Clinical trial results:
Assessing the Pharmacokinetics, Safety, Tolerability and Efficacy of Continuous Oral Levodopa via the DopaFuse Delivery System in Parkinson's Disease Patients

Summary

EudraCT number	2020-003372-41
Trial protocol	ES IT LU
Global end of trial date	02 August 2022

Results information

Result version number	v1 (current)
This version publication date	22 September 2023
First version publication date	22 September 2023

Trial information

Trial identification

Sponsor protocol code	TP-0007

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	SynAgile Corporation
Sponsor organisation address	628 river oaks parkway, San Jose, United States, CA
Public contact	Clinical Affairs, SynAgile Corporation, clinical@synagile.com
Scientific contact	Clinical Affairs, SynAgile Corporation, clinical@synagile.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	29 June 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 August 2022
Global end of trial reached?	Yes
Global end of trial date	02 August 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Pharmacokinetics - To compare plasma levodopa variability between intermittent vs. DopaFuse delivery system
Safety & Tolerability - To assess the safety and tolerability of DopaFuse delivery system
Efficacy - To assess the effect of DopaFuse delivery system on OFF time

Protection of trial subjects:

The Investigator could not deviate from the protocol without a formal protocol amendment having been established and approved by an appropriate IRB/IEC, except when necessary to eliminate immediate hazards to the patient or when the change involved only logistical or administrative aspects of the study.

Rescue medication in the form of rescue doses of apomorphine (Days 1-3) or additional standard oral LD/CD, inhaled LD/CD, or other medications routinely used by the patient to treat clinically significant OFF (Days 4-15), could be introduced at the judgment of the Investigator.

Background therapy:

For this study, a patient’s standard LD/CD regimen was considered background treatment.

Evidence for comparator: -

Actual start date of recruitment	12 October 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	Italy: 6
Country: Number of subjects enrolled	Luxembourg: 7
Country: Number of subjects enrolled	Spain: 4
Worldwide total number of subjects	17
EEA total number of subjects	17

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)	11
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients with Parkinson's Disease on stable LD/CD treatment who had experienced at least one hour of OFF time per day were invited to participate in the study. A qualified dentist assessed the patients' oral health and fit the retainers, which were worn without medication at home for 1-2 days to confirm tolerability prior to receiving IMP.

Pre-assignment

Screening details:

During screening, patients were evaluated for eligibility according to the protocol defined inclusion and exclusion criteria. Eligibility had to be approved by an Enrollment Authorization Committee prior to enrollment.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Arm 1 - Single group study

Arm description:

Single group study

Arm type	Experimental
Investigational medicinal product name	DopaFuse Delivery System
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral paste
Routes of administration	Oral use

Dosage and administration details:

DopaFuse treatment regimens were individualized in order to closely align with the patient's usual levodopa/carbidopa (LD/CD) dosing quantities and timetable. LD/CD was given at a 4:1 ratio using one of two flow rates, which were converted to reflect usual oral LD dosing for the 12-hour study window.

Number of subjects in period 1[1]	Arm 1 - Single group study
Started	16
Completed	16

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: One patient was enrolled in the study but not treated due to an adverse event (vomiting during the wearing of the retainer) and was not included in the baseline period or subsequent analysis.

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study
Reporting group description:	
Patients who were dosed at least once during the study	

Reporting group values	Overall Study	Total	
Number of subjects	16	16	
Age categorical Units: Subjects			
Adults (18-64 years)	10	10	
From 65-84 years	6	6	
Age continuous Units: years			
arithmetic mean	63.2		
standard deviation	± 9.1	-	
Gender categorical Units: Subjects			
Female	7	7	
Male	9	9	
Cognitive status: Units: Subjects			
Mini–Mental State Examination 30	8	8	
Mini–Mental State Examination 29	4	4	
Mini–Mental State Examination 28	4	4	
Mini–Mental State Examination 27	0	0	
Mini–Mental State Examination 26	0	0	
Mini–Mental State Examination < 26	0	0	
Ethnicity Units: Subjects			
Hispanic or Latino	1	1	
Not Hispanic or Latino	12	12	
Not reported / Unknown	3	3	
Race Units: Subjects			
White	16	16	
Weight Units: kg			
arithmetic mean	70.9		
standard deviation	± 14.8	-	
Body Mass Index Units: kg/m2			
arithmetic mean	25.2		
standard deviation	± 4.3	-	
Height Units: cm			
arithmetic mean	167.5		

standard deviation	± 8.8	-	

End points

End points reporting groups

Reporting group title	Arm 1 - Single group study
Reporting group description:	
Single group study	

Primary: Variability in plasma concentration of levodopa

End point title	Variability in plasma concentration of levodopa[1]
End point description:	
Variability in levodopa concentrations assessed by levodopa fluctuation index (FI) at 4-12 hours (steady state) with evaluations between Day 2 (DopaFuse alone) and Day 1 (oral LD/CD)	
End point type	Primary
End point timeframe:	
4-12 hours (steady state) for Day 2 (DopaFuse alone) vs. Day 1 (oral LD/CD)	

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: Single arm study - statistical analysis not reported in accordance with EudraCT & EU CTR Frequently asked questions (EMA/370102/2016) - Question 83

End point values	Arm 1 - Single group study			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Levodopa Fluctuation Index (FI)				
arithmetic mean (standard deviation)				
Day 2 (DopaFuse alone)	1.50 (± 0.55)			
Day 1 (Oral LD/CD)	2.15 (± 0.59)			

Statistical analyses

No statistical analyses for this end point

Primary: Variability in plasma concentration of levodopa

End point title	Variability in plasma concentration of levodopa[2]
End point description:	
Variability in levodopa concentrations assessed by levodopa fluctuation index (FI) at 4-12 hours (steady state) with evaluations between Day 3 (oral LD/CD morning dose + DopaFuse) and Day 1 (oral LD/CD)	
End point type	Primary
End point timeframe:	
At 4-12 hours (steady state) for Day 3 (oral LD/CD morning dose + DopaFuse) vs. Day 1 (oral LD/CD)	

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: Single arm study - statistical analysis not reported in accordance with EudraCT & EU CTR Frequently asked questions (EMA/370102/2016) - Question 83

End point values	Arm 1 - Single group study			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Levodopa Fluctuation index (FI)				
arithmetic mean (standard deviation)				
Day 3 (DopaFuse + LD/CD morning dose) Day 1 (Oral LD/CD)	1.03 (± 0.53) 1.84 (± 0.63)			

Statistical analyses

No statistical analyses for this end point

Primary: Safety and Tolerability

End point title	Safety and Tolerability[3]

End point description:

Number of Treatment-emergent adverse events (TEAEs)

End point type	Primary

End point timeframe:

Day 1 to Day 29

Notes:

[3] - 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: Single arm study - statistical analysis not reported in accordance with EudraCT & EU CTR Frequently asked questions (EMA/370102/2016) - Question 83

End point values	Arm 1 - Single group study			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Treatment Emergent Adverse Events (TEAE)	19			

Statistical analyses

No statistical analyses for this end point

Primary: Safety and Tolerability

End point title	Safety and Tolerability[4]

End point description:

Number of Serious Adverse Events (SAEs)

End point type	Primary

End point timeframe:

Day 1 to Day 29

Notes:

[4] - 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: Single arm study - statistical analysis not reported in accordance with EudraCT & EU CTR Frequently asked questions (EMA/370102/2016) - Question 83

End point values	Arm 1 - Single group study			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Serious adverse events (SAEs)	0			

Statistical analyses

No statistical analyses for this end point

Primary: Safety and Tolerability

End point title	Safety and Tolerability[5]

End point description:

Number of TEAEs leading to study discontinuation

End point type	Primary

End point timeframe:

Day 1 to Day 29

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: Single arm study - statistical analysis not reported in accordance with EudraCT & EU CTR Frequently asked questions (EMA/370102/2016) - Question 83

End point values	Arm 1 - Single group study			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: TEAEs leading to discontinuation	0			

Statistical analyses

No statistical analyses for this end point

Primary: Safety and Tolerability

End point title	Safety and Tolerability[6]

End point description:

% of patients that completed study

End point type	Primary

End point timeframe:

Day 1 to Day 29

Notes:

[6] - 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: Single arm study - statistical analysis not reported in accordance with EudraCT & EU CTR Frequently asked questions (EMA/370102/2016) - Question 83

End point values	Arm 1 - Single group study			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: % patients completing study	100			

Statistical analyses

No statistical analyses for this end point

Primary: Efficacy Endpoint - OFF Time

End point title	Efficacy Endpoint - OFF Time[7]

End point description:

OFF time based on in-person investigator ratings for Day 15 (oral LD/CD morning dose + DopaFuse) vs. Day 1 (oral LD/CD)

End point type	Primary

End point timeframe:

Day 1 to Day 15

Notes:

[7] - 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: Single arm study - statistical analysis not reported in accordance with EudraCT & EU CTR Frequently asked questions (EMA/370102/2016) - Question 83

End point values	Arm 1 - Single group study			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: OFF time (Hours)				
arithmetic mean (standard deviation)				
Day 1 - Oral LD/CD	3.23 (± 2.18)			
Day 2 - DopaFuse alone	3.07 (± 2.52)			
Day 3 - DopaFuse + morning LD/CD	1.60 (± 1.48)			
Day 15 - DopaFuse + morning LD/CD	1.51 (± 1.44)			

Statistical analyses

No statistical analyses for this end point

Secondary: Variability in plasma concentration of levodopa

End point title	Variability in plasma concentration of levodopa

End point description:

Variability in levodopa concentrations assessed by levodopa fluctuation index (FI) at 0-12 hours for Day 3 vs. and Day 1

End point type	Secondary

End point timeframe:

0-12 hours for Day 3 vs. Day 1

End point values	Arm 1 - Single group study			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Levodopa Fluctuation Index (FI)				
arithmetic mean (standard deviation)				
Day 3 (DopaFuse + LD/CD morning dose) Day 1 (Oral LD/CD)	2.06 (± 0.44) 2.47 (± 0.47)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were recorded from Day 1 until Day 29

Adverse event reporting additional description:

AEs and ADEs were collected at each clinic or telephone visit with a non-leading question, as well as by reporting those events directly observed and spontaneously reported by the patient.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Arm 1 - Single group study

Reporting group description:

Single arm study

Serious adverse events	Arm 1 - Single group study		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Arm 1 - Single group study		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 16 (50.00%)		
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
General disorders and administration site conditions			

Complication associated with device subjects affected / exposed occurrences (all) Vessel puncture site haematoma subjects affected / exposed occurrences (all)	 5 / 16 (31.25%) 9 1 / 16 (6.25%) 1		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Dry mouth subjects affected / exposed occurrences (all) Oral disorder subjects affected / exposed occurrences (all)	 2 / 16 (12.50%) 2 2 / 16 (12.50%) 2 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1		

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