EU Clinical Trials Register

Clinical trial results:

A Randomized, Controlled, Open-Label Comparison Study of the Efficacy and Safety of Slow Transitioning compared with Fast Transitioning from a Stimulant Medication to Atomoxetine in Pediatric and Adolescent Outpatients with DSM-IV Attention-Deficit/Hyperactivity Disorder (ADHD).

Summary

EudraCT number	2008-001767-11
Trial protocol	GB ES PT
Global end of trial date	08 September 2010

Results information

Result version number	v1 (current)
This version publication date	15 November 2020
First version publication date	15 November 2020

Trial information

Trial identification

Sponsor protocol code	12305

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 September 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 September 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Children and adolescents with Attention Deficit Hyperactivity Disorder (ADHD) who are not tolerating or not responding well to stimulant therapy will be included in this study. Two different strategies for transition from Stimulant to Atomoxetine will be used: Slow (10 weeks) and fast (2 weeks). Changes in ADHD symptoms and tolerability of medication will be compared between the two different switching approaches.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 September 2008
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	Portugal: 7
Country: Number of subjects enrolled	Spain: 57
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	Australia: 12
Country: Number of subjects enrolled	Mexico: 20
Worldwide total number of subjects	111
EEA total number of subjects	79

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)	62

Adolescents (12-17 years)	49
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study Period II was a 10-week treatment period. Study Period III was a 4-week period, during which participants continued on atomoxetine treatment at the same dose as given at the end of Study Period II or at a higher dose, up to a maximum of 1.8 mg/kg/day.

Pre-assignment

Screening details:

NA

Period 1

Period 1 title	Study Period II
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Slow Switching Group

Arm description:

Switch from full stimulants dose to atomoxetine 1.2 milligrams per kilogram per day (mg/kg/day) without stimulants, orally (PO), during (or over) 10 weeks then continue treatment up to 1.8mg/kg/day, PO to 14 weeks.

Arm type	Experimental
Investigational medicinal product name	Atomoxetine
Investigational medicinal product code	LY139603
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Atomoxetine 1.2 milligrams per kilogram per day (mg/kg/day), orally (PO), during 10 weeks then continue treatment up to 1.8mg/kg/day, PO to 14 weeks.

Arm title	Fast Switching Group

Arm description:

Switch from full stimulant dose to atomoxetine 1.2mg/kg/day, PO, without stimulants during the first 2 weeks. Continue atomoxetine 1.2 mg/kg/day to 10 weeks, followed by atomoxetine up to 1.8 mg/kg/day to 14 weeks.

Arm type	Experimental
Investigational medicinal product name	Atomoxetine
Investigational medicinal product code	LY139603
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Atomoxetine 1.2mg/kg/day, PO, within 2 weeks. Continue atomoxetine 1.2 mg/kg/day to 10 weeks, followed by atomoxetine up to 1.8 mg/kg/day to 14 weeks.

Number of subjects in period 1	Slow Switching Group	Fast Switching Group
Started	57	54
Completed	44	41
Not completed	13	13
Parent/Caregiver Decision	3	-
Consent withdrawn by subject	1	-
Adverse event, non-fatal	3	4
Protocol deviation	6	3
Lack of efficacy	-	6

Period 2

Period 2 title	Study Period III
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Slow Switching Group

Arm description:

Switch from full stimulant dose to atomoxetine 1.2 milligrams per kilogram per day (mg/kg/day) without stimulants, orally (PO), during 10 weeks then continue treatment up to 1.8mg/kg/day, PO to 14 weeks.

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:

Atomoxetine 1.2 milligrams per kilogram per day (mg/kg/day), orally (PO), during 10 weeks then continue treatment up to 1.8mg/kg/day, PO to 14 weeks.

Arm title	Fast Switching Group

Arm description:

Switch from full stimulant dose to atomoxetine 1.2mg/kg/day, PO, without stimulants during 2 weeks. Continue atomoxetine 1.2 mg/kg/day to 10 weeks, followed by atomoxetine up to 1.8 mg/kg/day to 14 weeks.

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:

Atomoxetine 1.2mg/kg/day, PO, during 2 weeks. Continue atomoxetine 1.2 mg/kg/day to 10 weeks, followed by atomoxetine up to 1.8 mg/kg/day to 14 weeks.

Number of subjects in period 2	Slow Switching Group	Fast Switching Group
Started	44	41
Completed	41	38
Not completed	3	3
Parent/Caregiver Decision	-	1
Physician decision	-	1
Adverse event, non-fatal	1	-
Lack of efficacy	1	-
Protocol deviation	1	1

Baseline characteristics

Reporting groups

Reporting group title	Slow Switching Group
Reporting group description:	
Switch from full stimulants dose to atomoxetine 1.2 milligrams per kilogram per day (mg/kg/day) without stimulants, orally (PO), during (or over) 10 weeks then continue treatment up to 1.8mg/kg/day, PO to 14 weeks.	
Reporting group title	Fast Switching Group
Reporting group description:	
Switch from full stimulant dose to atomoxetine 1.2mg/kg/day, PO, without stimulants during the first 2 weeks. Continue atomoxetine 1.2 mg/kg/day to 10 weeks, followed by atomoxetine up to 1.8 mg/kg/day to 14 weeks.	

Reporting group values	Slow Switching Group	Fast Switching Group	Total
Number of subjects	57	54	111
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	11.1	12.0	
standard deviation	± 2.51	± 2.16	-
Gender categorical			
Units: Subjects			
Female	8	10	18
Male	49	44	93
Race/Ethnicity			
Units: Subjects			
Caucasian	46	43	89
African	1	0	1
Hispanic	10	11	21
Attention Deficit Hyperactivity Disorder (ADHD) subtype			
ADHD subtype was classified by Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) criteria.			
Units: Subjects			
Combined	38	36	74
Hyperactive/Impulsive	1	3	4
Inattentive	17	15	32
Not otherwise categorized	1	0	1

End points

End points reporting groups

Reporting group title	Slow Switching Group
Reporting group description:	
Switch from full stimulants dose to atomoxetine 1.2 milligrams per kilogram per day (mg/kg/day) without stimulants, orally (PO), during (or over) 10 weeks then continue treatment up to 1.8mg/kg/day, PO to 14 weeks.	
Reporting group title	Fast Switching Group
Reporting group description:	
Switch from full stimulant dose to atomoxetine 1.2mg/kg/day, PO, without stimulants during the first 2 weeks. Continue atomoxetine 1.2 mg/kg/day to 10 weeks, followed by atomoxetine up to 1.8 mg/kg/day to 14 weeks.	
Reporting group title	Slow Switching Group
Reporting group description:	
Switch from full stimulant dose to atomoxetine 1.2 milligrams per kilogram per day (mg/kg/day) without stimulants, orally (PO), during 10 weeks then continue treatment up to 1.8mg/kg/day, PO to 14 weeks.	
Reporting group title	Fast Switching Group
Reporting group description:	
Switch from full stimulant dose to atomoxetine 1.2mg/kg/day, PO, without stimulants during 2 weeks. Continue atomoxetine 1.2 mg/kg/day to 10 weeks, followed by atomoxetine up to 1.8 mg/kg/day to 14 weeks.	

Primary: Change From Baseline in Attention Deficit Hyperactivity Disorder-Rating Scale (ADHD-RS-IV) Parent Version: Investigator Administered and Scored - Total Score at Week 10 Endpoint

End point title	Change From Baseline in Attention Deficit Hyperactivity Disorder-Rating Scale (ADHD-RS-IV) Parent Version: Investigator Administered and Scored - Total Score at Week 10 Endpoint

End point description:

Measures the 18 symptoms contained in the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition, Text Revision (DSM-IV-TR) diagnosis of Attention-Deficit/Hyperactivity Disorder (ADHD). Individual item scores range from 0 (none/never or rarely) to 3 (severe/very often). Total scores range from 0 to 54. Higher score indicates greater severity of disease. Least squares means are adjusted for baseline, site, treatment, visit and treatment by visit interaction.

Analysis Population Description (APD): Intention to treat (ITT) population includes all randomized participants who received at least 1 dose of study drug, that is, they have a non-missing dose for atomoxetine study treatment.

End point type	Primary
End point timeframe:	
Baseline, 10 weeks	

End point values	Slow Switching Group	Fast Switching Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	54		
Units: units on a scale				
arithmetic mean (standard deviation)	-14.3 (± 1.2)	-15.0 (± 1.2)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Slow Switching Group v Fast Switching Group
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.692
Method	Mixed models analysis
Parameter estimate	Least square mean differences at week 10
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	2.6
Variability estimate	Standard error of the mean
Dispersion value	1.7

Notes:

[1] - Superiority or Other (legacy)

Primary: Change From Baseline in ADHD-RS-IV Parent Version: Investigator Administered and Scored - Total Score at Week 2 Endpoint

End point title	Change From Baseline in ADHD-RS-IV Parent Version: Investigator Administered and Scored - Total Score at Week 2 Endpoint

End point description:

Measures the 18 symptoms contained in the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition, Text Revision (DSM-IV-TR) diagnosis of ADHD. Individual item scores range from 0 (none/never or rarely) to 3 (severe/very often). Total scores range from 0 to 54. Higher score indicates greater severity of disease. Least squares means are adjusted for baseline, site, treatment, visit and treatment by visit interaction.

APD:Intention to treat (ITT) population includes all randomized participants who received at least 1 dose of study drug, that is, they have a non-missing dose for atomoxetine study treatment.

End point type	Primary

End point timeframe:

Baseline, 2 weeks

End point values	Slow Switching Group	Fast Switching Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	54		
Units: Units on scale				
arithmetic mean (standard error)	-8.0 (± 1.0)	-8.1 (± 1.0)		

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Slow Switching Group v Fast Switching Group
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.927
Method	Mixed models analysis
Parameter estimate	Least square mean differences at week 2
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	2.6
Variability estimate	Standard error of the mean
Dispersion value	1.4

Notes:

[2] - Superiority or Other (legacy)

Secondary: Change From Baseline in Global Impression of Perceived Difficulties (GIPD) Rating Scale - Patient Total Score at Week 10 Endpoint

End point title	Change From Baseline in Global Impression of Perceived Difficulties (GIPD) Rating Scale - Patient Total Score at Week 10 Endpoint

End point description:

The GIPD scale is a 5-item rating of ADHD-related difficulties (overall difficulties perceived in the morning, during school, during homework, in the evening, and over the entire day and night). For each item, difficulties during the past week are rated on a 7-point scale (1 = normal, not difficult at all; 7 = extremely difficult) and the mean of the 5 items is reported. Least square means are adjusted for baseline, site, treatment, visit and treatment by visit interaction.

APD: Intention to treat (ITT) population includes all randomized participants who received at least 1 dose of study drug, that is, they have a non-missing dose for atomoxetine study treatment.

End point type	Secondary

End point timeframe:

Baseline, 10 weeks

End point values	Slow Switching Group	Fast Switching Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	54		
Units: Units on scale				
least squares mean (standard error)	-0.6 (± 0.2)	-0.4 (± 0.2)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Slow Switching Group v Fast Switching Group
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.456
Method	Mixed models analysis
Parameter estimate	Least square mean differences at week 10
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.7
Variability estimate	Standard error of the mean

Notes:

[3] - Superiority or Other (legacy)

Secondary: Change From Baseline in Global Impression of Perceived Difficulties (GIPD) Rating Scale- Parent Total Score at Week 10 Endpoint

End point title	Change From Baseline in Global Impression of Perceived Difficulties (GIPD) Rating Scale- Parent Total Score at Week 10 Endpoint

End point description:

The GIPD scale is a 5-item rating of ADHD-related difficulties (overall difficulties perceived in the morning, during school, during homework, in the evening, and over the entire day and night). For each item, difficulties during the past week are rated on a 7-point scale (1 = normal, not difficult at all; 7 = extremely difficult) and the mean of the 5 items is reported. Least square means are adjusted for baseline, site, treatment, visit and treatment by visit interaction.

APD: Intention to treat (ITT) population includes all randomized participants who received at least 1 dose of study drug, that is, they have a non-missing dose for atomoxetine study treatment.

End point type	Secondary

End point timeframe:

Baseline, 10 weeks

End point values	Slow Switching Group	Fast Switching Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	54		
Units: Units on a scale				
least squares mean (standard error)	-1.0 (± 0.2)	-0.8 (± 0.2)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Slow Switching Group v Fast Switching Group
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.517
Method	Mixed models analysis
Parameter estimate	Least square mean differences at week 10
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[4] - Superiority or Other (legacy)

Secondary: Change From Baseline in Global Impression of Perceived Difficulties (GIPD) Rating Scale- Investigator Total Score at Week 10 Endpoint

End point title	Change From Baseline in Global Impression of Perceived Difficulties (GIPD) Rating Scale- Investigator Total Score at Week 10 Endpoint

End point description:

The GIPD scale is a 5-item rating of ADHD-related difficulties (overall difficulties perceived in the morning, during school, during homework, in the evening, and over the entire day and night). For each item, difficulties during the past week are rated on a 7-point scale (1 = normal, not difficult at all; 7 = extremely difficult) and the mean of the 5 items is reported. Least square means are adjusted for baseline, site, treatment, visit and treatment by visit interaction.

APD: Intention to treat (ITT) population includes all randomized participants who received at least 1 dose of study drug, that is, they have a non-missing dose for atomoxetine study treatment.

End point type	Secondary

End point timeframe:

Baseline, 10 weeks

End point values	Slow Switching Group	Fast Switching Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	54		
Units: Units on a scale				
least squares mean (standard error)	-1.3 (± 0.2)	-1.2 (± 0.2)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Slow Switching Group v Fast Switching Group
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.526
Method	Mixed models analysis
Parameter estimate	Least square mean differences at week 10
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[5] - Superiority or Other (legacy)

Secondary: Change From Baseline in Clinical Global Impression Severity (CGI-S) Rating Scale - Total Score at Week 10 Endpoint

End point title	Change From Baseline in Clinical Global Impression Severity (CGI-S) Rating Scale - Total Score at Week 10 Endpoint

End point description:

The CGI- S is a single-item clinician rating of the severity of the participant's ADHD symptoms in relation to the clinician's total experience of ADHD participants. Severity is rated on a seven-point scale (1 = normal, not ill at all; 7 = among the most extremely ill patients). Least square means are adjusted for baseline, site, treatment, visit and treatment by visit interaction.

APD: Intention to treat (ITT) population includes all randomized participants who received at least 1 dose of study drug, that is, they have a non-missing dose for atomoxetine study treatment.

End point type	Secondary

End point timeframe:

Baseline, 10 weeks

End point values	Slow Switching Group	Fast Switching Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	54		
Units: Units on a scale				
least squares mean (standard error)	-1.7 (± 0.26)	-1.7 (± 0.2)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Fast Switching Group v Slow Switching Group
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 0.898
Method	Mixed models analysis
Parameter estimate	Least square mean differences at week 10
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[6] - Superiority or Other (legacy)

Secondary: Change From Baseline in Child Health and Illness Profile Child Edition-Parent Report Form (CHIP-CE-PRF) - Domain Scores at Week 10 Endpoint

End point title	Change From Baseline in Child Health and Illness Profile Child Edition-Parent Report Form (CHIP-CE-PRF) - Domain Scores at Week 10 Endpoint

End point description:

CHIP-CE-PRF consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format. Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation (SD) of 10. Standard scores are expressed in SD units. T-score=[(Score- Mean for the reference population [Ref Pop])*10/SD for the Ref Pop]+50. Higher scores mean better quality of life. Least square means are adjusted for baseline, site, treatment, visit and treatment by visit interaction.

APD: Intention to treat (ITT) population includes all randomized participants who received at least 1 dose of study drug, that is, they have a non-missing dose for atomoxetine study treatment.

End point type	Secondary

End point timeframe:

Baseline, 10 weeks

End point values	Slow Switching Group	Fast Switching Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	54		
Units: standard deviation units				
arithmetic mean (standard error)				
Satisfaction Domain	3.4 (± 1.6)	2.2 (± 1.6)		
Comfort Domain	0.7 (± 1.2)	4.1 (± 1.1)		
Risk Avoidance Domain	4.9 (± 1.4)	2.9 (± 1.4)		
Resilience Domain	1.8 (± 1.4)	-1.0 (± 1.4)		
Achievement Domain	3.5 (± 1.7)	-1.2 (± 1.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Treatment Satisfaction Preference Survey Mean Score at Week 10 Endpoint

End point title	Change From Baseline in Treatment Satisfaction Preference Survey Mean Score at Week 10 Endpoint

End point description:

The Treatment Satisfaction Survey consists of a five-question survey each rated on a 5 point scale (0=very satisfied/very likely, 4=very dissatisfied/not at all likely). The mean score over the items is reported.

APD: Intention to treat (ITT) population includes all randomized participants who received at least 1 dose of study drug, that is, they have a non-missing dose for atomoxetine study treatment. Last Observation Carried Forward (LOCF).

End point type	Secondary

End point timeframe:

Baseline, 10 weeks

End point values	Slow Switching Group	Fast Switching Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	53		
Units: units on a scale				
arithmetic mean (standard deviation)	-0.7 (± 1.16)	-0.5 (± 1.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Blood Pressure (BP) at Week 6 and Week 14 Endpoint

End point title	Change From Baseline in Blood Pressure (BP) at Week 6 and Week 14 Endpoint

End point description:

APD: Intention to treat (ITT) population includes all randomized participants who received at least 1 dose of study drug, that is, they have a non-missing dose for atomoxetine study treatment, and with both baseline and week 6 or 14 values.

End point type	Secondary

End point timeframe:

Baseline, 6 weeks, 14 weeks

End point values	Slow Switching Group	Fast Switching Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	54		
Units: mmHg				
arithmetic mean (standard deviation)				
Week 6 Change Diastolic BP (n=52, 52)	1.5 (± 7.21)	1.9 (± 8.31)		
Week 6 Change Systolic BP (n=52, 52)	1.2 (± 7.74)	0.5 (± 9.05)		
Week 14 Change Diastolic BP (n=43, 40)	2.3 (± 7.58)	3.1 (± 7.04)		
Week 14 Change Systolic BP (n= 43, 40)	-0.2 (± 8.62)	2.6 (± 9.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pulse Rate at Week 6 and Week 14 Endpoint

End point title	Change From Baseline in Pulse Rate at Week 6 and Week 14 Endpoint

End point description:

APD: Intention to treat (ITT) population includes all randomized participants who received at least 1 dose of study drug, that is, they have a non-missing dose for atomoxetine study treatment, and with both baseline and week 6 or 14 values.

End point type	Secondary

End point timeframe:

Baseline, 6 weeks, 14 weeks

End point values	Slow Switching Group	Fast Switching Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	54		
Units: beats per minute				
arithmetic mean (standard deviation)				
Week 6 Change (n=52, 52)	6.8 (± 11.12)	4.2 (± 8.83)		
Week 14 Change (n=43, 40)	3.4 (± 12.69)	5.9 (± 10.17)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Weight at Week 6 and Week 14 Endpoint

End point title	Change From Baseline in Body Weight at Week 6 and Week 14 Endpoint
End point description:	
APD: Intention to treat (ITT) population includes all randomized participants who received at least 1 dose of study drug, that is, they have a non-missing dose for atomoxetine study treatment, and with both baseline and week 6 or 14 values.	
End point type	Secondary
End point timeframe:	
Baseline, 6 weeks, 14 weeks	

End point values	Slow Switching Group	Fast Switching Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	54		
Units: kilogram(s)				
arithmetic mean (standard deviation)				
Week 6 Change (n=52, 52)	-0.4 (± 1.12)	0.6 (± 1.25)		
Week 14 Change (n=43, 40)	0.6 (± 1.64)	1.1 (± 2.15)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Suicidal Behaviors and Ideations

End point title	Number of Participants With Suicidal Behaviors and Ideations
End point description:	

Columbia Suicide Rating Scale (C-SSRS): scale capturing occurrence, severity, and frequency of suicide-related thoughts and behaviors. Number of participants with suicidal behaviors and ideations are provided. Suicidal behavior: a "yes" answer to any of 5 suicidal behavior questions: preparatory acts or behavior, aborted attempt, interrupted attempt, actual attempt, and completed suicide. Suicidal ideation: a "yes" answer to any one of 5 suicidal ideation questions, which includes wish to be dead, and 4 different categories of active suicidal ideation.

APD: Intention to treat (ITT) population includes all randomized participants who received at least 1 dose of study drug, that is, they have a non-missing dose for atomoxetine study treatment.

End point type	Secondary
End point timeframe:	
Baseline through 14 weeks	

End point values	Slow Switching Group	Fast Switching Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	54		
Units: Subjects				
number (not applicable)	1	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Entire Study

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups

Reporting group title	Slow Switching Group

Reporting group description:

Switch from full stimulant dose to atomoxetine 1.2mg/kg/day, PO, during 10 weeks then continue treatment up to 1.8mg/kg/day, PO to 14 weeks.

Reporting group title	Fast Switching Group

Reporting group description:

Switch from full stimulant dose to atomoxetine 1.2mg/kg/day, PO, during 2 weeks. Continue atomoxetine 1.2 mg/kg/day to 10 weeks, followed by atomoxetine up to 1.8 mg/kg/day to 14 weeks.

Serious adverse events	Slow Switching Group	Fast Switching Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 57 (1.75%)	1 / 54 (1.85%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
VIth nerve paralysis			
subjects affected / exposed	1 / 57 (1.75%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 57 (1.75%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide Attempt			
subjects affected / exposed	0 / 57 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Slow Switching Group	Fast Switching Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 57 (61.40%)	30 / 54 (55.56%)	
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 57 (19.30%)	12 / 54 (22.22%)	
occurrences (all)	16	19	
Somnolence			
subjects affected / exposed	4 / 57 (7.02%)	9 / 54 (16.67%)	
occurrences (all)	4	9	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 57 (5.26%)	4 / 54 (7.41%)	
occurrences (all)	3	4	
Irritability			
subjects affected / exposed	4 / 57 (7.02%)	3 / 54 (5.56%)	
occurrences (all)	5	3	
Pyrexia			
subjects affected / exposed	4 / 57 (7.02%)	2 / 54 (3.70%)	
occurrences (all)	4	3	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	3 / 57 (5.26%)	6 / 54 (11.11%)	
occurrences (all)	3	13	
Abdominal Pain Upper			
subjects affected / exposed	8 / 57 (14.04%)	5 / 54 (9.26%)	
occurrences (all)	11	5	
Nausea			
subjects affected / exposed	4 / 57 (7.02%)	0 / 54 (0.00%)	
occurrences (all)	4	0	
Vomiting			
subjects affected / exposed	1 / 57 (1.75%)	5 / 54 (9.26%)	
occurrences (all)	1	6	
Respiratory, thoracic and mediastinal			

disorders			
Cough			
subjects affected / exposed	3 / 57 (5.26%)	1 / 54 (1.85%)	
occurrences (all)	4	2	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 57 (1.75%)	3 / 54 (5.56%)	
occurrences (all)	1	3	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 57 (12.28%)	3 / 54 (5.56%)	
occurrences (all)	8	3	
Upper respiratory tract infection			
subjects affected / exposed	3 / 57 (5.26%)	0 / 54 (0.00%)	
occurrences (all)	3	0	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	11 / 57 (19.30%)	12 / 54 (22.22%)	
occurrences (all)	12	19	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 November 2008	Changes to exclusion criteria.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported