Clinical trial results:
Double-blind, randomized, crossover design for evaluation of efficacy and safety of methylphenidate in cognition in patients with Parkinson's disease using electrophysiological measures

Summary

EudraCT number	2020-005073-28
Trial protocol	ES
Global end of trial date	14 December 2024

Results information

Result version number	v1 (current)
This version publication date	01 January 2025
First version publication date	01 January 2025
Summary attachment (see zip file)	MPD2024 (MPDsummary2024.pdf)

Trial information

Trial identification

Sponsor protocol code	ParKMetil/001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University of Rey Juan Carlos
Sponsor organisation address	Avenida de Atenas,, Alcorcon, Spain, 28922
Public contact	Sponsor , Universidad Rey Juan Carlos, nfogelson@gmail.com
Scientific contact	Sponsor , Universidad Rey Juan Carlos, nfogelson@gmail.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	14 December 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 February 2024
Global end of trial reached?	Yes
Global end of trial date	14 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To examine the cognitive effects of a single 20 mg dose of methylphenidate (MPD) in non-demented patients with Parkinson's disease, using behavioural and electrophysiological measures, in a randomized, double-blind, placebo-controlled, single-dose, cross-over clinical trial study. Specifically we evaluated reaction time and event-related potentials associated with different types of stimuli and compared these for the MPD and placebo sessions in the patients.

Protection of trial subjects:

Patients with the following criteria were excluded from the study: dementia, clinically significant depression, patients who have suffered from hallucinations, delusions or psychosis, severe motor fluctuations and prominent ON dyskinesia, unbalanced arterial hypertension of more than 140/80 during siting on the day of the study, uncontrolled hypertension, hepatic or renal failure, uncontrolled malignancy, or untreated glaucoma, and patients treated with Monoamine Oxidase Inhibitors.

Background therapy:

Patients were asked to take their regular medication on the day of the experiment, including Parkinsonian treatment with levopdopa.

Evidence for comparator:

We recorded EEG, during the performance of the task, in PD patients after the administration of methylphenidate (MPD) and placebo. Each subject performed a total of two recording sessions, one after the administration of 20 mg of MPD and another after the administration of a placebo saccharine pill. Each session was performed on a different day, 7 to 14 days apart, using the same procedures. EEG recordings were performed 90 mins after the administration of either the MPD or placebo pill. The order of administration of MPD versus placebo was randomized and counterbalanced across the subjects. All the sessions were recorded in the morning hours to control for environmental effects on attention, while the patients were in ON state.

Actual start date of recruitment	01 February 2022
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: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	5
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Forty patients diagnosed with Parkinson's disease in Hospital Universitario Fundación Alcorcon, Spain fit the inclusion criteria and were contacted to participate in the study between February 2022 and 2024.

Pre-assignment

Screening details:

Patients diagnosed with PD fit the inclusion criteria and were contacted to participate in the study. Fourteen patients refused to participate, and four patients were unable to perform at least one of the recording sessions due to high blood pressure measurements on the day of the experiment.

Pre-assignment period milestones

Number of subjects started	40[1]
Number of subjects completed	22

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Physician decision: 4
Reason: Number of subjects	Consent withdrawn by subject: 14

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Fourteen subjects did not give their consent to proceed with the trial. Fouir subjects could not proceed on the day of the recordings due to high blood pressure.

Period 1

Period 1 title	Methylphenidate
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Carer, Assessor

Blinding implementation details:

Patients, clinicians assesing the patients, the researchers performing the EEG recordings and analyzing the data were blinded to the administration of either metghylphenidate or a placebo saccharine pill.

Arms

Arm title	Methylphenidate

Arm description:

Parkinson's disease patients administered 20 mg of methylphenidate

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

Dosage and administration details:

20 mg of methylphenidate swallowed orally

Number of subjects in period 1	Methylphenidate
Started	22
Completed	22

Period 2	
Period 2 title	Placebo
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Carer, Assessor

Arms

Arm title	Placebo

Arm description:

Placebo session

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

Dosage and administration details:

1 pill of saccarine swallowed with water

Number of subjects in period 2	Placebo
Started	22
Completed	22

Baseline characteristics

Reporting groups	
Reporting group title	Methylphenidate
Reporting group description:	
Twenty two patients performing two crossover sessions	

Reporting group values	Methylphenidate	Total	
Number of subjects	22	22	
Age categorical			
Parkinson's diasease patients age range 30-78 years			
Units: Subjects			

Age continuous			
Parkinson's disease patients 30-78 years old			
Units: years			
arithmetic mean	68		
standard deviation	± 8	-	
Gender categorical			
Units: Subjects			
Female	10	10	
Male	12	12	

End points

End points reporting groups

Reporting group title	Methylphenidate
Reporting group description:	
Parkinson's disease patients administered 20 mg of methylphenidate	
Reporting group title	Placebo
Reporting group description:	
Placebo session	

Primary: Change between MPD and placebo

End point title	Change between MPD and placebo
End point description:	
End point type	Primary
End point timeframe:	
P3b latency for targets for MPD session and placebo session in each subject	

End point values	Methylphenidate	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: ms				
arithmetic mean (standard deviation)	401 (± 51)	432 (± 57)		

Statistical analyses

Statistical analysis title	Comparison of P3b latency between MPD and placebo
Comparison groups	Placebo v Methylphenidate
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	ANOVA
Parameter estimate	Mean difference (final values)
Confidence interval	
sides	2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
No adverse events	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	regular
Dictionary version	1

Reporting groups	
Reporting group title	Methylphenidate
Reporting group description:	
Parkinson's disease patients administered 20 mg of methylphenidate	
Reporting group title	Placebo
Reporting group description:	
Parkinson's disease patients administered saccarine placebo pill	

Serious adverse events	Methylphenidate	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (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: 0 %

Non-serious adverse events	Methylphenidate	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	
Cardiac disorders			
Dizziness	Additional description: One adverse event was reported by a patient who experienced dizziness due to high blood pressure after completing the recording session, where methylphenidate was administered.		
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (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