



Clinical trial results:

A Double-Blind, Randomized, Placebo-Controlled, Crossover Study Evaluating the Academic, Behavioral, and Cognitive Effects of **CONCERTA** on Older Children with ADHD

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

Summary

EudraCT number	2015-001081-26
Trial protocol	Outside EU/EEA
Global end of trial date	12 June 2009

Results information

Result version number	v2 (current)
This version publication date	01 July 2016
First version publication date	31 July 2015
Version creation reason	<ul style="list-style-type: none">• Correction of full data set• Review of data

Trial information

Trial identification

Sponsor protocol code	CONCERTAATT4069
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00799409
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ortho-McNeil Janssen Scientific Affairs LLC
Sponsor organisation address	1125 Trenton-Harbourton Road, Titusville, New Jersey, United States, 08560- 0200
Public contact	Clinical Registry Group-JB BV, Janssen Research and Development, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group-JB BV, Janssen Research and Development, ClinicalTrialsEU@its.jnj.com

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	12 June 2009
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	12 June 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this trial is to determine if the study medication, CONCERTA (methylphenidate HCl), is safe and effective in improving academic performance and behavior in children with attention deficit hyperactivity disorder (ADHD), when compared to placebo.

Protection of trial subjects:

Safety were evaluated throughout the study by monitoring of adverse events (AEs), laboratory tests (complete blood count [CBC], complete chemistry panel, and liver function tests [LFTs]), vital signs body weight measurements, electrocardiogram and the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL) including items specifically examining suicidal thinking.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 November 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 78
Worldwide total number of subjects	78
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)	67
Adolescents (12-17 years)	11
Adults (18-64 years)	0
From 65 to 84 years	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Total 78 subjects were enrolled in the study and out of 78 only only 71 subjects completed the study.

Period 1

Period 1 title	Open-Label Dose Adjustment Period
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Concerta
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Arm description:

Subjects initiated with Concerta as 18 milligram/day (mg/day) once daily. Concerta dose was continuously increased until an optimal individualized dose was achieved, up to a maximum dose of 54 mg/day.

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

Dosage and administration details:

Concerta (18 mg, 36 mg, or 54 mg) tablet once daily orally was administered.

Number of subjects in period 1	Concerta
Started	78
Completed	71
Not completed	7
Consent withdrawn by subject	1
Other	5
Lost to follow-up	1

Period 2

Period 2 title	Double-Blind Assessment Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind

Roles blinded	Subject, Investigator
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Arms

Are arms mutually exclusive?	Yes
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Arm title	Placebo/Concerta
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Arm description:

Children randomized to receive Placebo at lab school day 1 and an individualized, optimal dose of Concerta (18 mg, 36 mg, or 54 mg tablet) once daily at lab school Day 2.

Arm type	Experimental
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Investigational medicinal product name	Placebo
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Tablet
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Routes of administration	Oral use
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Dosage and administration details:

Subject received placebo matching with Concerta orally once daily

Investigational medicinal product name	Concerta
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Capsule
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Routes of administration	Oral use
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Dosage and administration details:

Concerta (18mg, 36mg, or 54 mg) orally tablet was given once daily

Arm title	Concerta/Placebo
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Arm description:

Children randomized to receive an individualized, optimal dose of Concerta (18 mg, 36 mg, or 54 mg tablet) once daily at lab school Day 1 and Placebo at lab school Day 2.

Arm type	Experimental
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Investigational medicinal product name	Concerta
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Tablet
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Routes of administration	Oral use
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Dosage and administration details:

Concerta (18mg, 36mg, or 54 mg) orally tablet was given once daily.

Investigational medicinal product name	Placebo
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Tablet
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Routes of administration	Oral use
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Dosage and administration details:

Subject received placebo matching with Concerta orally once daily

Number of subjects in period 2	Placebo/Concerta	Concerta/Placebo
Started	36	35
Completed	36	35

Baseline characteristics

Reporting groups

Reporting group title	Open-Label Dose Adjustment Period
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Reporting group description:

Subjects initiated with Concerta as 18 milligram/day (mg/day) once daily. Concerta dose was continuously increased until an optimal individualized dose was achieved, up to a maximum dose of 54 mg/day.

Reporting group values	Open-Label Dose Adjustment Period	Total	
Number of subjects	78	78	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	67	67	
Adolescents (12-17 years)	11	11	
Adults (18-64 years)	0	0	
From 65 to 84 years	0	0	
85 years and over	0	0	
Title for AgeContinuous Units: years			
arithmetic mean	9.9		
standard deviation	± 0.69	-	
Title for Gender Units: subjects			
Female	23	23	
Male	55	55	

End points

End points reporting groups

Reporting group title	Concerta
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Reporting group description:

Subjects initiated with Concerta as 18 milligram/day (mg/day) once daily. Concerta dose was continuously increased until an optimal individualized dose was achieved, up to a maximum dose of 54 mg/day.

Reporting group title	Placebo/Concerta
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Reporting group description:

Children randomized to receive Placebo at lab school day 1 and an individualized, optimal dose of Concerta (18 mg, 36 mg, or 54 mg tablet) once daily at lab school Day 2.

Reporting group title	Concerta/Placebo
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Reporting group description:

Children randomized to receive an individualized, optimal dose of Concerta (18 mg, 36 mg, or 54 mg tablet) once daily at lab school Day 1 and Placebo at lab school Day 2.

Subject analysis set title	Intent-to-treat (ITT) population
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Intent-to-Treat for Placebo and Concerta columns in the primary and secondary results are comprised of the 36 children randomized to Placebo/Concerta (lab day 1/lab day 2) plus the 35 children randomized to Concerta/Placebo.

Subject analysis set title	Placebo
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Children randomized to receive Placebo at lab school day 1 or lab school day 2

Subject analysis set title	Concerta
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Children randomized to receive Concerta at lab school day 1 or lab school day 2

Primary: Hour 4 Permanent Product Math Test Attempted Score (PERMP-Attempted)

End point title	Hour 4 Permanent Product Math Test Attempted Score (PERMP-Attempted)
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End point description:

PERMP (range: 0, 400) is a measure of academic productivity in children up to 14 years of age. These seatwork math tasks provide an objective measure of attention and accuracy in calculations. The level of difficulty is established on a screening math pretest. The subsequent laboratory school day assessments employed a series of 10-minute math tests (5 pages of 80 math problem each for a total of 400 problems available). Children were graded on the number of attempted problems. A higher number of problems attempted was indicative of greater attention to detail (higher score is preferable)

End point type	Primary
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End point timeframe:

Hour 4 of the of the Lab School Day during Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[1]	71 ^[2]		
Units: Problems attempted				
arithmetic mean (standard deviation)	74.8 (± 42.05)	103.5 (± 38.51)		

Notes:

[1] - ITT Population

[2] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Concerta
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-28.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35
upper limit	-22.3

Notes:

[3] - Number of subjects included in the analysis were "71" instead of "142", as same subjects received both treatments (Placebo and Concerta), one in each treatment period.

Primary: Hour 4 Permanent Product Math Test Correct Score (PERMP-Correct)

End point title	Hour 4 Permanent Product Math Test Correct Score (PERMP-Correct)
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End point description:

PERMP (range: 0, 400) is a measure of academic productivity in children up to 14 years of age. These seatwork math tasks provide an objective measure of attention and accuracy in calculations. The level of difficulty is established on a screening math pretest performed at Visit 2. The subsequent laboratory school day assessments employed a series of 10-minute math tests (5 pages of 80 math problem each for a total of 400 problems available). Children were graded on the number of correct problems. A higher number of problems correct, of those attempted, was indicative of greater accuracy.

End point type	Primary
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End point timeframe:

Hour 4 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[4]	71 ^[5]		
Units: Problems correct				
arithmetic mean (standard deviation)	69 (± 41.02)	97.4 (± 38.99)		

Notes:

[4] - ITT Population

[5] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Concerta
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority ^[6]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-28.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.4
upper limit	-22.2

Notes:

[6] - Number of subjects included in the analysis were "71" instead of "142", as same subjects received both treatments (Placebo and Concerta), one in each treatment period.

Secondary: Hour 4 Swanson, Kotkin, Alger, M-Flynn and Pelham Scale for Department (SKAMP-Department)

End point title	Hour 4 Swanson, Kotkin, Alger, M-Flynn and Pelham Scale for Department (SKAMP-Department)
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End point description:

The SKAMP scale measures the manifestations of ADHD using an independent observer (teacher) rating of the child's impairment in classroom behavior. The SKAMP-Department (SKAMP-D) (range: 0, 36) is a sum of ratings on 6 department items (interacting with other children, interacting with adults, remaining quiet, staying seated, complying with the teacher's directions, and following the classroom rules). Each item was rated on a 7-point impairment scale (0=normal, 6=maximum impairment), with higher scores indicating more severe symptoms.

End point type	Secondary
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End point timeframe:

Hour 4 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[7]	71 ^[8]		
Units: Units on a scale				
arithmetic mean (standard deviation)	9 (± 6.68)	3.1 (± 4.1)		

Notes:

[7] - ITT Population

[8] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 4 Swanson, Kotkin, Alger, M-Flynn and Pelham Scale for Attention (SKAMP-Attention)

End point title	Hour 4 Swanson, Kotkin, Alger, M-Flynn and Pelham Scale for Attention (SKAMP-Attention)
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End point description:

The SKAMP scale measures the manifestations of ADHD using an independent observer (teacher) rating of the child's impairment in classroom behavior. The SKAMP-Attention (SKAMP-A) (range: 0, 42) is a sum of the ratings on 7 attention items (getting started, sticking with tasks, attending to an activity, making activity transitions, completing assigned tasks, performing work accurately, and being neat and careful while writing or drawing). Each item was rated on a 7-point impairment scale (0=normal, 6=maximum impairment), with higher scores indicating more severe symptoms.

End point type	Secondary
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End point timeframe:

Hour 4 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[9]	71 ^[10]		
Units: Units on a scale				
arithmetic mean (standard deviation)	11.8 (± 6.48)	6.7 (± 5.03)		

Notes:

[9] - ITT Population

[10] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 4 Swanson, Kotkin, Alger, M-Flynn and Pelham Scale for Composite (SKAMP-Composite)

End point title	Hour 4 Swanson, Kotkin, Alger, M-Flynn and Pelham Scale for Composite (SKAMP-Composite)
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End point description:

The SKAMP scale measures the manifestations of ADHD using an independent observer (teacher) rating of the child's impairment in classroom behavior. A composite score (range: 0, 78) for the SKAMP variable (13 items total) was obtained by summing the SKAMP-D and SKAMP-A subscale scores. A lower score was preferable, as a higher score represented greater behavioral impairment.

End point type	Secondary
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End point timeframe:

Hour 4 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[11]	71 ^[12]		
Units: Units on a scale				
arithmetic mean (standard deviation)	20.8 (± 11.23)	9.9 (± 7.44)		

Notes:

[11] - ITT Population

[12] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 5.5 Test of Variables of Attention (TOVA) ADHD Composite Cutoff Score

End point title	Hour 5.5 Test of Variables of Attention (TOVA) ADHD Composite Cutoff Score
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End point description:

The TOVA (range: unbounded) is a computerized, visual continuous performance test providing a measure of attention. The stimulus, presented for 100 milliseconds (ms) at the rate of 30 per minute, is a computer-presented square containing a square hole near the top (target) or bottom (non-target) edge. Higher scores indicate better performance, lower scores indicate worse performance. Clinical interpretation: an ADHD scores of -1.80 or lower (≤ -1.80) are considered not within normal limits scores above -1.80 (> -1.80) are considered inconclusive (meaning, neither like-ADHD nor like-normal).

End point type	Secondary
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End point timeframe:

Hour 5.5 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[13]	71 ^[14]		
Units: Units on a scale				
arithmetic mean (standard deviation)	-4.39 (± 3.31)	-1.34 (± 3.43)		

Notes:

[13] - ITT Population

[14] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 5.5 Test of Variables of Attention (TOVA) Reaction Time Standard Score

End point title	Hour 5.5 Test of Variables of Attention (TOVA) Reaction Time Standard Score
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End point description:

The TOVA (range: unbounded) is a computerized, visual continuous performance test providing a measure of attention. The stimulus, presented for 100 milliseconds (ms) at the rate of 30 per minute, is a computer-presented square containing a square hole near the top (target) or bottom (non-target) edge. Higher scores indicated better performance, lower scores indicate worse performance. Clinical interpretation: scores below 80 are considered abnormal, 80-85 are considered borderline, and scores above 85 are considered within normal limits.

End point type	Secondary
End point timeframe:	
Hour 5.5 of the Lab School Day During the Double-Blind Assessment Period	

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[15]	71 ^[16]		
Units: Units on a scale				
arithmetic mean (standard deviation)	73.8 (± 23.74)	89.72 (± 21.32)		

Notes:

[15] - ITT Population

[16] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 5.5 Test of Variables of Attention (TOVA) Reaction Time Variability Standard Score

End point title	Hour 5.5 Test of Variables of Attention (TOVA) Reaction Time Variability Standard Score
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End point description:

The TOVA (range: unbounded) is a computerized, visual continuous performance test providing a measure of attention. The stimulus, presented for 100 milliseconds (ms) at the rate of 30 per minute, is a computer-presented square containing a square hole near the top (target) or bottom (non-target) edge. Higher scores indicated better performance, lower scores indicate worse performance. Clinical interpretation: scores below 80 are considered abnormal, 80-85 are considered borderline, and scores above 85 are considered within normal limits.

End point type	Secondary
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End point timeframe:

Hour 5.5 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[17]	71 ^[18]		
Units: Units on a scale				
arithmetic mean (standard deviation)	62.87 (± 33.789)	85.14 (± 34.906)		

Notes:

[17] - ITT Population

[18] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Concerta

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-22.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.43
upper limit	-17.47

Secondary: Hour 5.5 Wide Range Assessment of Memory and Learning (WRAML-2) Finger Windows Backwards

End point title	Hour 5.5 Wide Range Assessment of Memory and Learning (WRAML-2) Finger Windows Backwards
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End point description:

End point type	Secondary
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End point timeframe:

Time Frame: Hour 5.5 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[19]	71 ^[20]		
Units: Correct Sequences				
arithmetic mean (standard deviation)	11.2 (± 4.25)	12.2 (± 3.57)		

Notes:

[19] - ITT Population

[20] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 5.5 Wide Range Assessment of Memory and Learning (WRAML-2) Finger Windows Forwards

End point title	Hour 5.5 Wide Range Assessment of Memory and Learning (WRAML-2) Finger Windows Forwards
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End point description:

WRAML-2 (range: 0, 28) is designed to evaluate a child's ability to learn and to memorize information, consists of 9 subtests from which 4 summary indexes can be calculated: verbal memory index, visual memory index, learning index, and general memory index. During this test the investigator pointed to a longer and longer series of windows on a card at the rate of 1 location per second, and then the child was asked to reproduce the sequence exactly. One point was given for each correctly recalled sequence, and the test was discontinued after 3 consecutive errors.

End point type	Secondary
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End point timeframe:

Hour 5.5 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[21]	71 ^[22]		
Units: Correct Sequences				
arithmetic mean (standard deviation)	12.9 (± 3.96)	14.3 (± 3.64)		

Notes:

[21] - ITT Population

[22] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 5.5 Test of Variables of Attention (TOVA) Commissions Standard Score

End point title	Hour 5.5 Test of Variables of Attention (TOVA) Commissions Standard Score
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End point description:

The TOVA (range: unbounded) is a computerized, visual continuous performance test providing a measure of attention. The stimulus, presented for 100 milliseconds (ms) at the rate of 30 per minute, is a computer-presented square containing a square hole near the top (target) or bottom (non-target) edge. Higher scores indicated better performance, lower scores indicate worse performance. Clinical interpretation: scores below 80 are considered abnormal, 80-85 are considered borderline, and scores above 85 are considered within normal limits.

End point type	Secondary
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End point timeframe:

Hour 5.5 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[23]	71 ^[24]		
Units: Units on a scale				
arithmetic mean (standard deviation)	86.42 (± 33.261)	92.58 (± 34.545)		

Notes:

[23] - ITT Population

[24] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 5.5 Wechsler Intelligence Scale for Children - 3rd ed. (WISC-III-PI) Digit Span Backwards

End point title	Hour 5.5 Wechsler Intelligence Scale for Children - 3rd ed.
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End point description:

Each child individually was given a sequence of numbers with the sequence becoming progressively longer. The child was then asked to repeat the digits in the same sequence, either forwards or backwards. Each sequence length was attempted twice. The test was complete after failure on both trials of any sequence length. One point was awarded if the participant passed only 1 trial of a sequence length. Zero points were given if the participant failed both trials. The maximum raw scores were 16 forwards and 14 backwards. A higher score was indicative of better recall and attention (range: 0, 14).

End point type	Secondary
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End point timeframe:

Hour 5.5 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[25]	71 ^[26]		
Units: Correct Trials				
arithmetic mean (standard deviation)	5.1 (± 1.97)	5.4 (± 2.12)		

Notes:

[25] - ITT Population

[26] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 8.75 Gray Silent Reading Test (GSRT) Reading Quotient

End point title	Hour 8.75 Gray Silent Reading Test (GSRT) Reading Quotient
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End point description:

Gray Silent Reading Test (GSRT) Reading Quotient is a reliable, validated measure of reading comprehension administered in the group setting during the first half hour of the homework session (range: 0, unbounded). A higher score is preferable as it means more questions were answered correctly.

End point type	Secondary
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End point timeframe:

Hour 8.75 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[27]	71 ^[28]		
Units: Units on a scale				
arithmetic mean (standard deviation)	85.9 (± 23.6)	91.9 (± 18.49)		

Notes:

[27] - ITT Population

[28] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 7.5 Test of Handwriting Skills (Revised) (THS-R) Standard Score

End point title	Hour 7.5 Test of Handwriting Skills (Revised) (THS-R) Standard Score
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End point description:

The THS-R (range: unbounded) is a standardized, untimed assessment designed to evaluate neurosensory integration manifested in manuscript and cursive writing. The test includes subtests: writing from memory or dictation the letters of the alphabet in order, single digit-numbers out of order, selected words, and copying selected letters, words, and sentences. Each subtest was scored from zero (poorly formed letters) to 3 (perfectly formed letters). 100 is the normal mean; scores lower than 100 indicate performance worse than normal, scores above 100 indicate performance better than normal.

End point type	Secondary
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End point timeframe:

Hour 7.5 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[29]	71 ^[30]		
Units: Units on a scale				
arithmetic mean (standard deviation)	93.6 (± 20.77)	98.3 (± 21.81)		

Notes:

[29] - ITT Population

[30] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 3.5 Dynamic Indicators of Basic Early Literacy Skills (DIBELS)

End point title	Hour 3.5 Dynamic Indicators of Basic Early Literacy Skills (DIBELS)
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End point description:

The DIBELS (range: 0, 376), used to assess reading fluency, consists of standardized, individually administered measures of early literacy development. These short (1 minute) fluency measures were developed based upon essential early literacy domains to assess development of phonological awareness, alphabetic understanding, and automaticity and fluency. Only the paragraph fluency component of an age/grade-appropriate DIBELS was used. A higher score indicated better performance, as it represented that the subject orally read a greater number of words correctly within the time allowed.

End point type	Secondary
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End point timeframe:

Hour 3.5 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[31]	71 ^[32]		
Units: Units on a scale				
arithmetic mean (standard deviation)	106.2 (± 35.15)	112 (± 35.51)		

Notes:

[31] - ITT Population

[32] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 5.5 Wechsler Intelligence Scale for Children - 3rd ed. (WISC-III-PI) Digit Span Forwards

End point title	Hour 5.5 Wechsler Intelligence Scale for Children - 3rd ed. (WISC-III-PI) Digit Span Forwards
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End point description:

Each child individually was given a sequence of numbers with the sequence becoming progressively longer. The child was then asked to repeat the digits in the same sequence, either forwards or backwards. Each sequence length was attempted twice. The test was complete after failure on both trials of any sequence length. One point was awarded if the participant passed only 1 trial of a sequence length. Zero points were given if the participant failed both trials. The maximum raw scores were 16 forwards and 14 backwards. A higher score was indicative of better recall and attention (range: 0, 14).

End point type	Secondary
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End point timeframe:

Hour 5.5 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[33]	71 ^[34]		
Units: Correct Trials				
arithmetic mean (standard deviation)	9.2 (± 1.88)	9.3 (± 1.7)		

Notes:

[33] - ITT Population

[34] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 5.5 Test of Variables of Attention (TOVA) Omissions Standard Score

End point title	Hour 5.5 Test of Variables of Attention (TOVA) Omissions Standard Score
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End point description:

The TOVA (range: unbounded) is a computerized, visual continuous performance test providing a measure of attention. The stimulus, presented for 100 milliseconds (ms) at the rate of 30 per minute, is a computer-presented square containing a square hole near the top (target) or bottom (non-target) edge. Higher scores indicated better performance, lower scores indicate worse performance. Clinical interpretation: scores below 80 are considered abnormal, 80-85 are considered borderline, and scores above 85 are considered within normal limits.

End point type	Secondary
End point timeframe:	
Hour 5.5 of the Lab School Day During the Double-Blind Assessment Period	

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[35]	71 ^[36]		
Units: Units on a scale				
arithmetic mean (standard deviation)	25.98 (± 126.281)	64.07 (± 88.77)		

Notes:

[35] - ITT population

[36] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 3.0 Grammar Task

End point title	Hour 3.0 Grammar Task
End point description:	
<p>This task, presented once during a laboratory school day, was designed to index "attention to detail" by determining how many grammatical mistakes each child could identify and circle in a brief paragraph. The errors were not difficult to identify and were designed to show attention to task, not comprehension. A higher number of errors identified, of those possible, was indicative of better attention - identification of grammatical errors(range: 0, 1 represents correct responses divided by the number of possible responses).</p>	
End point type	Secondary
End point timeframe:	
Hour 3.0 of the Lab School Day During the Double-Blind Assessment Period	

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[37]	71 ^[38]		
Units: Units on a scale				
arithmetic mean (standard deviation)	0.241 (± 0.1704)	0.327 (± 0.2204)		

Notes:

[37] - ITT Population

[38] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 8.75 Packet Activity Short Story With Questions for Comprehension

End point title	Hour 8.75 Packet Activity Short Story With Questions for Comprehension
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End point description:

Packet Activities: Assessment of ability to organize, listen to instructions, initiate task, complete task, and distractibility, by completing a word search, reading a short story for comprehension on a multiple choice test, reading a longer story for comprehension on a true/false test, decoding a mystery sentence, and completing various vocabulary assessments (word choice, homophones; base/root words, alphabetic order) (range: 0, 1 represents correct responses divided by the number of possible responses).

End point type	Secondary
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End point timeframe:

Hour 8.75 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[39]	71 ^[40]		
Units: Units on a scale				
arithmetic mean (standard deviation)	0.609 (± 0.2449)	0.629 (± 0.2843)		

Notes:

[39] - ITT Population

[40] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 8.75 Packet Activity Identify Root Word

End point title	Hour 8.75 Packet Activity Identify Root Word
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End point description:

Packet Activities: Assessment of ability to organize, listen to instructions, initiate task, complete task, and distractibility, by completing a word search, reading a short story for comprehension on a multiple choice test, reading a longer story for comprehension on a true/false test, decoding a mystery sentence, and completing various vocabulary assessments (word choice, homophones; base/root words, alphabetic order) (range: 0, 1 represents correct responses divided by the number of possible responses).

End point type	Secondary
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End point timeframe:

Hour 8.75 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[41]	71 ^[42]		
Units: Units on a scale				
arithmetic mean (standard deviation)	0.744 (± 0.3058)	0.76 (± 0.3054)		

Notes:

[41] - ITT Population

[42] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 8.75 Packet Activity Alphabetize List of Words

End point title	Hour 8.75 Packet Activity Alphabetize List of Words
End point description: Packet Activities: Assessment of ability to organize, listen to instructions, initiate task, complete task, and distractibility, by completing a word search, reading a short story for comprehension on a multiple choice test, reading a longer story for comprehension on a true/false test, decoding a mystery sentence, and completing various vocabulary assessments (word choice, homophones; base/root words, alphabetic order) (range: 0, 1 represents correct responses divided by the number of possible responses).	
End point type	Secondary
End point timeframe: Hour 8.75 of the Lab School Day During the Double-Blind Assessment Period	

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[43]	71 ^[44]		
Units: Units on a scale				
arithmetic mean (standard deviation)	0.676 (± 0.34)	0.676 (± 0.3369)		

Notes:

[43] - ITT Population

[44] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 8.75 Packet Activity Identify Multiple Meanings for Words

End point title	Hour 8.75 Packet Activity Identify Multiple Meanings for Words
End point description: Packet Activities: Assessment of ability to organize, listen to instructions, initiate task, complete task, and distractibility, by completing a word search, reading a short story for comprehension on a multiple choice test, reading a longer story for comprehension on a true/false test, decoding a mystery sentence, and completing various vocabulary assessments (word choice, homophones; base/root words, alphabetic order) (range: 0, 1 represents correct responses divided by the number of possible responses).	
End point type	Secondary
End point timeframe: Hour 8.75 of the Lab School Day During the Double-Blind Assessment Period	

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[45]	71 ^[46]		
Units: Units on a scale				
arithmetic mean (standard deviation)	0.694 (± 0.3123)	0.795 (± 0.3019)		

Notes:

[45] - ITT Population

[46] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 8.75 Packet Activity Complete Sentences Using Words Provided

End point title	Hour 8.75 Packet Activity Complete Sentences Using Words Provided
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End point description:

Packet Activities: Assessment of ability to organize, listen to instructions, initiate task, complete task, and distractibility, by completing a word search, reading a short story for comprehension on a multiple choice test, reading a longer story for comprehension on a true/false test, decoding a mystery sentence, and completing various vocabulary assessments (word choice, homophones; base/root words, alphabetic order) (range: 0, 1 represents correct responses divided by the number of possible responses).

End point type	Secondary
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End point timeframe:

Hour 8.75 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[47]	71 ^[48]		
Units: Units on a scale				
arithmetic mean (standard deviation)	0.652 (± 0.3251)	0.741 (± 0.3221)		

Notes:

[47] - ITT Population

[48] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 8.75 Packet Activity Word Search

End point title	Hour 8.75 Packet Activity Word Search
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End point description:

Packet Activities: Assessment of ability to organize, listen to instructions, initiate task, complete task, and distractibility, by completing a word search, reading a short story for comprehension on a multiple choice test, reading a longer story for comprehension on a true/false test, decoding a mystery sentence, and completing various vocabulary assessments (word choice, homophones; base/root words, alphabetic order) (range: 0, 1 represents correct responses divided by the number of possible responses).

End point type	Secondary
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End point timeframe:

Hour 8.75 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[49]	71 ^[50]		
Units: Units on a scale				
arithmetic mean (standard deviation)	0.935 (± 0.1952)	0.979 (± 0.1123)		

Notes:

[49] - ITT Population

[50] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hour 8.75 Packet Activity Decode the Mystery Sentence

End point title	Hour 8.75 Packet Activity Decode the Mystery Sentence
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End point description:

Packet Activities: Assessment of ability to organize, listen to instructions, initiate task, complete task, and distractibility, by completing a word search, reading a short story for comprehension on a multiple choice test, reading a longer story for comprehension on a true/false test, decoding a mystery sentence, and completing various vocabulary assessments (word choice, homophones; base/root words, alphabetic order) (range: 0, 1 represents correct responses divided by the number of possible responses).

End point type	Secondary
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End point timeframe:

Hour 8.75 of the Lab School Day During the Double-Blind Assessment Period

End point values	Placebo	Concerta		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71 ^[51]	71 ^[52]		
Units: Units on a scale				
arithmetic mean (standard deviation)	0.96 (± 0.1566)	0.987 (± 0.0501)		

Notes:

[51] - ITT Population

[52] - ITT Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 to End of treatment

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	11.1
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Reporting groups

Reporting group title	Concerta (Open-Label Dose Adjustment Period)
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Reporting group description:

Subjects initiated with Concerta as 18 milligram/day (mg/day) once daily. Concerta dose was continuously increased until an optimal individualized dose was achieved, up to a maximum dose of 54 mg/day.

Reporting group title	Placebo/Concerta
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Reporting group description:

Children randomized to receive Placebo at lab school day 1 and an individualized, optimal dose of Concerta (18mg, 36mg, or 54 mg tablet) once daily at lab school day 2

Reporting group title	Concerta/Placebo
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Reporting group description:

Children randomized to receive an individualized, optimal dose of Concerta (18mg, 36mg, or 54mg tablet) once daily at lab school day 1 and Placebo at lab school day 2

Serious adverse events	Concerta (Open-Label Dose Adjustment Period)	Placebo/Concerta	Concerta/Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Concerta (Open-Label Dose Adjustment Period)	Placebo/Concerta	Concerta/Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	20 / 36 (55.56%)	15 / 35 (42.86%)
General disorders and administration site conditions			
Chest Pain			
subjects affected / exposed	0 / 7 (0.00%)	3 / 36 (8.33%)	0 / 35 (0.00%)
occurrences (all)	0	4	0

Fatigue			
subjects affected / exposed	0 / 7 (0.00%)	2 / 36 (5.56%)	1 / 35 (2.86%)
occurrences (all)	0	4	1
Irritability			
subjects affected / exposed	0 / 7 (0.00%)	8 / 36 (22.22%)	3 / 35 (8.57%)
occurrences (all)	0	9	4
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Pyrexia			
subjects affected / exposed	0 / 7 (0.00%)	2 / 36 (5.56%)	2 / 35 (5.71%)
occurrences (all)	0	2	2
Thirst			
subjects affected / exposed	0 / 7 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Nasal Congestion			
subjects affected / exposed	0 / 7 (0.00%)	4 / 36 (11.11%)	1 / 35 (2.86%)
occurrences (all)	0	4	1
Cough			
subjects affected / exposed	0 / 7 (0.00%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	0	2	1
Pulmonary Congestion			
subjects affected / exposed	0 / 7 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal Pain			
subjects affected / exposed	0 / 7 (0.00%)	2 / 36 (5.56%)	1 / 35 (2.86%)
occurrences (all)	0	2	1
Rhinorrhoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	0	1	2
Psychiatric disorders			

Affective Disorder			
subjects affected / exposed	0 / 7 (0.00%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Aggression			
subjects affected / exposed	0 / 7 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Anger			
subjects affected / exposed	0 / 7 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Depressed Mood			
subjects affected / exposed	0 / 7 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Emotional Disorder			
subjects affected / exposed	0 / 7 (0.00%)	2 / 36 (5.56%)	1 / 35 (2.86%)
occurrences (all)	0	2	2
Impulse-Control Disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Initial Insomnia			
subjects affected / exposed	0 / 7 (0.00%)	3 / 36 (8.33%)	3 / 35 (8.57%)
occurrences (all)	0	3	3
Logorrhoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	0	1	2
Mental Status Changes			
subjects affected / exposed	0 / 7 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Mood Swings			
subjects affected / exposed	0 / 7 (0.00%)	0 / 36 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Onychophagia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	0	1	2

Sleep Terror subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 36 (2.78%) 1	0 / 35 (0.00%) 0
Social Avoidant Behaviour subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 36 (0.00%) 0	1 / 35 (2.86%) 1
Stereotypy subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 36 (2.78%) 1	1 / 35 (2.86%) 3
Trichotillomania subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 36 (2.78%) 1	1 / 35 (2.86%) 1
Investigations Weight Decreased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 36 (2.78%) 1	1 / 35 (2.86%) 1
Injury, poisoning and procedural complications Arthropod Bite subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 36 (2.78%) 1	0 / 35 (0.00%) 0
Contusion subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 36 (0.00%) 0	1 / 35 (2.86%) 1
Joint Sprain subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 36 (2.78%) 1	0 / 35 (0.00%) 0
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 36 (0.00%) 0	1 / 35 (2.86%) 1
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	3 / 36 (8.33%) 3	1 / 35 (2.86%) 1
Mental Impairment			

subjects affected / exposed	0 / 7 (0.00%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	0 / 7 (0.00%)	4 / 36 (11.11%)	7 / 35 (20.00%)
occurrences (all)	0	5	11
Paraesthesia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	0 / 7 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Abdominal Pain Lower			
subjects affected / exposed	0 / 7 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Abdominal Pain Upper			
subjects affected / exposed	0 / 7 (0.00%)	5 / 36 (13.89%)	8 / 35 (22.86%)
occurrences (all)	0	6	9
Defaecation Urgency			
subjects affected / exposed	0 / 7 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	0	1	2
Dyspepsia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Frequent Bowel Movements			
subjects affected / exposed	0 / 7 (0.00%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	0	1	2
Nausea			
subjects affected / exposed	0 / 7 (0.00%)	2 / 36 (5.56%)	1 / 35 (2.86%)
occurrences (all)	0	2	1

Vomiting subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	2 / 36 (5.56%) 2	0 / 35 (0.00%) 0
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 36 (2.78%) 1	0 / 35 (0.00%) 0
Renal and urinary disorders Urinary Incontinence subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 36 (2.78%) 1	0 / 35 (0.00%) 0
Musculoskeletal and connective tissue disorders Pain in Extremity subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 36 (0.00%) 0	1 / 35 (2.86%) 1
Infections and infestations Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 36 (2.78%) 1	0 / 35 (0.00%) 0
Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	9 / 36 (25.00%) 10	8 / 35 (22.86%) 9

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 October 2008	The first protocol amendment included removal of single-centre text and clarification that subscale scores could be considered to 1) allow subjects with 1 subtype of ADHD (attention deficit hyperactivity disorder) predominating and 2) be used in dose adjustments. Inclusion criteria#4 was updated and visit1 and visit 2 were included. Exclusion criteria #5 changed score to 3, clarified text. Dosage and administration was updated and subscales were allowed for dose adjustments.
11 December 2008	The second protocol amendment included clarification about optimal dose as both total and subscale scores \leq 75th percentile, Laboratory assessment days shortened to 1 month (28 days) from 6 weeks, In inclusion criteria #2 name of Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K- SADS PL) was corrected

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported