Clinical trial results:
Huntington's Disease Rilmenidine Safety Trial

Summary

EudraCT number	2009-018119-14
Trial protocol	GB
Global end of trial date	30 June 2015

Results information

Result version number	v1 (current)
This version publication date	16 July 2016
First version publication date	16 July 2016

Trial information

Trial identification

Sponsor protocol code	A091758

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Cambridge University Hospitals NHS Foundation Trust
Sponsor organisation address	Hills Road, Cambridge, United Kingdom, CB2 2PY
Public contact	Stephen Kelleher, Cambridge University NHS Foundation Trust, 01223 217418, stephen.kelleher@addenbrookes.nhs.uk
Scientific contact	Stephen Kelleher, Cambridge University NHS Foundation Trust, 01223 217418, stephen.kelleher@addenbrookes.nhs.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	13 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 June 2015
Global end of trial reached?	Yes
Global end of trial date	30 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate whether Rilmenidine (oral preparation) can safely be taken and is well tolerated by patients suffering from Huntington's Disease (HD).
This will be achieved by regular, periodic assessments of the patients' physical and mental health monitoring for adverse effects and disease progression.

Protection of trial subjects:

The patients were recruited from our normal NHS HD clinic, and on completion of the trial came back to this clinic.
They are well known to us and the trial itself was straightforward with no invasive procedures, but simple assessments, blood tests and imaging.
The only special measure was the monitoring of blood pressure given the agent being trialled is normally used as an anti-hypertensive.

Background therapy:

Patients were trialled with Rilmenidine 1mg for 6 months and 2mg for 18 month, taken once per day. No placebo arm.

Evidence for comparator:

N/A.

Actual start date of recruitment	03 September 2012
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: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	15
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All patients have been recruited from Cambridge University Hospital NHS FoundationTrust Huntington's disease clinic, which is run weekly at the Cambridge centre for Brain Repair. All patients have been recruited from Cambridge (single centre study) within one year of recruitment starting.

Pre-assignment

Screening details:

Known to have Huntington's disease, with a mild disease. Able to do MRI scan, which happened before and after medication was administered. Stable medication. no other ongoing medical or psychiatric problems and self caring. Not on hypertensive medication. Able to understand English.

Period 1

Period 1 title	Overall Trial Period
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Arm title	Active Treatment

Arm description: -

Arm type	Open Label drug repurposing
Investigational medicinal product name	Rilmenidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1mg for 6 months and 2 mg for following 18 months.

Number of subjects in period 1	Active Treatment
Started	16
None	16
Completed	16

Period 2

Period 2 title	Post intervention
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Active Treatment
Arm description: -	
Arm type	Open Label drug repurposing
Investigational medicinal product name	Rilmenidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1mg for 6 months and 2 mg for following 18 months.

Number of subjects in period 2	Active Treatment
Started	16
Completed	16

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial Period

Reporting group description: -

Reporting group values	Overall Trial Period	Total	
Number of subjects	16	16	
Age categorical			
Ambulant and able to self care independently. Males and Females, aged between 18 and 70. Women of childbearing age who are neither pregnant nor planning to conceive during the period of the study. Women will be required to use two forms of contraception, at least one of which to be a barrier method. English speaking and able to give written, informed consent.			
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)	15	15	
From 65-84 years	1	1	
85 years and over	0	0	
Study Subject	0	0	
Age continuous			
Units: years			
arithmetic mean	53		
full range (min-max)	37.8 to 69.9	-	
Gender categorical			
Males and Females with no selected gender bias for the trial			
Units: Subjects			
Female	5	5	
Male	11	11	
Demographics			
Age, gender, disease duration			
Units: Subjects			
Demographics	16	16	
Clinical Assessments			
UHDRS - Clinical scoring			
Units: out of 144			
arithmetic mean	24.2		
full range (min-max)	4 to 79	-	
Cognitive Assessment			
Mini Mental State			
Units: out of 30			
arithmetic mean	27.5		
full range (min-max)	21 to 30	-	

Total Functional Capacity Units: 0-13 arithmetic mean full range (min-max)	 9.6 5 to 13	 -	
Trail A Units: Seconds arithmetic mean full range (min-max)	 53.3 30 to 221	 -	
Trail B Units: seconds arithmetic mean full range (min-max)	 162 33 to 497	 -	

End points

End points reporting groups	
Reporting group title	Active Treatment
Reporting group description: -	
Reporting group title	Active Treatment
Reporting group description: -	
Subject analysis set title	Safety Popultion
Subject analysis set type	Safety analysis
Subject analysis set description: Any patients who received IMP	

Primary: Number of Serious Adverse Events	
End point title	Number of Serious Adverse Events
End point description:	
End point type	Primary
End point timeframe: 27 months	

End point values	Active Treatment	Active Treatment	Safety Popultion	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	16	16	
Units: Participants	3	3	3	

Statistical analyses

Statistical analysis title	Primary Analysis
Statistical analysis description: Comparison of SAE rate to a reference value of 5%	
Comparison groups	Active Treatment v Active Treatment v Safety Popultion
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.04
Method	exact binomial test, one-sided
Parameter estimate	Incidence rate of SAEs
Point estimate	0.18
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.053
upper limit	0.348

Secondary: MRI Volumetric Change

End point title	MRI Volumetric Change

End point description:

End point type	Secondary

End point timeframe:

27 months - trial duration

End point values	Active Treatment			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: ML				
arithmetic mean (standard deviation)				
MRI	13000 (± 10000)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mini Mental State Examination

End point title	Mini Mental State Examination

End point description:

End point type	Secondary

End point timeframe:

Collection over 27 months and collected at Baseline, 3, 6, 9 , 12, 18, 24 and 27 Months

End point values	Active Treatment			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: 30				
number (not applicable)				
MMSE	16			

Statistical analyses

No statistical analyses for this end point

Secondary: UHDRS motor score

End point title	UHDRS motor score

End point description:

End point type	Secondary

End point timeframe:

at all time points as specified in trial protocol.

End point values	Active Treatment			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: 0-144				
number (not applicable)	16			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

27 months

Assessment type	Non-systematic

Dictionary used

Dictionary name	None
Dictionary version	1

Reporting groups

Reporting group title	Active Treatment

Reporting group description: -

Serious adverse events	Active Treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 16 (18.75%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Migraine			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depressive delusion			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Fracture			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Active Treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 16 (87.50%)		
Injury, poisoning and procedural complications			
Thumb Injury			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	4		
Nervous system disorders			
Head discomfort	Additional description: Headache		
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Dizziness			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Fall			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Insomnia related to another mental condition			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Raised CPK			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Gastrointestinal disorders			

weight gain subjects affected / exposed occurrences (all) nausea subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1 1 / 16 (6.25%) 1		
Hepatobiliary disorders Alanine aminotransferase increased subjects affected / exposed occurrences (all) Alkaline Phosphatase Increased subjects affected / exposed occurrences (all)	 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1		
Psychiatric disorders Increased irritability subjects affected / exposed occurrences (all) Low Mood subjects affected / exposed occurrences (all)	 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 August 2011	Addition of patient ID card to the study.
18 August 2011	Update the Clinical Trials Authorisation with details of the company manufacturing and importing IMP.
10 December 2012	Increase the dose of the IMP that the patients take from 1mg to 2mg per day from 6 months for the remaining 18 months on the trial until month 24. Updates to the Patient Information sheets, protocol and patient Identification card and update to the original REC application form to correctly catagorise the trial as a phase II and not a phase IV as previously listed.

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.

Technical issues prevented saccadometer data from being recorded.
NeuroPsychiatry Inventory could not be analysed as subjects attended with different or no caregiver.
Hand tapping was collected over different time periods so couldn't be analysed.

Notes: