



## Clinical trial results:

### THE ROLE OF BUSPIRONE IN ATTENUATING LEVODOPA-INDUCED DYSKINESIAS IN PATIENTS WITH PARKINSON'S DISEASE: A CLINICAL AND POSITRON EMISSION TOMOGRAPHY STUDY WITH 11C-PHNO.

#### Summary

EudraCT number	2014-005422-35
Trial protocol	GB
Global end of trial date	23 January 2017

#### Results information

Result version number	v1 (current)
This version publication date	12 October 2018
First version publication date	12 October 2018
Summary attachment (see zip file)	2014-005422-35_Results_upload (2014-005422-35_EudraCT_results_report.pdf)

#### Trial information

##### Trial identification

Sponsor protocol code	14HH2382
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Imperial College Joint Research Compliance Office: 14HH2382, NIHR Portfolio Public database: 139087, Local Clinical Research Network: 139087

Notes:

#### Sponsors

Sponsor organisation name	Imperial College London
Sponsor organisation address	St Mary's Campus - JRCO, Praed Street, London, United Kingdom, W2 1NY
Public contact	Gary Roper, Imperial College London - Imperial College NHS Trust, +44 (0)2075941872, gary.roper@imperial.ac.uk
Scientific contact	Gary Roper, Imperial College London - Imperial College NHS Trust, +44 (0)2075941872, gary.roper@imperial.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	23 January 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 January 2017
Global end of trial reached?	Yes
Global end of trial date	23 January 2017
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate that buspirone which is a serotonin (5HT1A) antagonist will reduce the levels of synaptic dopamine generated from the serotonergic terminals after L-dopa administration. This will be associated with a reduction in dyskinesia intensity in PD patients.

Protection of trial subjects:

Patients were followed up clinically before, during and after their participation in this clinical study. The research team is the team directly involved in their medical care.

Background therapy:

n/a

Evidence for comparator:

n/a

Actual start date of recruitment	15 April 2015
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: 8
Worldwide total number of subjects	8
EEA total number of subjects	8

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)	3
From 65 to 84 years	5
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The proposed number of participants was originally 24. However, recruitment was slower than expected. When 8 participants were enrolled in the study, the Sponsor discussed with the research team whether to perform an interim analysis to assess the efficacy of Buspirone in order to apply for extending the recruitment period.

### Pre-assignment

Screening details:

At screening, all patients had a clinical diagnosis of idiopathic Parkinson's disease. Patients with other neurological conditions, psychiatric disorders, history of depression and or anxiety were excluded. All patients were recruited from Specialist NHS Movement Disorders outpatient clinics by the research team.

### Pre-assignment period milestones

Number of subjects started	8
Number of subjects completed	8

### Period 1

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

Blinding implementation details:

The subjects were randomised into two subgroups:

Group a: 12 PD patients with dyskinesias to receive 0.20mg/kg of Buspirone prior to LDOPA administration. The effects of Buspirone will be compared to placebo.

Group b: 12 PD patients with dyskinesias to receive 0.10mg/kg of Buspirone prior to LDOPA administration. The effects of Buspirone will be compared to placebo.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Buspirone 0.10mg/kg and Placebo
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Buspirone Hydrochloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0.10mg/kg oral

Investigational medicinal product name	Ascorbic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ascorbic acid 50mg oral

<b>Arm title</b>	Buspirone 0.20mg/kg and Placebo
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Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Buspirone Hydrochloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Buspirone 02.mg/kg oral	
Investigational medicinal product name	Ascorbic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Ascorbic acid 50mg oral	

<b>Number of subjects in period 1</b>	Buspirone 0.10mg/kg and	Buspirone 0.20mg/kg and
Started	4	4
Completed	4	4

## Baseline characteristics

### Reporting groups

Reporting group title	Treatment period
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Reporting group description: -

Reporting group values	Treatment period	Total	
Number of subjects	8	8	
Age categorical			
All subjects were aged between 40-80.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	3	3	
From 65-84 years	5	5	
85 years and over	0	0	
Age continuous			
The 8 patients who completed the study had a mean age of 67.99 ± 7.64 (1SD).			
Units: years			
arithmetic mean	67.99		
standard deviation	± 7.64	-	
Gender categorical			
3 Males and 5 Females were included in this study.			
Units: Subjects			
Female	5	5	
Male	3	3	

## End points

### End points reporting groups

Reporting group title	Buspirone 0.10mg/kg and Placebo
Reporting group description: -	
Reporting group title	Buspirone 0.20mg/kg and Placebo
Reporting group description: -	

### Primary: The effect of Buspirone in improving dyskinesias' severity

End point title	The effect of Buspirone in improving dyskinesias' severity
End point description:	
End point type	Primary
End point timeframe:	To see an effect of Buspirone in improving dyskinesias during the acute study.

End point values	Buspirone 0.10mg/kg and Placebo	Buspirone 0.20mg/kg and Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4 <sup>[1]</sup>	4 <sup>[2]</sup>		
Units: Improvement of AIMS scale scores				
number (not applicable)	4	4		

Notes:

[1] - 4 subjects were randomised in this treatment arm.

[2] - 4 subjects were randomised in this treatment arm.

### Statistical analyses

Statistical analysis title	Please see attached summary
Statistical analysis description:	
as above	
Comparison groups	Buspirone 0.20mg/kg and Placebo v Buspirone 0.10mg/kg and Placebo
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	other <sup>[3]</sup>
P-value	< 0.05 <sup>[4]</sup>
Method	paired t-tests
Parameter estimate	n/a

Notes:

[3] - please see attached summary

[4] - 0.731  
0.523

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

Adverse effects were reported immediately to the Principal Investigator and were assessed as minor adverse effects possibly related to the study procedures. Patients were all fine at the end of the clinical examinations and were discharged.

Adverse event reporting additional description:

The PI and the clinician in charge decided not to treat any of these AEs as they were mild and released within a couple of hours without any treatment. In addition, all patients were contacted 24 hours afterwards and a week later. No further adverse events were reported.

Assessment type	Systematic
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### Dictionary used

Dictionary name	Local Imperial JRCO
Dictionary version	1

### Reporting groups

Reporting group title	Buspirone 0.10mg/kg
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Reporting group description:

6 out of 8 reported mild drowsiness, fatigue and/or headache following the administration of the study drug.

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Reporting group description:

6 out of 8 reported mild drowsiness, fatigue and/or headache following the administration of the study drug.

Serious adverse events	Buspirone 0.10mg/kg	Buspirone 0.20mg/kg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (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: 1 %

Non-serious adverse events	Buspirone 0.10mg/kg	Buspirone 0.20mg/kg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	

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: 6 out of 8 reported mild drowsiness, fatigue and/or headache following the administration of the study drug.



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 May 2015	In this substantial amendment, -details on blinding/unblinding were included. -further exclusion criteria were included. -definitions of SAEs and SUSARs were refined to reflect local standard documentation.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported