Clinical trial results:
A trial of Guanfacine, an alpha 2 adrenergic agonist, for Spatial Neglect and Impaired Vigilance following Stroke and Focal Brain Damage

Summary

EudraCT number	2008-001160-36
Trial protocol	GB
Global end of trial date	28 March 2014

Results information

Result version number	v1 (current)
This version publication date	29 December 2019
First version publication date	29 December 2019

Trial information

Trial identification

Sponsor protocol code	2008-1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00955253
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Imperial College London
Sponsor organisation address	South Kensington Campus, London, United Kingdom, SW7 2AZ
Public contact	Paresh A Malhotra, Imperial College London, +44 2088467286, p.malhotra@imperial.ac.uk
Scientific contact	Paresh A Malhotra, Imperial College London, +44 2088467286, p.malhotra@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	03 August 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 March 2014
Global end of trial reached?	Yes
Global end of trial date	28 March 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To establich whether spatial neglect and impaired sustained attention (secondary to hemispheric stroke or brain injury) are improved by a single dose of oral guanfacine

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 April 2010
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: 13
Worldwide total number of subjects	13
EEA total number of subjects	13

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)	8
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Stroke patients with evidence of neglect on bedside testing were recruited from Imperial College Healthcare NHS Trust, the National Hospital for Neurology and Neurosurgery and Northwick Park Hospital. Patients were recruited during their inpatient rehabilitation or via the outpatient clinic.

Pre-assignment

Screening details:

Patients with robust visual neglect when tested twice with cancellation tests (specifically an overall score on one or both tests<75%total and/or five or more omissions on the left than on the right) were considered for inclusion.

Period 1

Period 1 title	First treatment (day 2)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Guanfacine

Arm description:

Participants received Guanfacine

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

Dosage and administration details:

On day 2, individuals received 2mg of active drug

Arm title	Placebo

Arm description:

Participants received placebo

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:

On day 2, individuals received 2mg of placebo

Number of subjects in period 1	Guanfacine	Placebo
Started	7	6
Completed	7	6

Period 2	
Period 2 title	Second intervention (day 4)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms	
Are arms mutually exclusive?	Yes
Arm title	Guanfacine

Arm description:

Participants received Guanfacine

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

Dosage and administration details:

On day 2, individuals received 2mg of active drug

Arm title	Placebo

Arm description:

Participants received placebo

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:

On day 2, individuals received 2mg of placebo

Number of subjects in period 2	Guanfacine	Placebo
Started	6	7
Completed	6	7

Baseline characteristics

Reporting groups	
Reporting group title	First treatment (day 2)

Reporting group description: -

Reporting group values	First treatment (day 2)	Total	
Number of subjects	13	13	
Age categorical Units: Subjects			
Adults (18-64 years)	8	8	
From 65-84 years	5	5	
Age continuous Units: years			
geometric mean	63.2		
standard deviation	± 10.3	-	
Gender categorical Units: Subjects			
Female	1	1	
Male	12	12	
Behavioural Inattention Test Star Cancellation Score			
This is a standard scale for measuring the severity of spatial neglect. Patients are asked to find and mark targets (which are embedded amongst distractors) on a piece of paper. The maximum number of targets that can be found is 54 (Therefore minimum score =0, maximum =54), which represents normal performance.			
Units: Number of targets found			
geometric mean	35.4		
standard deviation	± 15.9	-	
Touchscreen Cancellation			
This is a computerized scale for measuring the severity of spatial neglect as described in previous publications (Malhotra et al, Annals of Neurology 2006; Parton et al, Neuroreport 2006). Patients are asked to find and touch targets (which are embedded amongst distractors) on a touchscreen. In the variant of the task employed here, the targets are not marked when touched ("Invisible Cancellation").The maximum number of targets that can be found is 64 (Therefore minimum score = 0, maximum = 64), which represents normal performance.			
Units: Number of targets found			
geometric mean	28.4		
standard deviation	± 13.9	-	

Subject analysis sets	
Subject analysis set title	Guanfacine
Subject analysis set type	Full analysis

Subject analysis set description:

All participants who received Guanfacine

Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

All participants who received placebo

Reporting group values	Guanfacine	Placebo	
Number of subjects	13	13	
Age categorical Units: Subjects			
Adults (18-64 years) From 65-84 years			
Age continuous Units: years geometric mean standard deviation	±	±	
Gender categorical Units: Subjects			
Female Male			
Behavioural Inattention Test Star Cancellation Score			
This is a standard scale for measuring the severity of spatial neglect. Patients are asked to find and mark targets (which are embedded amongst distractors) on a piece of paper. The maximum number of targets that can be found is 54 (Therefore minimum score =0, maximum =54), which represents normal performance.			
Units: Number of targets found geometric mean standard deviation	35.4 ± 15.9	35.4 ± 15.9	
Touchscreen Cancellation			
This is a computerized scale for measuring the severity of spatial neglect as described in previous publications (Malhotra et al, Annals of Neurology 2006; Parton et al, Neuroreport 2006). Patients are asked to find and touch targets (which are embedded amongst distractors) on a touchscreen. In the variant of the task employed here, the targets are not marked when touched ("Invisible Cancellation").The maximum number of targets that can be found is 64 (Therefore minimum score = 0, maximum = 64), which represents normal performance.			
Units: Number of targets found geometric mean standard deviation	28.4 ± 13.9	28.4 ± 13.9	

End points

End points reporting groups

Reporting group title	Guanfacine
Reporting group description: Participants received Guanfacine	
Reporting group title	Placebo
Reporting group description: Participants received placebo	
Reporting group title	Guanfacine
Reporting group description: Participants received Guanfacine	
Reporting group title	Placebo
Reporting group description: Participants received placebo	
Subject analysis set title	Guanfacine
Subject analysis set type	Full analysis
Subject analysis set description: All participants who received Guanfacine	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description: All participants who received placebo	

Primary: Performance on Tests of Hemispatial Neglect and Sustained Attention

End point title	Performance on Tests of Hemispatial Neglect and Sustained Attention

End point description:

Touchscreen Cancellation: This is a computerized scale for measuring the severity of spatial neglect as described in previous publications (Malhotra et al, Annals of Neurology 2006; Parton et al, Neuroreport 2006). Patients are asked to find and touch targets (which are embedded amongst distractors) on a touchscreen. In the variant of the task employed here, the targets are not marked when touched ("Invisible Cancellation"). The maximum number of targets that can be found is 64 (Therefore minimum score =0, maximum = 64), which represents normal performance.

End point type	Primary

End point timeframe:

5 days

End point values	Guanfacine	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	13		
Units: Number of targets found				
geometric mean (standard deviation)	31.15 (± 15.1)	26.15 (± 41.29)		

Statistical analyses

Statistical analysis title	Hemispatial Neglect and Sustained Attention
Comparison groups	Guanfacine v Placebo
Number of subjects included in analysis	26
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.013
Method	t-test, 2-sided

Secondary: Sustained attention	
End point title	Sustained attention
End point description:	
The computed response time variability, which is commonly used as an index of sustained attention, with higher variability indicating poorer deployment of attention on the task. The main effect of the drug on response bias.	
End point type	Secondary
End point timeframe:	
5 days	

End point values	Guanfacine	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	13		
Units: signal detection				
median (standard deviation)	0.72 (± 0.42)	0.51 (± 0.45)		

Statistical analyses

Statistical analysis title	Sustained attention
Comparison groups	Placebo v Guanfacine
Number of subjects included in analysis	26
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.004
Method	t-test, 2-sided

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: 5 days	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10

Reporting groups	
Reporting group title	Guanfacine
Reporting group description: Participants received Guanfacine	
Reporting group title	Placebo
Reporting group description: Participants received placebo	

Serious adverse events	Guanfacine	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	0 / 13 (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	Guanfacine	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	0 / 13 (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: No adverse event reported

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29436486