Clinical trial results:
OPEN LABEL TRIAL OF ATOMOXETINE FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN CHILDREN WITH SPECIAL EDUCATIONAL NEEDS

Summary

EudraCT number	2008-004827-44
Trial protocol	GB
Global end of trial date	22 March 2013

Results information

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

Trial information

Trial identification

Sponsor protocol code	ATOM

Additional study identifiers

ISRCTN number	ISRCTN25691213
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	King's College London
Sponsor organisation address	The Strand, London, United Kingdom, WC2R 2LS
Public contact	Professor Emily Simonoff, King's College London, +44 02078485312, emily.simonoff@kcl.ac.uk
Scientific contact	Professor Emily Simonoff, King's College London, +44 02078485312, emily.simonoff@kcl.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	22 March 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 March 2013
Global end of trial reached?	Yes
Global end of trial date	22 March 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

What is the efficacy of atomoxetine in reducing the symptoms of ADHD among children with moderate and severe learning disabilities and ADHD?

Protection of trial subjects:

Following determination of eligibility, informed consent will be obtained from at least one parent with parental responsibility or legal guardian. Children and young people will be given developmentally appropriate information about the disorder, its treatment and the trial. Only exceptionally will children be enrolled where there is disagreement among the parents regarding consent to participate.

Background therapy:

None

Evidence for comparator:

not applicable

Actual start date of recruitment	11 November 2009
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: 11
Worldwide total number of subjects	11
EEA total number of subjects	11

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)	6
Adolescents (12-17 years)	5
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited at one site in the UK between 2009 and 2013

Pre-assignment

Screening details:

1 Aged 7 - 15 years,
2 Diagnosis of ADHD
3 Full-scale intelligence quotient (IQ) 30 - 69 or age equivalent estimate
4 Did not respond to methylphenidate either at high dose or because dose limited by unacceptable adverse effects
5 Child in stable care situation
6 Child regularly attending school (more than 75% of last school term)

Pre-assignment period milestones

Number of subjects started	11
Number of subjects completed	11

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Participants will be randomized immediate start atomoxetine or delayed start by 8 weeks.

Arms

Are arms mutually exclusive?	Yes
Arm title	Immediate

Arm description:

Immediate

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

Dosage and administration details:

Active treatment: Participants randomised to immediate treatment . All participants dosing regime as below:-
Week 1 - Strattera 0.5 mg/kg/day (starting dose) during the first week,
Week 2 – Strattera 0.8 mg/kg/day (low dose)
Week 3 to 16 - 1.2 mg/kg/day (standard dose)
or
Week 8 to 16 - Subjects showing less than “much improvement” on the CGI—Improvement (CGI-I) scale at the end of week 8, AND experiencing mild or no adverse effects, may have a further dose increase to 1.4 mg/kg/day (high dose).

Arm title	Delayed Treatment

Arm description:

Active treatment: Participants randomised to delayed (8 weeks treatment).

Arm type	Active comparator

Investigational medicinal product name	Atomoxetine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Active treatment: Participants randomised to treatment delayed for 8 weeks . All participants dosing regime as below:-
Week 1 - Strattera 0.5 mg/kg/day (starting dose) during the first week,
Week 2 – Strattera 0.8 mg/kg/day (low dose)
Week 3 to 16 - 1.2 mg/kg/day (standard dose)
or
Week 8 to 16 - Subjects showing less than "much improvement" on the CGI—Improvement (CGI-I) scale at the end of week 8, AND experiencing mild or no adverse effects, may have a further dose increase to 1.4 mg/kg/day (high dose).

Number of subjects in period 1	Immediate	Delayed Treatment
Started	5	6
Completed	5	6

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	11	11	
Age categorical Units: Subjects			
Children (2-12 years)	6	6	
Adolescents (13-16 years)	4	4	
Adolescents (17-18 years)	1	1	
Gender categorical Units: Subjects			
Female	3	3	
Male	8	8	

End points

End points reporting groups

Reporting group title	Immediate
Reporting group description:	
Immediate	
Reporting group title	Delayed Treatment
Reporting group description:	
Active treatment: Participants randomised to delayed (8 weeks treatment).	

Primary: Primary Efficacy Endpoint

End point title	Primary Efficacy Endpoint[1]
End point description:	
The primary efficacy criteria are reduction in symptoms of hyperactive behaviour (overactivity, poor concentration and impulsivity) as rated by parents and teachers on the ADHD index of the short version of the Conners scale (CRS-S; Conners, 1989). Average baseline ratings taken prior to treatment will be compared to average ratings taken during Week 16	
End point type	Primary
End point timeframe:	
0-16 weeks	

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: Due to insufficient recruitment, it was not possible to analyse the data obtained. However no safety concerns were raised.

End point values	Immediate	Delayed Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: whole	5	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary Efficacy Parameters

End point title	Secondary Efficacy Parameters
End point description:	
Secondary efficacy outcome variables: 1.Conners' hyperactivity scale (parent and teacher) 2.Clinical Global Impressions Scale (improvement) 3.Parent Aberrant Behaviour Scale 4.Teacher Aberrant Behaviour Scale	
End point type	Secondary
End point timeframe:	
0-16 weeks	

End point values	Immediate	Delayed Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: whole	5	6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Duraton of Trial	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1
Reporting groups	
Reporting group title	Immediate Treatment
Reporting group description: Participants introduced to atomoxetine straight after the reassessment.	
Reporting group title	Delayed Treatment
Reporting group description: introduced to atomoxetine 8 weeks after reassessment.	

Serious adverse events	Immediate Treatment	Delayed Treatment	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (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	Immediate Treatment	Delayed Treatment	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	6 / 6 (100.00%)	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Nervous system disorders			
Drowsiness			
subjects affected / exposed	3 / 5 (60.00%)	1 / 6 (16.67%)	
occurrences (all)	3	1	
Headache			

subjects affected / exposed	1 / 5 (20.00%)	2 / 6 (33.33%)	
occurrences (all)	1	2	
Immune system disorders			
Rash			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Mumps			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Appetite Loss			
subjects affected / exposed	3 / 5 (60.00%)	2 / 6 (33.33%)	
occurrences (all)	3	2	
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Upset Stomach			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Redness of face			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Being tearful, on and off not related to bad mood			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Irritability			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	

Sleep problems subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1	
Musculoskeletal and connective tissue disorders Leg trauma subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	
Infections and infestations Sore Throat subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 July 2010	Children and adolescents of both genders aged 7-18 years inclusive at the beginning of trial. Children over 16 should be in full-time education and not expected to leave school within 6 months. Additionally children over 16 will be assessed for their capacity to give consent to participate in the trial using the Mental Capacity Tool (Children over 16 appendix). This tool was designed for use with young adults with intellectual disability, neurodevelopmental or other disorders that might impair their ability to give informed consent. Evidence of potential impairment in capacity includes the diagnosis of learning disability, IQ <70, significant deficity in adaptive functioning, or other signs or symptoms of mental disorder that might compromise capacity to give informed consent. The assessment establishes understanding, retention of information, use of information to make the decision and communication of the decision. These reflect the limbs of the 'capacity test' as defined in the Mental Capacity Act 2005. We expect that the majority of the over 16 children would have difficulties in showing the necessary understanding in order to consent due to their special needs; in these cases a consultee will be appointed following the procedure described in the Children over 16 appendix.
31 January 2011	1) To change the period off-psychotropic medication from 3 months to 1 month in order for the children to have quicker access to the trial. 2) To clarify that children who ·use to be stimulants should be off them for at least a week.

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.

This trial was terminated early due to inability to recruit eligible participants, therefore insufficient data was obtained to perform robust analyses or meet the prirmary endpoints. No safety concerns were raised.

Notes: