[9] - Full analysis set.

[10] - Full analysis set.

Statistical analyses

No statistical analyses for this end point

Primary: Clinically significant changes (CS) from baseline in physical examinations

End point title	Clinically significant changes (CS) from baseline in physical examinations[11]

End point description:

Number of clinically significant changes in physical examination investigated by general appearance, head, ears, eyes, nose, throat, neck, skin, cardiovascular system, respiratory system, abdominal system, and nervous system. Any abnormalities were specified and documented as either clinically significant or not clinically significant.
There were no clinically relevant changes from baseline (screening) to Visit 9 (Day 70±7 days) in physical examination findings between the active treatment group or the placebo group as assessed by the Investigator. Fourteen of the 27 randomized patients had a physical examination assessed as abnormal, clinically significant for one or more organ system at either the screening visit (Visit 1) or Visit 9 or both. Clinically significant findings were most commonly associated with the nervous system and the underlying PD (12 patients, 8 on NLX-112 and 4 on placebo) and were observed both at screening and at Visit 9 (10 patients).

End point type	Primary

End point timeframe:

Visit 1 (Screening) and Visit 9 (Follow-up Clinic Visit, Day 70).

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, the end-point is reported using descriptive statistics only.

End point values	NLX-112	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[12]	9[13]		
Units: Number of patients with CS changes	8	4		

Notes:

[12] - Full analysis set.

[13] - Full analysis set.

Statistical analyses

No statistical analyses for this end point

Primary: Suicidal ideation/behavior as assessed by the Columbia Suicide Severity Rating Scale (C-SSRS)

End point title	Suicidal ideation/behavior as assessed by the Columbia Suicide Severity Rating Scale (C-SSRS)[14]

End point description:

Number of patients with changes from baseline in suicidal ideation/behavior as assessed by C-SSRS questionnaire with no total score summation. The scale contains 6 “yes” or “no” questions in which respondents were asked to indicate whether they have experienced several thoughts or feelings relating

to suicide over the past month and behavior over their lifetime and past 3 months. Each question addresses a different component of the respondent's suicide ideation severity and behavior. Q1: wish to be dead, Q2: non-specific suicidal thoughts, Q3-5: more specific suicidal thoughts and intent to act, Q6: suicidal behavior over the respondent's lifetime and past 3 months, If the respondent answered "yes" to Q2, he/she was instructed to answer Q 3-5. If the respondent answered "no" to Q2, he/she could skip to Q6.
No patient indicated a change in suicidal ideation/behavior from baseline until Visit 9 (Day 70±7 days).

End point type	Primary

End point timeframe:

The baseline scale was used at screening (Visit 1) and the follow-up scale at all subsequent visits (Visit 2, 4-7, 9)

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, the end-point is reported using descriptive statistics only.

End point values	NLX-112	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[15]	9[16]		
Units: Number of patients with changes	0	0		

Notes:

[15] - Full analysis set.

[16] - Full analysis set.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline at the final efficacy clinic visit (Day 42), after a 150% L-DOPA dose challenge, in the Unified Dyskinesia Rating Scale (UDysRS) total score - Absolute change from baseline

End point title	Change from baseline at the final efficacy clinic visit (Day 42), after a 150% L-DOPA dose challenge, in the Unified Dyskinesia Rating Scale (UDysRS) total score - Absolute change from baseline

End point description:

The UDysRS is a rating instrument designed to assess the core features of dyskinesia in PD. The UDysRS consists of 4 parts:
• Part 1, historical disability with regard to the patient's perceptions of the impact on activities of ADL of on-dyskinesia.
• Part 2, historical disability with regard to the patient's perceptions of the impact on ADL of off-dystonia.
• Part 3, objective impairment, which assesses severity of dyskinesia, affected body parts, and type of impairment (choreic vs. dystonic).
• Part 4, objective disability, based on an evaluation of Part 3 activities.
Each item in the UDysRS was scored from 0 to 4, with a possible maximum total score of 104.
The UDysRS Parts 3 and 4 were repeated 3 times after each L-DOPA challenge, 30 minutes apart, and were hence performed approximately 30, 60 and 90 minutes after each challenge.

End point type	Secondary

End point timeframe:

At baseline (Day 1, Visit 2), and Day 42 (Visits 7), starting approximately 30 minutes after the L-DOPA challenge.

End point values	NLX-112	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[17]	7[18]		
Units: UDysRS total score				
arithmetic mean (standard deviation)				
Visit 2 Baseline	31.6 (± 9.7)	39.9 (± 14.2)		
Visit 7 Clinic Efficacy Visit	-6.3 (± 7.0)	-2.4 (± 9.7)		

Notes:

[17] - Per protocol analysis set.

[18] - Per protocol analysis set.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in UDysRS total score at Day 28, after a 150% L-DOPA dose challenge - Absolute change from baseline

End point title	Change from baseline in UDysRS total score at Day 28, after a 150% L-DOPA dose challenge - Absolute change from baseline

End point description:

The UDysRS is a rating instrument designed to assess the core features of dyskinesia in PD. The UDysRS consists of 4 parts:
• Part 1, historical disability with regard to the patient's perceptions of the impact on activities of ADL of on-dyskinesia.
• Part 2, historical disability with regard to the patient's perceptions of the impact on ADL of off-dystonia.
• Part 3, objective impairment, which assesses severity of dyskinesia, affected body parts, and type of impairment (choreic vs. dystonic).
• Part 4, objective disability, based on an evaluation of Part 3 activities.
Each item in the UDysRS was scored from 0 to 4, with a possible maximum total score of 104.
The UDysRS Parts 3 and 4 were repeated 3 times after each L-DOPA challenge, 30 minutes apart, and were hence performed approximately 30, 60 and 90 minutes after each challenge.

End point type	Secondary

End point timeframe:

At baseline (Day 1, Visit 2) and Day 28 (Visits 6), starting approximately 30 minutes after the L-DOPA challenge.

End point values	NLX-112	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[19]	7[20]		
Units: UDysRS total score				
arithmetic mean (standard deviation)				
Visit 2 Baseline	31.6 (± 9.7)	39.9 (± 14.2)		
Visit 6 Clinic Efficacy Visit	-4.1 (± 9.3)	-2.0 (± 4.9)		

Notes:

[19] - Per protocol analysis set.

[20] - Per protocol analysis set.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in total objective score (Parts 3, 4) of the UDysRS at Day 28 and Day 42, after a 150% L-DOPA dose challenge - Absolute change from baseline

End point title	Change from baseline in total objective score (Parts 3, 4) of the UDysRS at Day 28 and Day 42, after a 150% L-DOPA dose challenge - Absolute change from baseline

End point description:

The UDysRS is a rating instrument designed to assess the core features of dyskinesia in PD. The UDysRS consists of 4 parts:
• Part 1, historical disability with regard to the patient's perceptions of the impact on activities of ADL of on-dyskinesia.
• Part 2, historical disability with regard to the patient's perceptions of the impact on ADL of off-dystonia.
• Part 3, objective impairment, which assesses severity of dyskinesia, affected body parts, and type of impairment (choreic vs. dystonic).
• Part 4, objective disability, based on an evaluation of Part 3 activities.
Each item in the UDysRS was scored from 0 to 4, with a possible maximum total score of 104.

End point type	Secondary

End point timeframe:

At baseline (Day 1, Visit 2), Day 28 and Day 42 (Visits 6 and 7), starting approximately 30 minutes after the L-DOPA challenge.

End point values	NLX-112	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[21]	7[22]		
Units: UDysRS total score				
arithmetic mean (standard deviation)				
Visit 2 Baseline	15.5 (± 6.2)	18.1 (± 7.9)		
Visit 6 Clinic Efficacy Visit	-1.7 (± 4.3)	-1.0 (± 1.8)		
Visit 7 Clinic Efficacy Visit	-3.1 (± 4.2)	-0.1 (± 3.8)		

Notes:

[21] - Per protocol analysis set.

[22] - Per protocol analysis set.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in ON Time Without Troublesome Dyskinesia (ON Without Dyskinesia plus ON With Non-troublesome Dyskinesia) based on a PD Home Dyskinesia Diary - Absolute change from baseline

End point title	Change from baseline in ON Time Without Troublesome Dyskinesia (ON Without Dyskinesia plus ON With Non-troublesome Dyskinesia) based on a PD Home Dyskinesia Diary - Absolute change from baseline

End point description:

A PD Home Dyskinesia Diary (electronic) as completed by the patient and/or caregiver with concordance in ON time with dyskinesia between study staff and patient. The diary was integrated in the Kinesia 360 wearable dyskinesia assessment system and was based on the PD Home Diary developed by Hauser et al 2004. The diary was used to score 5 different conditions in 30-minute time intervals during 2x24 hours prior to Visit 2, Visit 6 and Visit 7:
• ASLEEP;
• OFF;
• ON (i.e., adequate control of PD symptoms) without dyskinesia;
• ON with non-troublesome dyskinesia;
• ON with troublesome dyskinesia.

End point type	Secondary

End point timeframe:

The patient and/or caregiver completed a PD Home Dyskinesia eDiary diary in 30-minute time intervals during 2x24 hours prior to baseline (Visit 2), and during 4x24 hours prior to Day 28 (Visit 6) and Day 42 (Visit 7).

End point values	NLX-112	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[23]	7[24]		
Units: ON and OFF ratio				
arithmetic mean (standard deviation)				
Baseline	0.576 (± 0.199)	0.548 (± 0.192)		
Titration	0.0569 (± 0.158)	0.0245 (± 0.135)		
Steady-State	0.0523 (± 0.193)	0.0335 (± 0.154)		

Notes:

[23] - Per protocol analysis set.
Titration n = 13, Steady-State n = 12

[24] - Per protocol analysis set.
Titration n = 6, Steady-State n = 6

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Unified Parkinson’s Disease Rating Scale (UPDRS) scores (Part III, motor examination) - Absolute change from baseline

End point title	Change from baseline in Unified Parkinson’s Disease Rating Scale (UPDRS) scores (Part III, motor examination) - Absolute change from baseline

End point description:

The UPDRS is one of the most widely-used rating scales employed in the assessment of PD. The UPDRS consists of 4 parts:
• Part I assesses non-motor experiences of daily living, such as cognitive impairment and depressed mood.
• Part II assesses motor experiences of daily living, such as speech and eating tasks.
• Part III is a motor examination conducted by the clinician, including assessments of symptoms such as rigidity and tremor.
• Part IV is an assessment of motor complications, such as time spent with dyskinesia and functional impact of dyskinesias.
Each item in the UPDRS was scored from 0 to 4, and the individual scores were summed to give a total score that indicates the severity of the disease, with a score of 0 indicating no disability and a score of 199 being the most severe (indicating total disability).

End point type	Secondary

End point timeframe:

At baseline (Day 1, Visit 2), Day 28 (Visit 6), Day 42 (Visit 7) and Day 70 (Visit 9).

End point values	NLX-112	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[25]	7[26]		
Units: UPDRS total score				
arithmetic mean (standard deviation)				
Visit 2 Baseline	17.5 (± 9.4)	17.0 (± 10.3)		
Visit 6 Clinic Efficacy Visit	-3.7 (± 4.7)	1.3 (± 6.9)		
Visit 7 Clinic Efficacy Visit	-3.7 (± 4.6)	0.1 (± 8.2)		
Visit 9 Follow-up Clinic Visit	-2.7 (± 5.5)	-2.4 (± 2.9)		

Notes:

[25] - Per protocol analysis set.

[26] - Per protocol analysis set.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in UPDRS combined scores (Parts I, II, III and IV) - Absolute change from baseline

End point title	Change from baseline in UPDRS combined scores (Parts I, II, III and IV) - Absolute change from baseline

End point description:

The UPDRS is one of the most widely-used rating scales employed in the assessment of PD. The UPDRS consists of 4 parts:
• Part I assesses non-motor experiences of daily living, such as cognitive impairment and depressed mood.
• Part II assesses motor experiences of daily living, such as speech and eating tasks.
• Part III is a motor examination conducted by the clinician, including assessments of symptoms such as rigidity and tremor.
• Part IV is an assessment of motor complications, such as time spent with dyskinesia and functional impact of dyskinesias.
Each item in the UPDRS was scored from 0 to 4, and the individual scores were summed to give a total score that indicates the severity of the disease, with a score of 0 indicating no disability and a score of 199 being the most severe (indicating total disability).

End point type	Secondary

End point timeframe:

At baseline (Day 1, Visit 2), Day 28 (Visit 6), Day 42 (Visit 7) and Day 70 (Visit 9).

End point values	NLX-112	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[27]	7[28]		
Units: UPDRS total score				
arithmetic mean (standard deviation)				
Visit 2 Baseline	37.0 (± 13.3)	41.3 (± 15.0)		
Visit 6 Clinic Efficacy Visit	-6.5 (± 7.6)	-3.6 (± 7.0)		
Visit 7 Clinic Efficacy Visit	-5.7 (± 6.0)	-3.9 (± 9.3)		
Visit 9 Follow-up Clinic Visit	-4.4 (± 9.0)	-7.3 (± 5.4)		

Notes:

[27] - Per protocol analysis set.

[28] - Per protocol analysis set.

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression of Change (CGI-C) in overall PD symptoms

End point title	Clinical Global Impression of Change (CGI-C) in overall PD symptoms

End point description:

The CGI-C is a clinician-oriented scale that assesses the total improvement in the patient's condition relative to the clinical global impression of severity (CGI-S) scale conducted at baseline. The CGI-C rates the patient’s condition from 0 to 7, with a rating of 0 indicating “no assessment”, a rating of 1 indicating “very much better”, and a rating of 7 indicating “very much worse”.

End point type	Secondary

End point timeframe:

Patients rated their global condition using CGI-S at baseline (Day 1, Visit 2) and CGI-C at Day 28 (Visit 6) and Day 42 (Visit 7).

End point values	NLX-112	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[29]	7[30]		
Units: Number of subjects				
Visit 2 Baseline - Normal, not at all ill	3	2		
Visit 2 Baseline - Moderately ill	8	2		
Visit 2 Baseline - Markedly ill	3	2		
Visit 2 Baseline - Severely ill	1	1		
Visit 6 Clinic Efficacy Visit - Much improved	2	2		
Visit 6 Clinic Efficacy Visit - Minimally improved	3	0		
Visit 6 Clinic Efficacy Visit - No change	9	4		
Visit 6 Clinic Efficacy Visit - Minimally worse	1	1		
Visit 7 Clinic Efficacy Visit - Very much improved	1	0		
Visit 7 Clinic Efficacy Visit - Much improved	4	1		
Visit 7 Clinic Efficacy Visit - Minimally improved	3	1		
Visit 7 Clinic Efficacy Visit - No change	6	5		
Visit 7 Clinic Efficacy Visit - Minimally worse	1	0		

Notes:

[29] - Per protocol analysis set.

[30] - Per protocol analysis set.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in dyskinesia scores measured by the Kinesia 360 (Great Lakes Neurotechnologies, Inc) wearable dyskinesia assessment system - Absolute change from baseline

End point title	Change from baseline in dyskinesia scores measured by the Kinesia 360 (Great Lakes Neurotechnologies, Inc) wearable dyskinesia assessment system - Absolute change from baseline

End point description:

The Kinesia 360 (Great Lakes Neurotechnologies, Inc) wearable dyskinesia assessment system was used to monitor dyskinesias. The Kinesia 360 motor assessment system is intended to provide a low burden method for remote, continuous measurement of patient symptoms. Sensors worn on the wrist and ankle combined with a mobile application continuously record data for assessment of tremor, slowness, dyskinesia and mobility. Data from the motion sensors was uploaded to the Kinesia Web Portal and algorithms were used to detect symptoms and calculate severity scores every 2 minutes on a scale shown to be highly correlated with clinician ratings. Sensors recorded data all day and were recharged overnight for extended home use.

End point type	Secondary

End point timeframe:

Wearable data collection of dyskinesias took place during a 2-day period prior to the baseline visit (Day 1, Visit 2) and a 4-day period prior to Day 28 (Visit 6) and Day 42 (Visit 7).

End point values	NLX-112	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[31]	7[32]		
Units: Dyskinesia detect scores				
arithmetic mean (standard deviation)				
Baseline	0.1807 (± 0.1955)	0.2855 (± 0.3322)		
Titration	-0.06517 (± 0.06722)	-0.009172 (± 0.1353)		
Steady-State	-0.009327 (± 0.1243)	-0.01630 (± 0.3166)		

Notes:

[31] - Per protocol analysis set.
Baseline n = 12, Titration n = 8, Steady-State n = 6
[32] - Per protocol analysis set.
Baseline n = 5, Titration n = 3, Steady-State n = 3

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs (including SAEs) were collected from the start of IMP administration until the end-of-study visit.

Adverse event reporting additional description:

The grading of the severity/intensity (grade 1 to grade 5) of AEs followed the common terminology criteria for AEs (CTCAE) v5.0 [24]. AEs were assessed as unlikely, possibly or probably related to the IMP.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	NLX-112

Reporting group description:

Patients were randomized to receive either active treatment with NLX-112 or placebo. This arm represents the patients that received NLX-112.

Reporting group title	Placebo

Reporting group description:

Patients were randomized to receive either active treatment with NLX-112 or placebo. This arm represents the patients that received placebo.

Serious adverse events	NLX-112	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	NLX-112	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 18 (88.89%)	7 / 9 (77.78%)	
Vascular disorders			

Hypertension			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Orthostatic hypotension			
subjects affected / exposed	2 / 18 (11.11%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
Systolic hypertension			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Surgical and medical procedures			
Cataract operation			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	2 / 18 (11.11%)	2 / 9 (22.22%)	
occurrences (all)	2	3	
Psychiatric disorders			
Apathy			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Dissociation			
subjects affected / exposed	2 / 18 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Hallucination			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Illusion			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	

Insomnia			
subjects affected / exposed	2 / 18 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Irritability			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Rapid eye movement sleep behavior disorder			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Sleep disorder			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Stress			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Investigations			
Inflammatory marker increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 18 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	3	0	
Incorrect dose administered			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Lip injury			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Product communication issue			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	

Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 18 (11.11%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
Dyskinesia			
subjects affected / exposed	2 / 18 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Headache			
subjects affected / exposed	3 / 18 (16.67%)	2 / 9 (22.22%)	
occurrences (all)	4	3	
On and off phenomenon			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Parkinsonism			
subjects affected / exposed	3 / 18 (16.67%)	3 / 9 (33.33%)	
occurrences (all)	3	7	
Parosmia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Restless legs syndrome			
subjects affected / exposed	2 / 18 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Somnolence			
subjects affected / exposed	1 / 18 (5.56%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Taste disorder			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Vertigo			
subjects affected / exposed	2 / 18 (11.11%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
Eye disorders			

Binocular eye movement disorder			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Dry eye			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Erythema of eyelid			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Eye pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Swelling of eyelid			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Dry mouth			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Gastritis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	4 / 18 (22.22%)	0 / 9 (0.00%)	
occurrences (all)	4	0	
Oral pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	2 / 18 (11.11%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Pollakiuria			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	2 / 18 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Muscle spasms			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Neck pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	

Nasopharyngitis			
subjects affected / exposed	1 / 18 (5.56%)	2 / 9 (22.22%)	
occurrences (all)	1	2	
Respiratory tract infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
Hyperglycemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported