Clinical trial results:
The control of brain networks after traumatic brain injury: a neuroimaging and neuropsychological study of dopamine and cognition

Summary

EudraCT number	2013-004244-37
Trial protocol	GB
Global end of trial date	29 September 2016

Results information

Result version number	v1
This version publication date	15 November 2018
First version publication date	15 November 2018
Summary attachment (see zip file)	TBI Dopamine CSR (Clinical Study Report DREAM Trial_19.09.2018.pdf)

Trial information

Trial identification

Sponsor protocol code	13HH1824

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Imperial College London | Imperial College NHS Healthcare Trust
Sponsor organisation address	Kensington, London, London, United Kingdom, SW7 2AZ
Public contact	Youssouf, Imperial College London | Imperial College NHS Healthcare Trust, +44 0203 311 0213, nabila.youssouf@imperial.ac.uk
Scientific contact	Youssouf, Imperial College London | Imperial College NHS Healthcare Trust, +44 0203 311 0213, nabila.youssouf@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	18 September 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 September 2016
Global end of trial reached?	Yes
Global end of trial date	29 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To investigate the relationship between dopamine levels (a chemical in the brain which modulates brain functions) in the brain and its impact on cognition in patients who have suffered a traumatic brain injury.

Protection of trial subjects:

No specific measures were implemented to protect participants, but adverse events were closely monitored and participants were free to withdraw at any time.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2014
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: 46
Worldwide total number of subjects	46
EEA total number of subjects	46

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)	46
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

158 TBI participants were screened. 62 chose not to participate and 50 met one or more of the exclusion criteria.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo First

Arm description:

participants in this arm received placebo first.

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:

As per IMP

Arm title	Methylphenidate First

Arm description:

participants in this arm received the active IMP first before crossing over to placebo

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:

0.3mg/kg (rounded to nearest 5mg and capped at maximum dose of 25mg/day) twice per day.

Number of subjects in period 1[1]	Placebo First	Methylphenidate First
Started	20	20
Completed	20	20

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 46 participants were enrolled but 6 withdrew, leaving 40 in the final analysis set.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo First
Reporting group description: participants in this arm received placebo first.	
Reporting group title	Methylphenidate First
Reporting group description: participants in this arm received the active IMP first before crossing over to placebo	

Reporting group values	Placebo First	Methylphenidate First	Total
Number of subjects	20	20	40
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	20	20	40
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	4	2	6
Male	16	18	34

Subject analysis sets	
Subject analysis set title	Normal Caudate
Subject analysis set type	Sub-group analysis
Subject analysis set description: Normal caudate 123I-ioflupane specific binding ratio (N=22) Comparison of IMP group median score vs placebo group median score	
Subject analysis set title	Low Caudate Group
Subject analysis set type	Sub-group analysis
Subject analysis set description: Low caudate 123I-ioflupane specific binding ratio (N=18) Comparison of IMP group median score vs placebo group median score	

Reporting group values	Normal Caudate	Low Caudate Group	
Number of subjects	22	18	
Age categorical 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)	22	18	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	5	1	
Male	17	17	

End points

End points reporting groups

Reporting group title	Placebo First
Reporting group description: participants in this arm received placebo first.	
Reporting group title	Methylphenidate First
Reporting group description: participants in this arm received the active IMP first before crossing over to placebo	
Subject analysis set title	Normal Caudate
Subject analysis set type	Sub-group analysis
Subject analysis set description: Normal caudate 123I-ioflupane specific binding ratio (N=22) Comparison of IMP group median score vs placebo group median score	
Subject analysis set title	Low Caudate Group
Subject analysis set type	Sub-group analysis
Subject analysis set description: Low caudate 123I-ioflupane specific binding ratio (N=18) Comparison of IMP group median score vs placebo group median score	

Primary: Primary Outcome Measure

End point title	Primary Outcome Measure[1]
End point description:	
End point type	Primary
End point timeframe: Assessed by comparing scores at placebo visit to those at active IMP visit.	

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: A complete case analysis was conducted (i.e. for each analysis only cases with the relevant outcome data were included). There was no imputation for missing data. See full clinical study report for further details.

End point values	Normal Caudate	Low Caudate Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22	18		
Units: Milliseconds				
median (inter-quartile range (Q1-Q3))				
Placebo	357 (325 to 392)	382 (359 to 429)		
Methylphenidate	362 (331 to 378)	369 (347 to 398)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From consent to the final MRI study visit.

Assessment type	Systematic

Dictionary used

Dictionary name	None
Dictionary version	0

Reporting groups

Reporting group title	All participants

Reporting group description:

All participants affected by adverse events (n=24/40).

Serious adverse events	All participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 40 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	All participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 40 (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: There were no SAEs and no AEs of a sufficient frequency to require reporting. In total, 24 of the 40 participants exposed suffered adverse events, however I was unable to add that information into the relevant section.
See the attached CSR for a full list of AEs.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 February 2014	Protocol amendment 1
05 March 2014	Protocol amendment 2
13 June 2014	Protocol amendment 3
21 October 2014	Protocol amendment 4
12 November 2014	Protocol amendment 5
19 July 2016	Protocol amendment 6

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

See the attached CSR for a complete description of the study, results and conclusions.

Notes: