

**Clinical trial results:****A Phase IIA Prospective, Single-Centre, Open Label Clinical Trial to Evaluate the Safety, Tolerability and Pharmacodynamic Effects of Ambroxol in Patients with Parkinson Disease: Ambroxol in Disease Modification in Parkinson Disease****Summary**

EudraCT number	2015-002571-24
Trial protocol	GB
Global end of trial date	26 April 2018

Results information

Result version number	v1 (current)
This version publication date	24 July 2019
First version publication date	24 July 2019
Summary attachment (see zip file)	AiM-PD Summary Upload (AiM-PD trial clean 14Jun2019.pdf)

Trial information**Trial identification**

Sponsor protocol code	15/0118
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02941822
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Univeristy College London
Sponsor organisation address	Gower Street, London, United Kingdom, WC1E 6BT
Public contact	Joshua Elflein, Leonard Wolfson Experimental Neurology Centre Clinical Research Facility , +44 02034484541, joshua.elflein@ucl.ac.uk
Scientific contact	Joshua Elflein, Leonard Wolfson Experimental Neurology Centre Clinical Research Facility , +44 2034484541, joshua.elflein@ucl.ac.uk

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	26 April 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 April 2018
Global end of trial reached?	Yes
Global end of trial date	26 April 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To assess the central nervous system (CNS), cerebrospinal fluid (CSF) penetration and binding to GCase of ambroxol by the parameters outline (modulation of GCase activity & ambroxol level) at 5 intra-participant dose escalations from day 1 to day 186 at 60 mg TID (day 1-7), 120 mg TID (day 8-14), 180 mg TID (day 15-21), 300 mg TID (day 22-28) and 420 mg TID (day 29-186).
 - To assess the safety and tolerability of the Glucocerebrosidase (GCase) modulating chaperone ambroxol in Parkinson disease participants with and without Gaucher gene (GBA) mutation at 5 intra-participant dose escalations from day 1 to 186.
 - To measure the pharmacodynamic effects of ambroxol on GCase activity in blood and CSF following ambroxol oral administration at 5 intra-participant dose escalations from day 1 to 186.
 - To quantify the effect of ambroxol on biomarkers of Parkinson and neurodegeneration at 5 intra-participant dose escalations from day 1 to 186.
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Protection of trial subjects:

Data will be reported in accordance to the protocol and local reporting regulations (REC/MHRA) which is covered by Good Pharmacovigilance Practice. There will be regular Trial Management Group (TMG) which will meet regularly throughout the course of the study to assess the study progress and all AEs and the minutes will be accessed and recorded. The protocol also specifies criterias for the following:

- IMP discontinuations
- Participant stopping criteria
- Participant Termination criteria

The purpose of the TMG is to ensure participant safety is not compromised during the course of the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 July 2016
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	United Kingdom: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	19
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at the Leonard Wolfson Experimental Neurology Centre Clinical Research Facility, which is based at the National Hospital for Neurology and Neurosurgery and is part of the University College London Hospitals NHS Foundation Trust. All participants recruited to this study had a confirmed diagnosis of Parkinson Disease.

Pre-assignment

Screening details:

Twenty participants to be recruited in total, 10 with a GBA positive status and 10 with a GBA negative status. Informed consent, Medical history, Physical and neurological examinations, Screening genotyping, Vital signs, Height and weight, ECG, pregnancy test, blood collection, Adverse event review, Concomitant medication review, etc.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Arm title	Interventional
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Ambroxol hydrochloride
Investigational medicinal product code	
Other name	Ambrosan
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants will be instructed to self-administer 5 intra-participant dose escalations at 60 mg TID (day 1-7), 120 mg TID (day 8-14), 180 mg TID (day 15-21), 300 mg TID (day 22-28) and 420 mg TID (day 29-186). The study drug should be administered with or without a meal and rinsed down with sufficient amount of fluid for each daily morning, afternoon and evening in accordance to the instructions provided by the Investigator.

Number of subjects in period 1	Interventional
Started	24
Completed	18
Not completed	6
Consent withdrawn by subject	3
Screen Failures	3

Baseline characteristics

End points

End points reporting groups

Reporting group title	Interventional
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Reporting group description: -

Primary: To assess the central nervous system (CNS), cerebrospinal fluid (CSF) penetration and binding to GCase of ambroxol by the parameters outline (modulation of GCase activity & ambroxol level)

End point title	To assess the central nervous system (CNS), cerebrospinal fluid (CSF) penetration and binding to GCase of ambroxol by the parameters outline (modulation of GCase activity & ambroxol level) ^[1]
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End point description:

End point type	Primary
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End point timeframe:

Baseline to Day 186

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: Comprehensive information regarding the statistical analysis can be referenced in the attached trial summary.

End point values	Interventional			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: ng/mL	156			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

All AEs assessed upon reporting.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21
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Frequency threshold for reporting non-serious adverse events: 5 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: All AEs reported in attached AiM-PD Trial Summary.

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