

**Clinical trial results:**

Randomized, double-blind, placebo-controlled crossover study to validate finger tapping tasks for the quantification of levodopa/carbidopa effects in Parkinson's Disease patients.

Summary

EudraCT number	2020-000686-16
Trial protocol	NL
Global end of trial date	05 November 2020

Results information

Result version number	v1 (current)
This version publication date	16 October 2022
First version publication date	16 October 2022
Summary attachment (see zip file)	Movement Disord Clin Pract - 2022 - Thijssen (Movement Disord Clin Pract - 2022 - Thijssen - A PlaceboControlled Study to Assess the Sensitivity of Finger Tapping to.pdf)

Trial information**Trial identification**

Sponsor protocol code	CHDR1953
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Centre of Human Drug Research
Sponsor organisation address	Zernikedreef 8, Leiden, Netherlands, 2333 CL
Public contact	Principal Investigator, Centre for Human Drug Research, +31 715246400, clintrials@chdr.nl
Scientific contact	Principal Investigator, Centre for Human Drug Research, +31 715246400, clintrials@chdr.nl

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	25 July 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 November 2020
Global end of trial reached?	Yes
Global end of trial date	05 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Assess whether the finger tapping task endpoints:

- Differentiate between ON and OFF states in PD patients
- Correlate with the golden standard MDS-UPDRS part III total score
- Differentiate between placebo and levodopa/carbidopa treatment

Protection of trial subjects:

Patients enrolled in this study were already using levodopa or had used it in the past. Therefore, they were expected to tolerate the study treatment well. Nonetheless, subject safety was evaluated by monitoring of adverse events throughout the study, and by examining the patient's vital signs, ECG and physical/neurological examination before discharge.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 April 2020
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	Netherlands: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	15
From 65 to 84 years	5

Subject disposition

Recruitment

Recruitment details:

The clinical phase of this study started on July 20, 2020 (screening of first subject) and ended on 05 November, 2020 (last follow-up visit).

Pre-assignment

Screening details:

PD patients with self-described motor fluctuations and recognizable OFF periods aged between 20-85 years with Hoehn and Yahr stage I-III were eligible for participation. Patients had to be levodopa responsive as evidenced by current or historical use of levodopa.

Period 1

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

Blinding implementation details:

To ensure blinding, levodopa/carbidopa 100/25 mg (Sinemet) tablets were over-encapsulated in 00 gelatin (Swedish orange) capsules. Similarly, placebo tablets were over-encapsulated.

Arms

Are arms mutually exclusive?	No
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Arm title	Active drugs
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	Levodopa/carbidopa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Levodopa/carbidopa 100/25 mg (Sinemet) tablets. Patients receive a semi-individualized dose, meaning they will be administered 1-5 capsules depending on their own dosing regimen. E.g. if patients only use levodopa as anti-Parkinson medication, they will be administered the number of capsules that most closely matches the dose they usually take. When patients receive other anti-Parkinson medication (as well), a levodopa equivalent dose (LED) of the medication they take in the morning will be calculated. This LED will then indicate the number of capsules that will be administered.

Arm title	Placebo
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Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo, over-encapsulated oral tablets similar in appearance as the active drug. The number of capsules is matched to that of the active drug.

Number of subjects in period 1	Active drugs	Placebo
Started	20	20
Completed	20	20

Baseline characteristics

Reporting groups

Reporting group title	Overall trial period
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Reporting group description: -

Reporting group values	Overall trial period	Total	
Number of subjects	20	20	
Age categorical Units: Subjects			
Adults (18-64 years)	16	16	
From 65-84 years	4	4	
Gender categorical Units: Subjects			
Female	6	6	
Male	14	14	

End points

End points reporting groups

Reporting group title	Active drugs
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: MDS-UPDRS III

End point title	MDS-UPDRS III ^[1]
End point description:	

End point type	Primary
End point timeframe:	
Day -1, Day 1 (pre-dose, 10 min, 30 min, 60 min, 90 min, 3,5 hrs)	

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: See attachment.

End point values	Active drugs	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: total score	20	20		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From screening until last follow up visit.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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Reporting groups

Reporting group title	Sinemet (Active)
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	Sinemet (Active)	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Sinemet (Active)	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 20 (10.00%)	2 / 20 (10.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Orthostatic hypotension			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 July 2020	Study start was postponed due to SARS-CoV-2 outbreak. This amendment concerned the updated ICF, advertisement material and protocol conform the CCMO guideline: 'Conditions (re)start studies in clinical research units, dd 24 june2020'.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported