Clinical trial results:
Assessing the Effect of Missing Doses (Off-Days) of Daily Medication in Patients Stable on Pharmacotherapy for ADHD Receiving Atomoxetine or OROS Methylphenidate: A Parallel Matched Group Clinical Study (On/Off Study)

Summary

EudraCT number	2009-011426-33
Trial protocol	ES NL SE
Global end of trial date	03 May 2011

Results information

Result version number	v1 (current)
This version publication date	10 June 2018
First version publication date	10 June 2018

Trial information

Trial identification

Sponsor protocol code	B4Z-EW-LYEN

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01127646
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 13070

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	03 May 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 May 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of the study is to help to understand the effect on children and adolescents who are stable on treatment with atomoxetine or osmotic-release oral system (OROS) methylphenidate for attention-deficit/hyperactivity disorder (ADHD) of not taking the medication for a maximum of 6 days over a 28-day study treatment period.

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	22 June 2010
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	Netherlands: 1
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	Sweden: 2
Worldwide total number of subjects	23
EEA total number of subjects	23

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)	14
Adolescents (12-17 years)	9
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Not Applicable

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Atomoxetine

Arm description:

Participants received 25-80 milligrams (mg) of atomoxetine orally, once daily for 4 weeks (on/off period), except for the off-days, where participants received 1 or 2 oral once daily placebo doses per week, with 6 nonconsecutive, double-blinded placebo doses in total over the 4-week on/off period.

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

Dosage and administration details:

Participants received 25-80 milligrams (mg) of atomoxetine orally, once daily for 4 weeks (on/off period), except for the off-days, where participants received 1 or 2 oral once daily placebo doses per week, with 6 nonconsecutive, double-blinded placebo doses in total over the 4-week on/off period.

Arm title	Osmotic-Release Oral System (OROS) Methylphenidate

Arm description:

Participants received 18-54 mg of OROS methylphenidate orally, once daily for 4 weeks (on/off period), except for the off-days, where participants received 1 or 2 oral once daily placebo doses per week, with 6 nonconsecutive, double-blinded placebo doses in total over the 4-week on/off period.

Arm type	Active comparator
Investigational medicinal product name	Osmotic-Release Oral System (OROS) Methylphenidate
Investigational medicinal product code	
Other name	Concerta
Pharmaceutical forms	Prolonged-release tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 18-54 mg of OROS methylphenidate orally, once daily for 4 weeks (on/off period), except for the off-days, where participants received 1 or 2 oral once daily placebo doses per week, with 6 nonconsecutive, double-blinded placebo doses in total over the 4-week on/off period.

Number of subjects in period 1	Atomoxetine	Osmotic-Release Oral System (OROS) Methylphenidate
Started	15	8
Completed	14	7
Not completed	1	1
Entry Criteria Not Met	1	-
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Atomoxetine
Reporting group description:	
Participants received 25-80 milligrams (mg) of atomoxetine orally, once daily for 4 weeks (on/off period), except for the off-days, where participants received 1 or 2 oral once daily placebo doses per week, with 6 nonconsecutive, double-blinded placebo doses in total over the 4-week on/off period.	
Reporting group title	Osmotic-Release Oral System (OROS) Methylphenidate
Reporting group description:	
Participants received 18-54 mg of OROS methylphenidate orally, once daily for 4 weeks (on/off period), except for the off-days, where participants received 1 or 2 oral once daily placebo doses per week, with 6 nonconsecutive, double-blinded placebo doses in total over the 4-week on/off period.	

Reporting group values	Atomoxetine	Osmotic-Release Oral System (OROS) Methylphenidate	Total
Number of subjects	15	8	23
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	10.8	10.9	
standard deviation	± 2.65	± 2.80	-
Gender, Male/Female Units: Participants			
Female	3	2	5
Male	12	6	18
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	15	7	22
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
Netherlands	1	0	1
Spain	12	8	20
Sweden	2	0	2
Attention-Deficit/Hyperactivity Disorder (ADHD) Subtype: Current Episode Units: Subjects			
Combined	7	4	11
Hyperactive/Impulsive	0	1	1
Inattentive	1	0	1
Subtype not present	6	3	9

Missing	1	0	1
Attention-Deficit/Hyperactivity Disorder (ADHD) Subtype: Lifetime Episode			
Lifetime episode refers to the most severe episode in the past.			
Units: Subjects			
Combined	8	7	15
Hyperactive/Impulsive	0	1	1
Inattentive	5	0	5
Subtype not present	1	0	1
Missing	1	0	1

End points

End points reporting groups

Reporting group title	Atomoxetine

Reporting group description:

Participants received 25-80 milligrams (mg) of atomoxetine orally, once daily for 4 weeks (on/off period), except for the off-days, where participants received 1 or 2 oral once daily placebo doses per week, with 6 nonconsecutive, double-blinded placebo doses in total over the 4-week on/off period.

Reporting group title	Osmotic-Release Oral System (OROS) Methylphenidate

Reporting group description:

Participants received 18-54 mg of OROS methylphenidate orally, once daily for 4 weeks (on/off period), except for the off-days, where participants received 1 or 2 oral once daily placebo doses per week, with 6 nonconsecutive, double-blinded placebo doses in total over the 4-week on/off period.

Primary: Daily Parent Report of Evening and Morning Behavior-Revised (DPREMB-R) Scale Mean Total Score (On-Days versus Off-Days) During the 4-Week Treatment Period

End point title	Daily Parent Report of Evening and Morning Behavior-Revised (DPREMB-R) Scale Mean Total Score (On-Days versus Off-Days) During the 4-Week Treatment Period[1]

End point description:

Parent-completed 11-item questionnaire; measures difficulty level of and 8 common evening behaviors (such as, sit through dinner) and 3 common morning behaviors (such as, get out of bed). Each item is scored on a 4-point Likert scale ranging from 0 (no difficulty) to 3 (a lot of difficulty). Total score (evening+morning) range is 0 to 33. Higher scores indicate greater difficulty in evening and morning behavior. DPREMB-R total score between days without missing doses (on-days) and days with missing doses (off-days) was not analyzed due to the insufficient sample size.
Analysis Population Description: No participants had data analyzed due to the termination of the trial and the insufficient sample size.

End point type	Primary

End point timeframe:

Baseline through 4 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: Zero participants were analyzed due to trial termination. Therefore, no inferential statistics were planned or conducted for this endpoint.

End point values	Atomoxetine	Osmotic-Release Oral System (OROS) Methylphenidate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: Not Applicable (NA)				

Notes:

[2] - Zero participants were analyzed due to trial termination.

[3] - Zero participants were analyzed due to trial termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Global Impression of Perceived Difficulties (GIPD) Scale-Patient Version Total Score and Individual Items (On-Days Versus Off-Days) During the 4-Week Treatment Period

End point title	Global Impression of Perceived Difficulties (GIPD) Scale-Patient Version Total Score and Individual Items (On-Days Versus Off-Days) During the 4-Week Treatment Period

End point description:

Assesses attention-deficit/hyperactivity disorder (ADHD)-related difficulties (overall difficulties perceived in morning, during school, during homework, in evening, over entire day and night). Participant rates difficulties during past week on 7-point scale (1=normal, not difficult at all; 7=extremely difficult) for each of 5 items. Total score=sum of all subscores (items); range: 5 to 35. Higher scores=greater impairment. GIPD-Pat total score and item scores between days without missing doses (on-days) and days with missing doses (off-days) were not analyzed due to insufficient sample size.
Analysis Population Description: No data displayed because Outcome Measure has zero total participants analyzed.

End point type	Secondary

End point timeframe:

Baseline through 4 weeks

End point values	Atomoxetine	Osmotic-Release Oral System (OROS) Methylphenidate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: Not Applicable (NA)				

Notes:

[4] - Zero participants were analyzed due to trial termination.

[5] - Zero participants were analyzed due to trial termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Conners' Global Index-Teacher Rating Scale Total Score (On-Days Versus Off-Days) During the 4-Week Treatment Period

End point title	Conners' Global Index-Teacher Rating Scale Total Score (On-Days Versus Off-Days) During the 4-Week Treatment Period

End point description:

The teacher version of Conners' Global Index consists of 10 items with each item being scored on a 4-point scale ranging from 0 (not true at all, or never/seldom) to 3 (very much true, or very often/very frequent). The total score ranges from 0 to 30. Higher scores indicate greater impairment. The Conner's Global Index-Teacher Rating Scale total score between days without missing doses (on-days) and days with missing doses (off-days) was not analyzed due to the insufficient sample size.
Analysis Population Description: No participants had data analyzed due to the termination of the trial and the insufficient sample size.

End point type	Secondary

End point timeframe:

Baseline through 4 weeks

End point values	Atomoxetine	Osmotic-Release Oral System (OROS) Methylphenidate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: Not Applicable (NA)				

Notes:

[6] - Zero participants were analyzed due to trial termination.

[7] - Zero participants were analyzed due to trial termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Global Impression of Perceived Difficulties Scale-Patient Version (GIPD-Pat) Scale Total Score and Individual Items during the 4-Week Treatment Period

End point title	Global Impression of Perceived Difficulties Scale-Patient Version (GIPD-Pat) Scale Total Score and Individual Items during the 4-Week Treatment Period

End point description:

Assesses attention-deficit/hyperactivity disorder (ADHD)-related difficulties (overall difficulties perceived in morning, during school, during homework, in evening, over entire day and night). Difficulties during past week are rated by participant on a 7-point scale (1=normal, not difficult at all; 7=extremely difficult) for each of 5 items. Total score=sum of all subscores (items); range: 5 to 35. Higher scores=greater impairment. Mean GIPD-Pat total score and individual item scores for days with missing doses (off-days) between both groups were not analyzed due to insufficient sample size.
Analysis Population Description: No participants had data analyzed due to the termination of the trial and the insufficient sample size.

End point type	Secondary

End point timeframe:

Baseline through 4 weeks

End point values	Atomoxetine	Osmotic-Release Oral System (OROS) Methylphenidate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: Not Applicable (NA)				

Notes:

[8] - Zero participants were analyzed due to trial termination.

[9] - Zero participants were analyzed due to trial termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Attention-Deficit/Hyperactivity Disorder Rating Scale-Parent Version: Investigator Administered and Scored (ADHD-RS-IV Parent:Inv) Total Score and Subscores at Weeks 2, 3, and 4

End point title	Attention-Deficit/Hyperactivity Disorder Rating Scale-Parent Version: Investigator Administered and Scored (ADHD-RS-IV Parent:Inv) Total Score and Subscores at Weeks 2, 3, and 4

End point description:

Assesses 18 Diagnostic and Statistical Manual of Mental Disorders Fourth Edition, Text Revision (DSM-IV-TR) ADHD diagnosis symptoms/severity in past week. Each item: 0 (none/never, rarely) to 3 (severe/very often). Total score ranges from 0 to 54. Higher total scores indicate greater illness severity. This outcome measure was not analyzed due to the insufficient sample size.
Analysis Population Description: No participants had data analyzed due to the termination of the trial and the insufficient sample size.

End point type	Secondary

End point timeframe:

Weeks 2, 3, and 4

End point values	Atomoxetine	Osmotic-Release Oral System (OROS) Methylphenidate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[10]	0[11]		
Units: Not Applicable (NA)				

Notes:

[10] - Zero participants were analyzed due to trial termination.

[11] - Zero participants were analyzed due to trial termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression-Attention Deficit/Hyperactivity Disorder-Severity Scale (CGI-ADHD-S) at Weeks 2, 3, and 4

End point title	Clinical Global Impression-Attention Deficit/Hyperactivity Disorder-Severity Scale (CGI-ADHD-S) at Weeks 2, 3, and 4

End point description:

This instrument is a single-item expert rating of the severity of the participant's attention-deficit/hyperactivity disorder (ADHD) symptoms in relation to the assessor's total experience of participants with ADHD. Severity is rated on a 7-point scale (1=normal, not ill at all; 7=among the most extremely ill participants). Higher scores represent greater illness severity. This outcome measure was not analyzed due to the insufficient sample size.
Analysis Population Description: No data displayed because Outcome Measure has zero total participants analyzed.

End point type	Secondary

End point timeframe:

Weeks 2, 3, and 4

End point values	Atomoxetine	Osmotic-Release Oral System (OROS) Methylphenidate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[12]	0[13]		
Units: Not Applicable (NA)				

Notes:

[12] - Zero participants were analyzed due to trial termination.

[13] - Zero participants were analyzed due to trial termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Emotion Expression Scale for Children (EESC)-Parent Rated Total Score up to Week 5

End point title	Emotion Expression Scale for Children (EESC)-Parent Rated Total Score up to Week 5

End point description:

29-item parent-reported measure used to monitor effect of attention-deficit/hyperactivity disorder (ADHD) medication; examines 3 aspects of emotion expression: positive emotions, emotional flatness, and emotional lability. Each item rated on 5-point Likert scale (1="not at all true" to 5="very much true"). Positive emotional subscale items reversed scored (6-raw score). Total score=transformed positive emotion + emotional flatness+ emotional lability subscales. Total scores range: 29 to 145. Higher scores=emotional impairment. This outcome measure not analyzed due to insufficient sample size.
Analysis Population Description: No participants had data analyzed due to the termination of the trial and the insufficient sample size.

End point type	Secondary

End point timeframe:

Up to Week 5

End point values	Atomoxetine	Osmotic-Release Oral System (OROS) Methylphenidate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[14]	0[15]		
Units: Not Applicable (NA)				

Notes:

[14] - Zero participants were analyzed due to trial termination.

[15] - Zero participants were analyzed due to trial termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Daily Parent Report of Evening and Morning Behavior-Revised (DPREMB-R) Scale Subscores (On-Days Versus Off-Days) During the 4-Week Treatment Period

End point title	Daily Parent Report of Evening and Morning Behavior-Revised

	(DPREMB-R) Scale Subscores (On-Days Versus Off-Days) During the 4-Week Treatment Period

End point description:

Parent-completed 11-item questionnaire; measures difficulty level of 8 common evening behaviors (such as, sit through dinner) and 3 common morning behaviors (such as, get out of bed) from 0 (no difficulty) to 3 (a lot of difficulty). Evening behavior total score range is 0 to 24. Morning behavior total score range is 0 to 9. Higher scores indicate greater difficulty in evening and morning behavior. DPREMB-R subscores between days without missing doses (on-days) and days with missing doses (off-days) not analyzed due to insufficient sample size.

End point type	Secondary

End point timeframe:

Baseline through 4 weeks

End point values	Atomoxetine	Osmotic-Release Oral System (OROS) Methylphenidate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[16]	0[17]		
Units: Not Applicable (NA)				

Notes:

[16] - Zero participants were analyzed due to trial termination.

[17] - Zero participants were analyzed due to trial termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Outcomes Questions (On-Days Versus Off-Days) During the 4-Week Treatment Period

End point title	Patient Outcomes Questions (On-Days Versus Off-Days) During the 4-Week Treatment Period

End point description:

6-item questionnaire from attention-deficit/hyperactivity disorder (ADHD) advocacy group evaluates treatment outcomes ADHD participant's perspective. Parent completed on each day of on/off period. Each item ranged from 1 ("I totally agree") to 5 ("I totally disagree"). Items 1 and 2 pertain to sleeping and eating; high scores=better outcome. Items 3-6 pertain to behavior; high scores=worse outcome. The mean scores for analysis would have been created for each question across the days of each of the on and off phases; however, mean scores were not analyzed due to insufficient sample size.
Analysis Population Description: No participants had data analyzed due to the termination of the trial and the insufficient sample size.

End point type	Secondary

End point timeframe:

Baseline through 4 weeks

End point values	Atomoxetine	Osmotic-Release Oral System (OROS) Methylphenidate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[18]	0[19]		
Units: Not Applicable (NA)				

Notes:

[18] - Zero participants were analyzed due to trial termination.

[19] - Zero participants were analyzed due to trial termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Daily Parent Report of Evening and Morning Behavior-Revised (DPREMB-R) Scale Total Score and Subscores During the 4-Week Treatment Period

End point title	Daily Parent Report of Evening and Morning Behavior-Revised (DPREMB-R) Scale Total Score and Subscores During the 4-Week Treatment Period

End point description:

Parent-completed 11-item questionnaire; measures difficulty level of 3 common morning behaviors (such as, get out of bed) and 8 common evening behaviors (such as, sit through dinner) from 0 (no difficulty) to 3 (a lot of difficulty). Evening behavior total score range is 0 to 24. Morning behavior total score range is 0 to 9. Total score (evening+morning) range is 0 to 33. Higher scores indicate greater difficulty in evening and morning behavior. Mean DPREMB-R total score and subscores for days with missing doses (off-days) between both groups were not analyzed due to insufficient sample size.
Analysis Population Description: No participants had data analyzed due to the termination of the trial and the insufficient sample size.

End point type	Secondary

End point timeframe:

Baseline through 4 weeks

End point values	Atomoxetine	Osmotic-Release Oral System (OROS) Methylphenidate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[20]	0[21]		
Units: Not Applicable (NA)				

Notes:

[20] - Zero participants were analyzed due to trial termination.

[21] - Zero participants were analyzed due to trial termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Conners' Global Index-Teacher Rating Scale Total Score During the 4-Week Treatment Period

End point title	Conners' Global Index-Teacher Rating Scale Total Score During

	the 4-Week Treatment Period

End point description:

The teacher version of Conners' Global Index consists of 10 items with each item being scored on a 4-point scale ranging from 0 (not true at all, or never/seldom) to 3 (very much true, or very often/very frequent). The total score ranges from 0 to 30. Higher scores indicate greater impairment. The Conners' Global Index-Teacher Rating Scale total score for days with missing doses (off-days) between both groups were not analyzed due to insufficient sample size.
Analysis Population Description: No participants had data analyzed due to the termination of the trial and the insufficient sample size.

End point type	Secondary

End point timeframe:

Baseline through 4 weeks

End point values	Atomoxetine	Osmotic-Release Oral System (OROS) Methylphenidate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[22]	0[23]		
Units: Not Applicable (NA)				

Notes:

[22] - Zero participants were analyzed due to trial termination.

[23] - Zero participants were analyzed due to trial termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Global Impression of Perceived Difficulties Investigator Version (GIPD-Inv) Total Score and Subscores At Weeks 2, 3, and 4

End point title	Global Impression of Perceived Difficulties Investigator Version (GIPD-Inv) Total Score and Subscores At Weeks 2, 3, and 4

End point description:

Assesses attention-deficit/hyperactivity disorder (ADHD)-related difficulties (overall difficulties perceived in morning, during school, during homework, in evening, and over entire day and night). Difficulties during past week are rated by investigator on a 7-point scale (1=normal, not difficult at all; 7=extremely difficult) for each of 5 items. Total score=sum of all subscores (items) and ranges from 5 to 35. Higher scores indicate greater impairment. This outcome measure was not analyzed due to the insufficient sample size.
Analysis Population Description: No participants had data analyzed due to the termination of the trial and the insufficient sample size.

End point type	Secondary

End point timeframe:

Weeks 2, 3, and 4

End point values	Atomoxetine	Osmotic-Release Oral System (OROS) Methylphenidate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[24]	0[25]		
Units: Not Applicable (NA)				

Notes:

[24] - Zero participants were analyzed due to trial termination.

[25] - Zero participants were analyzed due to trial termination.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline in Heart Rate up to 5 Weeks

End point title	Change from Baseline in Heart Rate up to 5 Weeks

End point description:

Analysis Population Description: Safety population: all participants who entered the study and took at least 1 dose of study medication.

End point type	Other pre-specified

End point timeframe:

Baseline, up to 5 weeks

End point values	Atomoxetine	Osmotic-Release Oral System (OROS) Methylphenidate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	8		
Units: beats per minute (bpm)				
arithmetic mean (standard deviation)	-1.2 (± 7.65)	2.5 (± 12.74)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline in Systolic and Diastolic Blood Pressure up to 5 Weeks

End point title	Change from Baseline in Systolic and Diastolic Blood Pressure up to 5 Weeks

End point description:

Analysis Population Description: Safety population: all participants who entered the study and took at least 1 dose of study medication.

End point type	Other pre-specified

End point timeframe:
Baseline, up to 5 weeks

End point values	Atomoxetine	Osmotic-Release Oral System (OROS) Methylphenidate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	7		
Units: millimeters of mercury (mm Hg)				
arithmetic mean (standard deviation)				
Diastolic Blood Pressure	1.9 (± 6.14)	-1.5 (± 4.67)		
Systolic Blood Pressure	-0.1 (± 9.00)	-3.7 (± 3.75)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected for the entire study period, which included the following: 3-14 day screening period, a run-in period of up to 7 days, a 4-week on/off period, and a 1-5 day run-out period for a maximum of 54 days.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	Osmotic-Release Oral System (OROS) Methylphenidate

Reporting group description:

Participants received 18-54 mg of OROS methylphenidate orally, once daily during the run-in period for up to 7 days. The run-in period was followed by the 4-week on/off period in which participants received 18-54 mg of OROS methylphenidate orally, once daily for 4 weeks, except for the off-days, where participants received 1 or 2 oral once daily placebo doses per week, with 6 nonconsecutive, double-blinded placebo doses in total over the 4-week on/off period. The on/off period was followed by a run-out period in which participants received 18-54 mg of OROS methylphenidate orally, once daily for 1-5 days.

Reporting group title	Atomoxetine

Reporting group description:

Participants received 25-80 milligrams (mg) of atomoxetine orally, once daily during the run-in period for up to 7 days. The run-in period was followed by the 4-week on/off period in which participants received 25-80 mg of atomoxetine orally, once daily for 4 weeks, except for the off-days, where participants received 1 or 2 oral once daily placebo doses per week, with 6 nonconsecutive, double-blinded placebo doses in total over the 4-week on/off period. The on/off period was followed by a run-out period in which participants received 25-80 mg of atomoxetine orally, once daily for 1-5 days.

Serious adverse events	Osmotic-Release Oral System (OROS) Methylphenidate	Atomoxetine	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 15 (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	Osmotic-Release Oral System (OROS) Methylphenidate	Atomoxetine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 8 (50.00%)	7 / 15 (46.67%)	
Nervous system disorders			

Disturbance in attention			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Dizziness			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 8 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Headache			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 8 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	8	
Somnolence			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	3	
General disorders and administration site conditions			
Fatigue			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Pyrexia			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 8 (12.50%)	1 / 15 (6.67%)	
occurrences (all)	1	6	
Abdominal pain upper			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Nausea			

alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 8 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	3	
Toothache			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Vomiting			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 8 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	10	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Psychiatric disorders			
Affect lability			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Impulsive behaviour			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	2 / 8 (25.00%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Insomnia			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Nervousness			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			

Pain in extremity alternative dictionary used: MedDRA 14.0 subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1	 0 / 15 (0.00%) 0	
Infections and infestations Herpes zoster alternative dictionary used: MedDRA 14.0 subjects affected / exposed occurrences (all)	 0 / 8 (0.00%) 0	 1 / 15 (6.67%) 1	
Metabolism and nutrition disorders Decreased appetite alternative dictionary used: MedDRA 14.0 subjects affected / exposed occurrences (all)	 0 / 8 (0.00%) 0	 1 / 15 (6.67%) 2	

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This study (Study LYEN) was terminated after enrolling 23 participants due to lack of availability of study participants to accommodate the study design.

Notes: