



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 |
|-----------------------|---------|

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.

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 |
| 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] |
|-----------------|---|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

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.

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|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|----|
| Dictionary version | 21 |
|--------------------|----|

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