Clinical trial results:
Evaluation of Academic Performance in Asian Children Aged 8 to 11 Years With Attention-Deficit/Hyperactivity Disorder Treated With Atomoxetine Hydrochloride

Summary

EudraCT number	2017-000740-18
Trial protocol	Outside EU/EEA
Global end of trial date	01 November 2008

Results information

Result version number	v1 (current)
This version publication date	22 December 2021
First version publication date	22 December 2021

Trial information

Trial identification

Sponsor protocol code	B4Z-CR-S018

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00471354
WHO universal trial number (UTN)	-
Other trial identifiers	Trial ID: 11098

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 8772854559,
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	01 April 2007
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 November 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of the study is to investigate the relationship of changes in measures of academic performance and problem behaviors, to changes in core Attention-Deficit/Hyperactivity Disorder (ADHD) symptoms in Asian children treated with atomoxetine.

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	01 April 2007
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	Taiwan: 76
Country: Number of subjects enrolled	China: 82
Country: Number of subjects enrolled	Korea, Republic of: 70
Worldwide total number of subjects	228
EEA total number of subjects	0

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)	228
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

No text entered

Pre-assignment

Screening details:

No text entered

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Atomoxetine

Arm description:

0.5 mg/kg/day once a day (QD), by mouth (PO), starting dose titrated over 1 week to target dose 1.2 mg/kg/day QD, PO for 23 weeks.

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

Dosage and administration details:

Atomoxetine 0.5 mg/kg/day once a day (QD), by mouth (PO) starting dose titrated over 1 week to target dose 1.2 mg/kg/day QD, PO for 23 weeks.

Number of subjects in period 1	Atomoxetine
Started	228
Completed	176
Not completed	52
Patient/Caregiver Decision	12
Consent withdrawn by subject	1
Physician decision	4
Adverse event, non-fatal	13
Sponsor Decision	1
Lost to follow-up	3
Protocol Entry Criteria Not Met	1
Protocol deviation	12
Lack of efficacy	5

Baseline characteristics

Reporting groups	
Reporting group title	Atomoxetine
Reporting group description:	
0.5 mg/kg/day once a day (QD), by mouth (PO), starting dose titrated over 1 week to target dose 1.2 mg/kg/day QD, PO for 23 weeks.	

Reporting group values	Atomoxetine	Total	
Number of subjects	228	228	
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	9.6		
standard deviation	± 0.96	-	
Gender categorical Units: Subjects			
Female	34	34	
Male	194	194	
Race/Ethnicity Units: Subjects			
East Asian	228	228	
Region of Enrollment Units: Subjects			
Taiwan	76	76	
China	82	82	
Korea, Republic of	70	70	

End points

End points reporting groups

Reporting group title	Atomoxetine

Reporting group description:

0.5 mg/kg/day once a day (QD), by mouth (PO), starting dose titrated over 1 week to target dose 1.2 mg/kg/day QD, PO for 23 weeks.

Primary: Correlation Between Change From Baseline and 24 Week Endpoint in Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Parent:Investigator-Administered and Scored (ADHDRS-IV-Parent:Inv) Total Score and School Grade Average (SGA)

End point title	Correlation Between Change From Baseline and 24 Week Endpoint in Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Parent:Investigator-Administered and Scored (ADHDRS-IV-Parent:Inv) Total Score and School Grade Average (SGA)[1]

End point description:

Correlation was calculated between change from baseline and endpoint in ADHD-RS Total Score and change in SGA total score. ADHD-RS measures 18 symptoms associated with 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. SGA: Grades (0 to 100) in classes of Language, Math, and Science were obtained and average taken to get SGA Total Score between 0 and 100; higher scores indicating better grades/apptitude. Any ordinal grades were imputed to numerical grades based on communication with relevant schools.
Analysis Population Description (APD): All patients with baseline and at least one non-missing post-baseline score for each of the variables, regardless of them having or not having received any ordinal grades (for the SGA).

End point type	Primary

End point timeframe:

Baseline, 24 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: No statistical analysis planned for this outcome.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	164			
Units: Spearman Correlation Coefficient				
number (not applicable)	-0.083			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation Between Change From Baseline to 24 Week Endpoint in ADHDRS-IV-Parent:Inv Total Score and School Grade Averages in Separate Language, Math and Science Classes

End point title	Correlation Between Change From Baseline to 24 Week Endpoint in ADHDRS-IV-Parent:Inv Total Score and School Grade Averages in Separate Language, Math and Science Classes

End point description:

Correlation was calculated between change from baseline and endpoint in ADHD-RS Total Score and change in separate SGA language, math, and science scores. ADHD-RS measures 18 symptoms associated with 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. SGA: separate language, math, and science school grades on a scale of 0-100, with higher scores indicating better grades/apptitude in the respective class. Any ordinal grades were imputed to numerical grades based on communication with relevant schools. APD: All patients with baseline and at least one non-missing post-baseline score for each of the variables, regardless of them having or not having received any ordinal grades (for the SGA).

End point type	Secondary

End point timeframe:

Baseline, 24 weeks

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	164			
Units: Spearman Correlation Coefficient				
number (not applicable)				
Correlation with Language Scores	-0.086			
Correlation with Math Scores	-0.126			
Correlation with Science Scores	-0.058			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to 24 Week Endpoint in Academic Performance by School Grade Average (SGA) Total, and Separate Language, Math, and Science Scores

End point title	Change From Baseline to 24 Week Endpoint in Academic Performance by School Grade Average (SGA) Total, and Separate Language, Math, and Science Scores

End point description:

Separate school grades in the classes of Language, Math, and Science were obtained. A score between 0 and 100 was provided for each of the three classes, and the average taken to get a SGA Total Score between 0 and 100, with higher scores indicating better grades/apptitude in each class and overall. Any ordinal grades were imputed to numerical grades based on communication with relevant schools.

End point type	Secondary

End point timeframe:

Baseline, 24 weeks

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	177			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change from Baseline in Language Scores	3.9 (± 13.35)			
Change from Baseline in Math Scores	4.1 (± 16.58)			
Change from Baseline in Science Scores	6.1 (± 14.98)			
Change from Baseline in Total Scores	4.7 (± 10.68)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to 24 Week Endpoint in Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Parent Version:Investigator-Administered and Scored - Total Score

End point title	Change From Baseline to 24 Week Endpoint in Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Parent Version:Investigator-Administered and Scored - Total Score

End point description:

Measures the 18 symptoms contained in the DSM-IV diagnosis of Attention-Deficit/Hyperactivity Disorder. Individual item scores range from 0 (none/never or rarely) to 3 (severe/very often). Total scores range from 0 to 54.
APD: All patients with baseline and at least one non-missing post-baseline score for each of the variables. Last observation carried forward.

End point type	Secondary

End point timeframe:

Baseline, 24 weeks

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	205			
Units: units on a scale				
arithmetic mean (standard deviation)	-18.8 (± 9.27)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to 24 Week Endpoint in Clinical Global Impressions - Attention-Deficit/Hyperactivity Disorder - Severity Scale (CGI-ADHD-S)

End point title	Change From Baseline to 24 Week Endpoint in Clinical Global

	Impressions - Attention-Deficit/Hyperactivity Disorder - Severity Scale (CGI-ADHD-S)

End point description:

Measures severity of the patient's overall severity of ADHD symptoms (1=normal, not at all ill; 7=among the most extremely ill patients).

End point type	Secondary

End point timeframe:

Baseline, 24 weeks

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	228			
Units: units on a scale				
geometric mean (standard deviation)	-2.1 (± 1.25)			

Statistical analyses

No statistical analyses for this end point

Secondary: CGI-ADHD-Improvement Scale (CGI-ADHD-I) at 24 Week Endpoint

End point title	CGI-ADHD-Improvement Scale (CGI-ADHD-I) at 24 Week Endpoint

End point description:

Measures total improvement (or worsening) of a patient's ADHD symptoms from the beginning of treatment (1=very much improved, 7=very much worsened).

End point type	Secondary

End point timeframe:

24 weeks

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	228			
Units: units on a scale				
arithmetic mean (standard deviation)	2.3 (± 1.05)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to 24 Week Endpoint in Revised Conners' Parent Rating Scale: Short Form (CPRS-R:S) Attention-Deficit/Hyperactivity Disorder Index Score

End point title	Change From Baseline to 24 Week Endpoint in Revised Conners' Parent Rating Scale: Short Form (CPRS-R:S) Attention-Deficit/Hyperactivity Disorder Index Score

End point description:

A 27-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the parent to assess problem behaviors related to ADHD. Subscale assessed: ADHD Index. ADHD Index is the sum of items 1, 5, 7, 10, 13, 15, 17, 19, 21, 23, 25, and 27. Subscale total scores range from 0 to 36. Higher scores reflect more severe problem behaviors related to ADHD.

End point type	Secondary

End point timeframe:

Baseline, 24 weeks

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	204			
Units: units on a scale				
arithmetic mean (standard deviation)	-9.8 (± 7.94)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Entire Study	
Adverse event reporting additional description:	
B4Z-CR-S018	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups	
Reporting group title	Atomoxetine

Reporting group description: -

Serious adverse events	Atomoxetine		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 228 (0.44%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Endocrine disorders			
hyperthyroidism			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Atomoxetine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	175 / 228 (76.75%)		
Investigations			
weight decreased			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	16 / 228 (7.02%)		
occurrences (all)	19		
Nervous system disorders			

dizziness			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	31 / 228 (13.60%)		
occurrences (all)	36		
headache			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	29 / 228 (12.72%)		
occurrences (all)	33		
somnolence			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	46 / 228 (20.18%)		
occurrences (all)	54		
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	25 / 228 (10.96%)		
occurrences (all)	28		
irritability			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	20 / 228 (8.77%)		
occurrences (all)	24		
Gastrointestinal disorders			
abdominal pain upper			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	15 / 228 (6.58%)		
occurrences (all)	16		
nausea			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	49 / 228 (21.49%)		
occurrences (all)	57		
vomiting			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	26 / 228 (11.40%)		
occurrences (all)	32		
Infections and infestations			

nasopharyngitis alternative dictionary used: MedDRA 11.0 subjects affected / exposed occurrences (all)	15 / 228 (6.58%) 15		
Metabolism and nutrition disorders anorexia alternative dictionary used: MedDRA 11.0 subjects affected / exposed occurrences (all)	55 / 228 (24.12%) 61		
decreased appetite alternative dictionary used: MedDRA 11.0 subjects affected / exposed occurrences (all)	74 / 228 (32.46%) 91		

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