Clinical trial results:
Aggression Following TBI: Effectiveness of Risperidone (AFTER)-a feasibility RCT.

Summary

EudraCT number	2015-000641-23
Trial protocol	GB
Global end of trial date	08 June 2018

Results information

Result version number	v1 (current)
This version publication date	24 May 2019
First version publication date	24 May 2019

Trial information

Trial identification

Sponsor protocol code	CNWL/MC/AFT/01

Additional study identifiers

ISRCTN number	ISRCTN30191436
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Central and North West London NHS Foundation Trust
Sponsor organisation address	1st Floor, Bloomsbury Building St Pancras Hospital, London, United Kingdom, NW1 0PE
Public contact	Angela Williams, Central and North West London NHS Foundation Trust, 44 20 3317 3765, after.noclor@nhs.net
Scientific contact	Angela Williams, Central and North West London NHS Foundation Trust, 44 20 3317 3765, after.noclor@nhs.net

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	24 October 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 June 2018
Global end of trial reached?	Yes
Global end of trial date	08 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Using the Modified Overt Aggression Scale (MOAS) to assess aggression at 12 weeks in order to estimate sample size for future full RCT, and gauge the potential recruitment and drop-out rates.

Protection of trial subjects:

Thorough monitoring of adverse events and participant wellbeing occurred as part of the assessment process. During assessment and testing breaks were provided to minimise possible fatigue or stress, and if indicated, the assessment were spread over more than one visit.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

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)	14
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Exclusions included post-traumatic amnesia, severe mental illness, contraindications to risperidone, pregnancy/breastfeeding, cardiovascular disease, low white blood cell count, drug-induced leukopenia/neutropenia, history of seizures. For those already prescribed an antipsychotic, a wash-out period of two weeks was required prior to randomisation.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Risperidone

Arm description: -

Arm type	Experimental
Investigational medicinal product name	risperidone
Investigational medicinal product code	N05AX08
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Dosing started with 1 mg once daily and was titrated in 1mg increments, not more than once every 7 days, to a maximum of 4mg a day.

Arm title	Placebo

Arm description: -

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:

Administration was matched to the active (risperidone) arm.

Number of subjects in period 1	Risperidone	Placebo
Started	6	8
Completed	5	7
Not completed	1	1
Physician decision	1	-

Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Risperidone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Risperidone	Placebo	Total
Number of subjects	6	8	14
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	39.3	43.1	
standard deviation	± 8.7	± 11.3	-
Gender categorical Units: Subjects			
Female	1	3	4
Male	5	5	10
Modified Overt Aggression Scale			
The MOAS is a simple but widely used 4-item scale that measures verbal aggression along with physical aggression towards other people, property and self.			
Units: Score			
arithmetic mean	5.5	13.9	
standard deviation	± 2.9	± 11.0	-

End points

End points reporting groups

Reporting group title	Risperidone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: MOAS at 12-week assessment

End point title	MOAS at 12-week assessment[1]
End point description:	
End point type	Primary
End point timeframe:	
Modified Overt Aggression Scale score at 12 week follow-up	

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: As this was a feasibility study the primary aim was to work out the standard deviation of the MOAS score at 12 week follow up to inform a sample size calculation for a future full scale RCT.

End point values	Risperidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	7		
Units: score				
arithmetic mean (standard deviation)	2.2 (± 3.9)	2.0 (± 2.4)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Timeframe for reporting adverse events was 17th January 2017 to 6th June 2018

Adverse event reporting additional description:

Participants were assessed for the known side effects of antipsychotic medication using a published scale- the UKU scale (Lingjaerde et al, 1987) at study visits. Ad hoc spontaneous adverse event reporting was also used.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	Risperidone
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	Risperidone	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (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: 5 %

Non-serious adverse events	Risperidone	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	4 / 8 (50.00%)	
Injury, poisoning and procedural complications			
Injury			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness	Additional description: dizziness resulting in a fall		
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	
occurrences (all)	0	2	
General disorders and administration site conditions			

Chest pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	2 / 6 (33.33%)	1 / 8 (12.50%)	
occurrences (all)	5	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anger			
subjects affected / exposed	2 / 6 (33.33%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Anxiety			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 November 2015	A change to the protocol to clarify existing eligibility criteria, and a change of sites.
17 July 2017	A change to the inclusion criterion "a history of seizures" changed to only exclude patients that have experienced a neurogenic seizure in the past three months

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported