Clinical trial results:
An Open-Label Study of the Efficacy of Atomoxetine Hydrochloride on Quality of Life of Children and Adolescents with Attention-Deficit/Hyperactivity Disorder with or without comorbid conditions

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2005-005701-32
Trial protocol	IT
Global end of trial date	06 October 2008

Results information

Result version number	v2 (current)
This version publication date	24 July 2016
First version publication date	05 August 2015
Version creation reason	• Correction of full data set Correction needed to Full Data Set
Summary attachment (see zip file)	EudraCT Full Data Set Results PDF (LYDS_RR_Approval_EudraCT_16JUL2015.pdf)

Trial information

Trial identification

Sponsor protocol code	B4Z-IT-LYDS

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00320528
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 9867, Trial Alias: B4Z-IT-LYDS

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-CTLILLY,
Scientific contact	Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-285-4559,

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	06 October 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 October 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Please Note: The Agency is aware of a bug when posting the summary of the clinical trial results: the order in which the arms/reporting groups are provided may not be maintained when the results are viewed online, downloaded as a PDF or downloaded as a XML. This inconsistency may exist in other areas like subject disposition, end points, baseline characteristics etc. where the reporting groups are referenced. Please see attached results summary for correctly reported baseline characteristics data.

Main Objective: This study aims to assess the effectiveness of atomoxetine on psychosocial functioning and emotional well being of children and adolescents with Attention-Deficit/Hyperactivity Disorder (ADHD) and to evaluate whether and in what measure the presence of comorbid conditions (internalizing and externalizing disorders) influences atomoxetine's ability to improve the quality of life of ADHD subjects.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (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	29 April 2006
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	Italy: 269
Worldwide total number of subjects	269
EEA total number of subjects	269

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)	187
Adolescents (12-17 years)	82
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:

Study Period I was a 3-day screening period. Study Period II was 12 weeks long. Study Period III was an optional additional 12 week open-label extension. Results are presented for Period II (patients who received at least one dose of study drug).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Pure ADHD (Period II)

Arm description:

Attention-Deficit/Hyperactivity Disorder (ADHD) alone. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

Arm type	Experimental
Investigational medicinal product name	atomoxetine
Investigational medicinal product code	
Other name	LY139603, Strattera
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

Arm title	ADHD+Internalizing Disorders (Period II)

Arm description:

Attention-Deficit/Hyperactivity Disorder (ADHD) plus internalizing disorders. Received atomoxetine:... more 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeksless

Arm type	Experimental
Investigational medicinal product name	atomoxetine
Investigational medicinal product code	
Other name	LY139603, Strattera
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

Arm title	ADHD+Externalizing Disorders (Period II)

Arm description:

Attention-Deficit/Hyperactivity Disorder (ADHD) plus internalizing disorders. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

Arm type	Experimental

Investigational medicinal product name	atomoxetine
Investigational medicinal product code	
Other name	LY139603, Strattera
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

Number of subjects in period 1	Pure ADHD (Period II)	ADHD+Internalizing Disorders (Period II)	ADHD+Externalizing Disorders (Period II)
Started	98	41	130
Received at Least One Dose of Study Drug	97	38	128
Completed	87	31	108
Not completed	11	10	22
Parent/Caregiver Decision	8	3	11
Consent withdrawn by subject	-	1	1
Adverse event, non-fatal	3	4	8
Entry Criteria Exclusion	-	2	2

Period 2

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

Arms

Are arms mutually exclusive?	No
Arm title	Pure ADHD (Period III)

Arm description:

Attention-Deficit/Hyperactivity Disorder (ADHD) alone. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

Arm type	Experimental
Investigational medicinal product name	atomoxetine
Investigational medicinal product code	
Other name	LY139603, Strattera
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

Arm title	ADHD+Internalizing Disorders (Period III)

Arm description:

Attention-Deficit/Hyperactivity Disorder (ADHD) plus internalizing disorders. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

Arm type	Experimental
Investigational medicinal product name	atomoxetine
Investigational medicinal product code	
Other name	LY139603, Strattera
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

Arm title	ADHD+Externalizing Disorders (Period III)

Arm description:

Attention-Deficit/Hyperactivity Disorder (ADHD) plus externalizing disorders. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

Arm type	Experimental
Investigational medicinal product name	atomoxetine
Investigational medicinal product code	
Other name	LY139603, Strattera
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

Number of subjects in period 2	Pure ADHD (Period III)	ADHD+Internalizing Disorders (Period III)	ADHD+Externalizing Disorders (Period III)
Started	87	31	108
Completed	0	0	2
Not completed	87	31	106
Parent/Caregiver Decision	14	3	11
Consent withdrawn by subject	1	-	-
Atomoxetine Commercially Available	68	25	90
Physician decision	-	1	2
Adverse event, non-fatal	1	-	-
Withdrawal by Subject	-	1	2
Sponsor Decision	-	-	1
Protocol Violation	-	1	-
Lost to follow-up	1	-	-
Lack of efficacy	2	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Pure ADHD (Period II)
Reporting group description:	
Attention-Deficit/Hyperactivity Disorder (ADHD) alone. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks	
Reporting group title	ADHD+Internalizing Disorders (Period II)
Reporting group description:	
Attention-Deficit/Hyperactivity Disorder (ADHD) plus internalizing disorders. Received atomoxetine:... more 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeksless	
Reporting group title	ADHD+Externalizing Disorders (Period II)
Reporting group description:	
Attention-Deficit/Hyperactivity Disorder (ADHD) plus internalizing disorders. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks	

Reporting group values	Pure ADHD (Period II)	ADHD+Internalizing Disorders (Period II)	ADHD+Externalizing Disorders (Period II)
Number of subjects	98	41	130
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	10.12	10.42	10
standard deviation	± 2.51	± 2.41	± 2.57
Gender categorical Units: Subjects			
Female	14	3	9
Male	83	35	119
Not Recorded	1	3	2
Region of Enrollment Units: Subjects			
Italy	98	41	130
Race/Ethnicity Units: Subjects			
Caucasian	90	36	124
Hispanic	1	2	2
African	3	0	0
Native American	1	0	2
East Asian	2	0	0
Not Recorded	1	3	2
Child Health and Illness Profile - Child Edition (CHIP-CE) - Achievement Domain (N=96, N=33, N=121)			
Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to			

67.7. Higher scores mean greater health or level of functioning in achievement.			
Units: T-Score			
arithmetic mean	29.27	27.72	25.83
standard deviation	± 7.89	± 7.73	± 7.6
Child Health and Illness Profile - Child Edition (CHIP-CE) - Satisfaction Domain (N=96, N=24, N=122)			
Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement.			
Units: T-Score			
arithmetic mean	39.26	30.11	31.69
standard deviation	± 13.89	± 14.83	± 14.78
Child Health and Illness Profile - Child Edition (CHIP-CE) - Comfort Domain (N=96, N=35, N=122)			
Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement.			
Units: T-Score			
arithmetic mean	51.31	46.76	44.74
standard deviation	± 9.4	± 12.28	± 9.38
Child Health and Illness Profile - Child Edition (CHIP-CE) - Resilience Domain (N=96, N=34, N=123)			
Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement.			
Units: T-Score			
arithmetic mean	39.34	34.96	31.4
standard deviation	± 10.15	± 10.89	± 11.85
Child Health and Illness Profile - Child Edition (CHIP-CE) - Risk Avoidance (N=96, N=33, N=121)			
Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement.			
Units: T-Score			
arithmetic mean	32.03	30.48	22.85
standard deviation	± 9.7	± 12.29	± 12
Children's Depression Rating Scale-Revised (CDRS-R)			
Measures presence and severity of depression. Consists of 17 items scored on a 1-5 or 1-7 scale. A rating of 1 indicates normal, thus the minimum score is 17. The maximum score is 113. In general, scores below 20 indicate an absence of depression; scores of 20 or 30 indicate borderline depression; scores of 40 to 60 indicate moderate depression.			
Units: units on a scale			
arithmetic mean	37.93	43.76	43.06
standard deviation	± 12.26	± 13.48	± 13.69

Clinical Global Impression-Attention Deficit Hyperactivity Disorder-Severity Scale (CGI-ADHD-S)			
Measures severity of the patient's overall severity of ADHD symptoms (1=normal, not at all ill; 7=among the most extremely ill patients).			
Units: units on a scale			
arithmetic mean	4.64	4.97	4.98
standard deviation	± 0.79	± 0.79	± 0.78
Conners' Teacher Rating Scale-Revised:Short Form (CTRS-R:S)			
A 28-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the teacher to assess problem behaviors related to ADHD. Subscale total scores range from 0 to 15 for Oppositional and Cognitive Problems, 0 to 21 for Hyperactivity, and 0 to 36 for ADHD Index.			
Units: units on a scale			
arithmetic mean	5.97	4.97	8.62
standard deviation	± 4.93	± 4.66	± 4.83
Conners' Teacher Rating Scale-Revised:Short Form (CTRS-R:S) Cognitive Problems			
A 28-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the teacher to assess problem behaviors related to ADHD. Subscale total scores range from 0 to 15 for Oppositional and Cognitive Problems, 0 to 21 for Hyperactivity, and 0 to 36 for ADHD Index.			
Units: units on a scale			
arithmetic mean	7.86	7.68	7.96
standard deviation	± 3.73	± 3.8	± 3.61
Conners' Teacher Rating Scale-Revised:Short Form (CTRS-R:S)			
A 28-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the teacher to assess problem behaviors related to ADHD. Subscale total scores range from 0 to 15 for Oppositional and Cognitive Problems, 0 to 21 for Hyperactivity, and 0 to 36 for ADHD Index.			
Units: units on a scale			
arithmetic mean	11.38	12.03	14.67
standard deviation	± 6.09	± 5.21	± 5.15
Conners' Teacher Rating Scale-Revised:Short Form (CTRS-R:S) ADHD			
A 28-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the teacher to assess problem behaviors related to ADHD. Subscale total scores range from 0 to 15 for Oppositional and Cognitive Problems, 0 to 21 for Hyperactivity, and 0 to 36 for ADHD Index.			
Units: units on a scale			
arithmetic mean	22.14	22.94	25.18
standard deviation	± 6.86	± 6.01	± 6.07
Pediatric Anxiety Rating Scale (PARS)			
The Pediatric Anxiety Rating Scale (PARS) is used to rate the severity of anxiety in children and adolescents, ages 6 to 17 years. The total score for the PARS is derived by summing 5 of the 7 severity/impairment/interference items (2,3,5,6,7). The total score ranges from 0 (none) to 25 (extreme severity). Items 1 (overall number of anxiety symptoms) and 4 (overall severity of physical symptoms) are not included in the total score calculation.			
Units: units on a scale			
arithmetic mean	2.5	7.5	4.67
standard deviation	± 2.67	± 5.68	± 5.12
Swanson, Nolan, and Pelham Rating Scale Revised (SNAP-IV) Inattention Subscale (N=97, N=38, N=127)			
The SNAP-IV is a 26-item scale that includes 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD and 1 item for each of the 8 symptoms contained in the DSM-IV diagnosis of ODD. Each item is score on 0 to 3 scale (0 = "Not at All", 1 = "Just a Little", 2 = "Pretty Much", 3 = "Very Much"). The SNAP-IV yields scores in three domains: Inattention (items 1-9: subscore range=0-27), Hyperactivity/impulsivity (items 10-18: subscale range=0-27), and Oppositional (items 19-26: subscale range=0-24). Combined type (inattention + hyperactivity/impulsivity) scores range from 0-54.			
Units: units on a scale			

arithmetic mean	20.28	21.03	21.87
standard deviation	± 4.19	± 3.72	± 3.48
SNAP-IV Hyperactivity/Impulsivity Subscale (N=97, N=38)			
The SNAP-IV is a 26-item scale that includes 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD and 1 item for each of the 8 symptoms contained in the DSM-IV diagnosis of ODD. Each item is score on 0 to 3 scale (0 = "Not at All", 1 = "Just a Little", 2 = "Pretty Much", 3 = "Very Much"). The SNAP-IV yields scores in three domains: Inattention (items 1-9: subscore range=0-27), Hyperactivity/impulsivity (items 10-18: subscale range=0-27), and Oppositional (items 19-26: subscale range=0-24). Combined type (inattention + hyperactivity/impulsivity) scores range from 0-54.			
Units: units on a scale			
arithmetic mean	17.21	19.66	21.04
standard deviation	± 6.1	± 5.54	± 3.48
Swanson, Nolan, and Pelham Rating Scale Revised (SNAP-IV) Combined Type Subscale (N=97, N=38, N=127)			
The SNAP-IV is a 26-item scale that includes 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD and 1 item for each of the 8 symptoms contained in the DSM-IV diagnosis of ODD. Each item is score on 0 to 3 scale (0 = "Not at All", 1 = "Just a Little", 2 = "Pretty Much", 3 = "Very Much"). The SNAP-IV yields scores in three domains: Inattention (items 1-9: subscore range=0-27), Hyperactivity/impulsivity (items 10-18: subscale range=0-27), and Oppositional (items 19-26: subscale range=0-24). Combined type (inattention + hyperactivity/impulsivity) scores range from 0-54.			
Units: units on a scale			
arithmetic mean	37.48	40.68	42.91
standard deviation	± 7.78	± 7.87	± 5.51
Swanson, Nolan, and Pelham Rating Scale Revised (SNAP-IV) Oppositional Subscale (N=97, N=38, N=127)			
The SNAP-IV is a 26-item scale that includes 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD and 1 item for each of the 8 symptoms contained in the DSM-IV diagnosis of ODD. Each item is score on 0 to 3 scale (0 = "Not at All", 1 = "Just a Little", 2 = "Pretty Much", 3 = "Very Much"). The SNAP-IV yields scores in three domains: Inattention (items 1-9: subscore range=0-27), Hyperactivity/impulsivity (items 10-18: subscale range=0-27), and Oppositional (items 19-26: subscale range=0-24). Combined type (inattention + hyperactivity/impulsivity) scores range from 0-54.			
Units: units on a scale			
arithmetic mean	10.15	12.32	17.99
standard deviation	± 4.54	± 4.67	± 3.57

Reporting group values	Total		
Number of subjects	269		
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	26		
Male	237		
Not Recorded	6		
Region of Enrollment			
Units: Subjects			
Italy	269		
Race/Ethnicity			
Units: Subjects			

Caucasian	250		
Hispanic	5		
African	3		
Native American	3		
East Asian	2		
Not Recorded	6		
Child Health and Illness Profile - Child Edition (CHIP-CE) - Achievement Domain (N=96, N=33, N=121)			
Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement.			
Units: T-Score			
arithmetic mean			
standard deviation	-		
Child Health and Illness Profile - Child Edition (CHIP-CE) - Satisfaction Domain (N=96, N=24, N=122)			
Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement.			
Units: T-Score			
arithmetic mean			
standard deviation	-		
Child Health and Illness Profile - Child Edition (CHIP-CE) - Comfort Domain (N=96, N=35, N=122)			
Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement.			
Units: T-Score			
arithmetic mean			
standard deviation	-		
Child Health and Illness Profile - Child Edition (CHIP-CE) - Resilience Domain (N=96, N=34, N=123)			
Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement.			
Units: T-Score			
arithmetic mean			
standard deviation	-		
Child Health and Illness Profile - Child Edition (CHIP-CE) - Risk Avoidance (N=96, N=33, N=121)			
Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of			

10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement.			
Units: T-Score arithmetic mean standard deviation	- -		
Children's Depression Rating Scale-Revised (CDRS-R)			
Measures presence and severity of depression. Consists of 17 items scored on a 1-5 or 1-7 scale. A rating of 1 indicates normal, thus the minimum score is 17. The maximum score is 113. In general, scores below 20 indicate an absence of depression; scores of 20 or 30 indicate borderline depression; scores of 40 to 60 indicate moderate depression.			
Units: units on a scale arithmetic mean standard deviation	- -		
Clinical Global Impression-Attention Deficit Hyperactivity Disorder-Severity Scale (CGI-ADHD-S)			
Measures severity of the patient's overall severity of ADHD symptoms (1=normal, not at all ill; 7=among the most extremely ill patients).			
Units: units on a scale arithmetic mean standard deviation	- -		
Conners' Teacher Rating Scale-Revised:Short Form (CTRS-R:S)			
A 28-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the teacher to assess problem behaviors related to ADHD. Subscale total scores range from 0 to 15 for Oppositional and Cognitive Problems, 0 to 21 for Hyperactivity, and 0 to 36 for ADHD Index.			
Units: units on a scale arithmetic mean standard deviation	- -		
Conners' Teacher Rating Scale-Revised:Short Form (CTRS-R:S) Cognitive Problems			
A 28-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the teacher to assess problem behaviors related to ADHD. Subscale total scores range from 0 to 15 for Oppositional and Cognitive Problems, 0 to 21 for Hyperactivity, and 0 to 36 for ADHD Index.			
Units: units on a scale arithmetic mean standard deviation	- -		
Conners' Teacher Rating Scale-Revised:Short Form (CTRS-R:S)			
A 28-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the teacher to assess problem behaviors related to ADHD. Subscale total scores range from 0 to 15 for Oppositional and Cognitive Problems, 0 to 21 for Hyperactivity, and 0 to 36 for ADHD Index.			
Units: units on a scale arithmetic mean standard deviation	- -		
Conners' Teacher Rating Scale-Revised:Short Form (CTRS-R:S) ADHD			
A 28-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the teacher to assess problem behaviors related to ADHD. Subscale total scores range from 0 to 15 for Oppositional and Cognitive Problems, 0 to 21 for Hyperactivity, and 0 to 36 for ADHD Index.			
Units: units on a scale arithmetic mean standard deviation	- -		
Pediatric Anxiety Rating Scale (PARS)			
The Pediatric Anxiety Rating Scale (PARS) is used to rate the severity of anxiety in children and adolescents, ages 6 to 17 years. The total score for the PARS is derived by summing 5 of the 7 severity/impairment/interference items (2,3,5,6,7). The total score ranges from 0 (none) to 25			

(extreme severity). Items 1 (overall number of anxiety symptoms) and 4 (overall severity of physical symptoms) are not included in the total score calculation.			
Units: units on a scale arithmetic mean standard deviation	- 		
Swanson, Nolan, and Pelham Rating Scale Revised (SNAP-IV) Inattention Subscale (N=97, N=38, N=127)			
The SNAP-IV is a 26-item scale that includes 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD and 1 item for each of the 8 symptoms contained in the DSM-IV diagnosis of ODD. Each item is score on 0 to 3 scale (0 = "Not at All", 1 = "Just a Little", 2 = "Pretty Much", 3 = "Very Much"). The SNAP-IV yields scores in three domains: Inattention (items 1-9: subscore range=0-27), Hyperactivity/impulsivity (items 10-18: subscale range=0-27), and Oppositional (items 19-26: subscale range=0-24). Combined type (inattention + hyperactivity/impulsivity) scores range from 0-54.			
Units: units on a scale arithmetic mean standard deviation	- 		
SNAP-IV Hyperactivity/Impulsivity Subscale (N=97, N=38)			
The SNAP-IV is a 26-item scale that includes 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD and 1 item for each of the 8 symptoms contained in the DSM-IV diagnosis of ODD. Each item is score on 0 to 3 scale (0 = "Not at All", 1 = "Just a Little", 2 = "Pretty Much", 3 = "Very Much"). The SNAP-IV yields scores in three domains: Inattention (items 1-9: subscore range=0-27), Hyperactivity/impulsivity (items 10-18: subscale range=0-27), and Oppositional (items 19-26: subscale range=0-24). Combined type (inattention + hyperactivity/impulsivity) scores range from 0-54.			
Units: units on a scale arithmetic mean standard deviation	- 		
Swanson, Nolan, and Pelham Rating Scale Revised (SNAP-IV) Combined Type Subscale (N=97, N=38, N=127)			
The SNAP-IV is a 26-item scale that includes 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD and 1 item for each of the 8 symptoms contained in the DSM-IV diagnosis of ODD. Each item is score on 0 to 3 scale (0 = "Not at All", 1 = "Just a Little", 2 = "Pretty Much", 3 = "Very Much"). The SNAP-IV yields scores in three domains: Inattention (items 1-9: subscore range=0-27), Hyperactivity/impulsivity (items 10-18: subscale range=0-27), and Oppositional (items 19-26: subscale range=0-24). Combined type (inattention + hyperactivity/impulsivity) scores range from 0-54.			
Units: units on a scale arithmetic mean standard deviation	- 		
Swanson, Nolan, and Pelham Rating Scale Revised (SNAP-IV) Oppositional Subscale (N=97, N=38, N=127)			
The SNAP-IV is a 26-item scale that includes 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD and 1 item for each of the 8 symptoms contained in the DSM-IV diagnosis of ODD. Each item is score on 0 to 3 scale (0 = "Not at All", 1 = "Just a Little", 2 = "Pretty Much", 3 = "Very Much"). The SNAP-IV yields scores in three domains: Inattention (items 1-9: subscore range=0-27), Hyperactivity/impulsivity (items 10-18: subscale range=0-27), and Oppositional (items 19-26: subscale range=0-24). Combined type (inattention + hyperactivity/impulsivity) scores range from 0-54.			
Units: units on a scale arithmetic mean standard deviation	- 		

End points

End points reporting groups

Reporting group title	Pure ADHD (Period II)
Reporting group description:	
Attention-Deficit/Hyperactivity Disorder (ADHD) alone. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks	
Reporting group title	ADHD+Internalizing Disorders (Period II)
Reporting group description:	
Attention-Deficit/Hyperactivity Disorder (ADHD) plus internalizing disorders. Received atomoxetine:... more 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeksless	
Reporting group title	ADHD+Externalizing Disorders (Period II)
Reporting group description:	
Attention-Deficit/Hyperactivity Disorder (ADHD) plus internalizing disorders. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks	
Reporting group title	Pure ADHD (Period III)
Reporting group description:	
Attention-Deficit/Hyperactivity Disorder (ADHD) alone. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks	
Reporting group title	ADHD+Internalizing Disorders (Period III)
Reporting group description:	
Attention-Deficit/Hyperactivity Disorder (ADHD) plus internalizing disorders. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks	
Reporting group title	ADHD+Externalizing Disorders (Period III)
Reporting group description:	
Attention-Deficit/Hyperactivity Disorder (ADHD) plus externalizing disorders. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks	

Primary: 1: Change From Baseline to 12 Week Endpoint in Child Health and Illness Profile - Child Edition (CHIP-CE), Achievement Domain

End point title	1: Change From Baseline to 12 Week Endpoint in Child Health and Illness Profile - Child Edition (CHIP-CE), Achievement Domain
End point description:	
Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement.	
End point type	Primary
End point timeframe:	
Baseline, 12 Weeks	

End point values	Pure ADHD (Period II)	ADHD+Internalizing Disorders (Period II)	ADHD+Externalizing Disorders (Period II)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83[1]	28[2]	97[3]	
Units: T-Score				
arithmetic mean (confidence interval 95%)	2.65 (0.93 to 4.37)	0.51 (-1.38 to 2.39)	3.89 (2.22 to 5.57)	

Notes:

[1] - Number of patients with baseline and at least one nonmissing post-baseline measurement.

[2] - Number of patients with baseline and at least one nonmissing post-baseline measurement.

[3] - Number of patients with baseline and at least one nonmissing post-baseline measurement.

Statistical analyses

Statistical analysis title	Statistical Analysis for End Point 1
Comparison groups	ADHD+Internalizing Disorders (Period II) v ADHD+Externalizing Disorders (Period II) v Pure ADHD (Period II)
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	LOCF analysis

Secondary: 2: Change From Baseline to 12 Week Endpoint in the Attention-Deficit/Hyperactivity Disorder (ADHD) Subscales of 18-Item Swanson, Nolan and Pelham Rating Scale (SNAP-IV)

End point title	2: Change From Baseline to 12 Week Endpoint in the Attention-Deficit/Hyperactivity Disorder (ADHD) Subscales of 18-Item Swanson, Nolan and Pelham Rating Scale (SNAP-IV)

End point description:

Items from the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) criteria for ADHD are included for the two subsets of symptoms: inattention (items #1-#9: total score=0-27) and hyperactivity/impulsivity (items #11-#19: total score=0-27). The SNAP-IV is based on a 0 (not at all) to 3 (very much) rating scale. Total combined type (inattention plus hyperactivity/impulsivity) subscale scores range from 0 to 54.

End point type	Secondary

End point timeframe:

Baseline, 12 Weeks

End point values	Pure ADHD (Period II)	ADHD+Internalizing Disorders (Period II)	ADHD+Externalizing Disorders (Period II)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	33	111	
Units: units on a scale				
arithmetic mean (confidence interval 95%)				
Inattention Subscale	-5.88 (-7.25 to -5.13)	-5.52 (-7.34 to -3.69)	-7.58 (-8.69 to -6.46)	

Hyperactivity/Impulsivity Subscale	-12.1 (-13.9 to -10.3)	-5.67 (-7.41 to -3.92)	-8.08 (-9.09 to -7.07)	
Combined Type (ADHD) Subscale	-6.19 (-6.97 to -4.78)	-11.2 (-14.4 to -7.92)	-15.7 (-17.6 to -13.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: 3: Change From Baseline to 12 Week Endpoint in Clinical Global Impressions-ADHD-Severity (CGI-ADHD-S)

End point title	3: Change From Baseline to 12 Week Endpoint in Clinical Global Impressions-ADHD-Severity (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, 12 Weeks

End point values	Pure ADHD (Period II)	ADHD+Internalizing Disorders (Period II)	ADHD+Externalizing Disorders (Period II)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	32	112	
Units: units on a scale				
arithmetic mean (confidence interval 95%)	-1.23 (-1.46 to -0.99)	-1.63 (-1.99 to -1.26)	-1.42 (-1.63 to -1.21)	

Statistical analyses

No statistical analyses for this end point

Secondary: 4: Change From Baseline to 12 Week Endpoint in CHIP-CE Satisfaction, Comfort, Resilience and Risk Avoidance Domains

End point title	4: Change From Baseline to 12 Week Endpoint in CHIP-CE Satisfaction, Comfort, Resilience and Risk Avoidance Domains

End point description:

Parent-rated assessment of a child’s health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, ‘how good is your child at making friends?’ 1=never, 5=always). Standard scores (t-value) were established, with all domains having a mean score of 50 and standard deviation of 10. Satisfaction range=-25.7 to 66.3; Comfort=-28.6 to 67.2; Resilience=-36.3 to 71.8; Risk Avoidance=-23.5 to 62.5. Higher scores mean greater health or level of functioning in that domain.

End point type	Secondary

End point timeframe:

Baseline, 12 Weeks

End point values	Pure ADHD (Period II)	ADHD+Internalizing Disorders (Period II)	ADHD+Externalizing Disorders (Period II)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	97	38	128	
Units: T-Score				
arithmetic mean (confidence interval 95%)				
Satisfaction Domain (N=88, N=31, N=105)	2.14 (-0.06 to 4.34)	0.81 (-3.33 to 4.95)	3.78 (1.18 to 6.39)	
Comfort Domain (N=86, N=28, N=103)	1.01 (-0.88 to 2.9)	5.72 (1.24 to 10.19)	4.94 (3.14 to 6.73)	
Resilience Domain (N=87, N=30, N=106)	1.21 (-0.85 to 3.27)	2.18 (-1.31 to 5.67)	3.07 (1.1 to 5.03)	
Risk Avoidance Domain (N=82, N=28, N=94)	4.72 (2.93 to 6.51)	5.7 (1.96 to 9.45)	9.88 (7.88 to 11.88)	

Statistical analyses

No statistical analyses for this end point

Secondary: 5: Change From Baseline to 12 Week Endpoint in Pediatric Anxiety Rating Scale (PARS)

End point title	5: Change From Baseline to 12 Week Endpoint in Pediatric Anxiety Rating Scale (PARS)

End point description:

The Pediatric Anxiety Rating Scale (PARS) is used to rate the severity of anxiety in children and adolescents, ages 6 to 17 years. The total score for the PARS is derived by summing 5 of the 7 severity/impairment/interference items (2,3,5,6,7). The total score ranges from 0 (none) to 25 (extreme severity). Items 1 (overall number of anxiety symptoms) and 4 (overall severity of physical symptoms) are not included in the total score calculation.

End point type	Secondary

End point timeframe:

Baseline, 12 Weeks

End point values	Pure ADHD (Period II)	ADHD+Internalizing Disorders (Period II)	ADHD+Externalizing Disorders (Period II)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	33	112	
Units: units on a scale				
arithmetic mean (confidence interval 95%)	-0.18 (-0.7 to 0.34)	-1.88 (-3.4 to -0.36)	-1.18 (-1.9 to -0.46)	

Statistical analyses

No statistical analyses for this end point

Secondary: 6: Change From Baseline to 12 Week Endpoint in Children's Depression Rating Scale-Revised (CDRS-R)

End point title	6: Change From Baseline to 12 Week Endpoint in Children's Depression Rating Scale-Revised (CDRS-R)

End point description:

Measures presence and severity of depression. Consists of 17 items scored on a 1-5 or 1-7 scale. A rating of 1 indicates normal, thus the minimum score is 17. The maximum score is 113. In general, scores below 20 indicate an absence of depression; scores of 20 or 30 indicate borderline depression; scores of 40 to 60 indicate moderate depression.

End point type	Secondary

End point timeframe:

Baseline, 12 Weeks

End point values	Pure ADHD (Period II)	ADHD+Internalizing Disorders (Period II)	ADHD+Externalizing Disorders (Period II)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	97	38	128	
Units: units on a scale				
arithmetic mean (confidence interval 95%)	-1.6 (-3.54 to 0.34)	-2.56 (-6.38 to 1.25)	-3.13 (-4.64 to -1.62)	

Statistical analyses

No statistical analyses for this end point

Secondary: 7: Change From Baseline to 12 Week Endpoint in SNAP-IV Oppositional Scale

End point title	7: Change From Baseline to 12 Week Endpoint in SNAP-IV Oppositional Scale

End point description:

Items are included from the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) criteria for Oppositional Defiant Disorder. The SNAP-IV is based on a 0 (not at all) to 3 (very much) rating scale. Total subscale scores range from 0 to 24.

End point type	Secondary

End point timeframe:

Baseline, 12 Weeks

End point values	Pure ADHD (Period II)	ADHD+Internalizing Disorders (Period II)	ADHD+Externalizing Disorders (Period II)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	33	111	
Units: units on a scale				
arithmetic mean (confidence interval 95%)	-2.01 (-2.86 to -1.16)	-2.12 (-3.95 to -0.29)	-5.54 (-6.43 to -4.65)	

Statistical analyses

No statistical analyses for this end point

Secondary: 8: Change From Baseline to 12 Week Endpoint in Adolescent Symptom Inventory-4: Parent Checklist (ASI-4)

End point title	8: Change From Baseline to 12 Week Endpoint in Adolescent Symptom Inventory-4: Parent Checklist (ASI-4)

End point description:

Parent-completed ASI-4 contains 120 items on 18 emotional and behavioral disorders in adolescents (12-18 years old). Item score range:0 (no symptoms) to 3 (maximum impairment). Categories: A=ADHD (0-54); B=Conduct (0-60); C=Oppositional Defiant (0-24); D=Generalized Anxiety (0-18); E=Specific Phobia/Panic Attack/Obsessions/Compulsions/Somatization (0-30); F=Social Phobia (0-6); G=Separation Anxiety (0-24); H=Schizoid Personality (0-9); I=Schizophrenia (0-6); J=Enuresis (0-18); K=Major Depressive (0-42); L=Bipolar (0-27); M=Anorexia (0-12); N=Bulimia (0-12); O=Substance Abuse (0-18).

End point type	Secondary

End point timeframe:

Baseline, 12 Weeks

End point values	Pure ADHD (Period II)	ADHD+Internalizing Disorders (Period II)	ADHD+Externalizing Disorders (Period II)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	10	30	
Units: units on a scale				
arithmetic mean (standard deviation)				
Category A - Baseline	32.73 (± 11.42)	38.33 (± 10.32)	38.13 (± 8.3)	
Category A - Change from Baseline	-11.4 (± 9.88)	-10.4 (± 11.55)	-11.6 (± 9.5)	
Category B - Baseline	4.04 (± 4.25)	6 (± 5.62)	10.8 (± 5.41)	
Category B - Change from Baseline	-0.73 (± 2.92)	-0.6 (± 5.83)	-5.57 (± 5.58)	
Category C- Baseline	7.92 (± 4.77)	10.5 (± 3.72)	15.6 (± 5.24)	
Category C - Change from Baseline	-0.88 (± 3.85)	-1.4 (± 6.15)	-5.47 (± 5.51)	
Category D- Baseline	4.73 (± 3.14)	9.2 (± 3.58)	8.37 (± 3.54)	
Category D - Change from Baseline	-0.58 (± 3.09)	-1.7 (± 3.65)	-2.97 (± 3.67)	
Category E- Baseline	3.58 (± 4)	7.6 (± 7.85)	3.63 (± 3.16)	
Category E - Change from Baseline	-0.38 (± 4.01)	-4.5 (± 8.72)	-1.3 (± 2.35)	
Category F- Baseline	1.19 (± 1.27)	2.6 (± 1.43)	1.2 (± 1.37)	
Category F - Change from Baseline	-0.58 (± 0.81)	-1.4 (± 1.43)	-0.53 (± 1.25)	
Category G- Baseline	2.27 (± 3.5)	4.5 (± 5.25)	2.1 (± 2.63)	

Category G - Change from Baseline	-0.46 (± 2.49)	-3.2 (± 4.71)	-0.97 (± 2.4)	
Category H- Baseline	0.73 (± 1.28)	1.6 (± 2.27)	1.7 (± 1.74)	
Category H - Change from Baseline	-0.38 (± 1.2)	0.2 (± 2.86)	-0.67 (± 1.69)	
Category I- Baseline	1 (± 1.92)	3.2 (± 3.65)	2.13 (± 2.22)	
Category I - Change from Baseline	-0.19 (± 0.8)	-1.3 (± 3.89)	-0.93 (± 1.7)	
Category J- Baseline	0.42 (± 0.99)	0.4 (± 0.97)	0.5 (± 0.78)	
Category J - Change from Baseline	0 (± 0.69)	-0.3 (± 0.67)	-0.23 (± 0.43)	
Category K- Baseline	3.73 (± 3.99)	4.9 (± 2.85)	4.23 (± 4.05)	
Category K - Change from Baseline	-1.04 (± 2.9)	-1 (± 3.5)	-1.6 (± 3.5)	
Category L- Baseline	3.54 (± 4.68)	5.1 (± 5)	6.03 (± 5.02)	
Category L - Change from Baseline	-1.08 (± 3.46)	-0.2 (± 6.03)	-1.97 (± 4.3)	
Category M- Baseline	0.73 (± 1.22)	1.3 (± 2.06)	0.5 (± 1.41)	
Category M - Change from Baseline	0.15 (± 1.08)	-0.1 (± 3.21)	0.3 (± 1.39)	
Category N- Baseline	1.31 (± 1.54)	2.2 (± 3.05)	2.3 (± 1.84)	
Category N - Change from Baseline	-0.38 (± 1.7)	-0.9 (± 2.23)	-0.8 (± 1.49)	
Category O- Baseline	0.23 (± 0.71)	0.3 (± 0.95)	0.53 (± 0.97)	
Category O - Change from Baseline	0.15 (± 0.37)	-0.2 (± 0.63)	-0.13 (± 0.51)	

Statistical analyses

No statistical analyses for this end point

Secondary: 9: Change From Baseline to 12 Week Endpoint in Child Symptom Inventory-4: Parent Checklist (CSI-4)

End point title	9: Change From Baseline to 12 Week Endpoint in Child Symptom Inventory-4: Parent Checklist (CSI-4)

End point description:

The CSI-4 contains 97 items that screen for 15 emotional and behavioral disorders in children between 5 and 12 years old. Item score range:0 (no symptoms) to 3 (maximum impairment). Categories: A=ADHD (0-54); B=Conduct (0-60); C=Oppositional Defiant (0-24); D=Generalized Anxiety (0-18); E=Specific Phobia/Panic Attack/Obsessions/Compulsions/Somatization (0-30); F=Social Phobia (0-6); G=Separation Anxiety (0-24); H=Schizoid Personality (0-9); I=Schizophrenia (0-6); J=Enuresis (0-18).

End point type	Secondary

End point timeframe:

Baseline, 12 Weeks

End point values	Pure ADHD (Period II)	ADHD+Internalizing Disorders (Period II)	ADHD+Externalizing Disorders (Period II)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	58	22	78	
Units: units on a scale				
arithmetic mean (standard deviation)				
Category A - Baseline	34 (± 10.43)	36 (± 9.32)	38.95 (± 8.68)	
Category A - Change from Baseline	-10.6 (± 9.76)	-9.68 (± 9.54)	-12.7 (± 12.06)	
Category B - Baseline	9.29 (± 4.72)	11.05 (± 4.13)	15.65 (± 4.4)	
Category B - Change from Baseline	-2.12 (± 3.88)	-1.14 (± 5.25)	-3.76 (± 5.56)	
Category C - Baseline	2.1 (± 2.44)	2.23 (± 2.25)	4.63 (± 3.69)	

Category C - Change from Baseline	-0.88 (± 2.11)	-0.05 (± 3.06)	-1.99 (± 3.17)	
Category D - Baseline	5.83 (± 3.37)	8.23 (± 3.96)	7.41 (± 3.94)	
Category D - Change from Baseline	-0.84 (± 3.16)	-2.23 (± 3.01)	-1.63 (± 3.86)	
Category E - Baseline	2.07 (± 1.87)	2.09 (± 1.95)	2.79 (± 2.69)	
Category E - Change from Baseline	-0.38 (± 1.9)	-0.41 (± 1.75)	-0.85 (± 2.43)	
Category F - Baseline	0.48 (± 0.86)	0.32 (± 0.57)	0.91 (± 1.35)	
Category F - Change from Baseline	-0.17 (± 0.94)	-0.14 (± 0.64)	-0.24 (± 1.28)	
Category G - Baseline	3.02 (± 2.7)	4.05 (± 2.79)	3.51 (± 3.3)	
Category G - Change from Baseline	-0.62 (± 2.4)	-0.91 (± 2)	-0.46 (± 2.52)	
Category H - Baseline	3.66 (± 4.14)	4.64 (± 4.02)	4.45 (± 4.39)	
Category H - Change from Baseline	-1.1 (± 2.21)	-1.09 (± 2.93)	-1.54 (± 4.31)	
Category I - Baseline	2.76 (± 1.85)	2.77 (± 1.38)	2.94 (± 1.93)	
Category I - Change from Baseline	-0.03 (± 1.83)	-0.45 (± 1.47)	-0.32 (± 1.75)	
Category J - Baseline	3.92 (± 3.98)	5.58 (± 6.05)	5.22 (± 4.47)	
Category J - Change from Baseline	-1.34 (± 3.64)	-0.83 (± 2.61)	-1.55 (± 4.34)	

Statistical analyses

No statistical analyses for this end point

Secondary: 10: Change From Baseline to 12 Week Endpoint in Conners' Teacher Rating Scale-Revised: Short Form (CTRS-R:S)

End point title	10: Change From Baseline to 12 Week Endpoint in Conners' Teacher Rating Scale-Revised: Short Form (CTRS-R:S)

End point description:

A 28-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the teacher to assess problem behaviors related to ADHD. Subscale total scores range from 0 to 15 for Oppositional and Cognitive Problems, 0 to 21 for Hyperactivity, and 0 to 36 for ADHD Index.

End point type	Secondary

End point timeframe:

Baseline, 12 Weeks

End point values	Pure ADHD (Period II)	ADHD+Internalizing Disorders (Period II)	ADHD+Externalizing Disorders (Period II)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	15	53	
Units: units on a scale				
arithmetic mean (confidence interval 95%)				
Oppositional	-1.42 (-2.22 to -0.61)	1.07 (-0.33 to 2.46)	-2.35 (-3.55 to -1.15)	
Cognitive Problems	-1.08 (-1.72 to -0.45)	-0.47 (-1.74 to 0.8)	-0.94 (-1.77 to -0.11)	
Hyperactivity	-2.87 (-4.04 to -1.69)	-2.34 (-4.8 to 0.11)	-4.09 (-5.52 to -2.67)	
ADHD Index	-4.96 (-6.36 to -3.52)	-3.6 (-6.65 to -0.55)	-6.62 (-8.59 to -4.65)	

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-IT-LYDS	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups	
Reporting group title	Pure ADHD
Reporting group description: -	
Reporting group title	ADHD plus internalizing disorders
Reporting group description: -	
Reporting group title	ADHD plus externalizing disorders
Reporting group description: -	

Serious adverse events	Pure ADHD	ADHD plus internalizing disorders	ADHD plus externalizing disorders
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 97 (1.03%)	0 / 38 (0.00%)	2 / 128 (1.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
facial bones fracture			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	0 / 97 (0.00%)	0 / 38 (0.00%)	1 / 128 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fall			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	0 / 97 (0.00%)	0 / 38 (0.00%)	1 / 128 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
idiosyncratic drug reaction			

alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	0 / 97 (0.00%)	0 / 38 (0.00%)	1 / 128 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
vomiting			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	0 / 97 (0.00%)	0 / 38 (0.00%)	1 / 128 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
appendicitis			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 97 (1.03%)	0 / 38 (0.00%)	0 / 128 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
dehydration			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	0 / 97 (0.00%)	0 / 38 (0.00%)	1 / 128 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Pure ADHD	ADHD plus internalizing disorders	ADHD plus externalizing disorders
Total subjects affected by non-serious adverse events			
subjects affected / exposed	70 / 97 (72.16%)	28 / 38 (73.68%)	87 / 128 (67.97%)
Investigations			
weight decreased			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	11 / 97 (11.34%)	1 / 38 (2.63%)	12 / 128 (9.38%)
occurrences (all)	15	1	15
Nervous system disorders			

headache			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	20 / 97 (20.62%)	10 / 38 (26.32%)	26 / 128 (20.31%)
occurrences (all)	34	17	35
somnolence			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	22 / 97 (22.68%)	11 / 38 (28.95%)	34 / 128 (26.56%)
occurrences (all)	23	15	44
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	5 / 97 (5.15%)	6 / 38 (15.79%)	7 / 128 (5.47%)
occurrences (all)	6	6	7
fatigue			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	5 / 97 (5.15%)	0 / 38 (0.00%)	2 / 128 (1.56%)
occurrences (all)	5	0	3
irritability			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	4 / 97 (4.12%)	6 / 38 (15.79%)	12 / 128 (9.38%)
occurrences (all)	4	6	16
pyrexia			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	3 / 97 (3.09%)	0 / 38 (0.00%)	8 / 128 (6.25%)
occurrences (all)	3	0	8
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	9 / 97 (9.28%)	8 / 38 (21.05%)	18 / 128 (14.06%)
occurrences (all)	13	9	32
abdominal pain upper			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	5 / 97 (5.15%)	6 / 38 (15.79%)	12 / 128 (9.38%)
occurrences (all)	5	8	17
constipation			

alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	2 / 97 (2.06%)	2 / 38 (5.26%)	1 / 128 (0.78%)
occurrences (all)	2	2	1
diarrhoea			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 97 (1.03%)	2 / 38 (5.26%)	3 / 128 (2.34%)
occurrences (all)	3	2	3
nausea			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	12 / 97 (12.37%)	10 / 38 (26.32%)	26 / 128 (20.31%)
occurrences (all)	17	19	36
vomiting			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	13 / 97 (13.40%)	6 / 38 (15.79%)	15 / 128 (11.72%)
occurrences (all)	23	13	20
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	3 / 97 (3.09%)	0 / 38 (0.00%)	8 / 128 (6.25%)
occurrences (all)	3	0	10
Psychiatric disorders			
aggression			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	4 / 97 (4.12%)	1 / 38 (2.63%)	9 / 128 (7.03%)
occurrences (all)	5	1	9
Infections and infestations			
gastroenteritis			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	2 / 97 (2.06%)	2 / 38 (5.26%)	0 / 128 (0.00%)
occurrences (all)	2	2	0
Metabolism and nutrition disorders			
anorexia			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	24 / 97 (24.74%)	11 / 38 (28.95%)	33 / 128 (25.78%)
occurrences (all)	26	15	39

decreased appetite			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	11 / 97 (11.34%)	7 / 38 (18.42%)	14 / 128 (10.94%)
occurrences (all)	13	7	20

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.

The original intent was to also calculate change and 95% confidence intervals at end of Period III; however, due to low number of patients completing Period III, variations from baseline (LOCF), are not suitable for further analysis or description.

Notes: