



Clinical trial results:

Neurophysiology of Attention-Deficit/Hyperactivity Disorder (ADHD) and Comorbid Dyslexia: Functional Magnetic Resonance Imaging (fMRI) Measures of Brain Activation During Attention and Reading Tasks Pre- and Post-Atomoxetine Treatment

Summary

EudraCT number	2019-000419-98
Trial protocol	Outside EU/EEA
Global end of trial date	01 July 2016

Results information

Result version number	v1 (current)
This version publication date	16 August 2024
First version publication date	16 August 2024

Trial information

Trial identification

Sponsor protocol code	B4Z-US-LYEI
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00716274
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 12212

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 July 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	01 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will evaluate the effects of atomoxetine on brain activation during attention and reading tasks via functional Magnetic Resonance Imaging (fMRI) in participants ages 10 to 16 years old with ADHD and comorbid dyslexia

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 110
Worldwide total number of subjects	110
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)	64
Adolescents (12-17 years)	46
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

No Text Available

Pre-assignment

Screening details:

Participants were randomized to either atomoxetine or placebo during study period II. Placebo participants were then assigned to atomoxetine in study period III. Atomoxetine participants were re-randomized to atomoxetine or placebo in study period III. Participants assigned to the healthy control group did not receive any study drug.

Period 1

Period 1 title	Study Period II (16-Weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Atomoxetine

Arm description:

Atomoxetine (ATX) 1.0 to 1.4 milligram/kilogram/day (mg/kg/day) was administered orally once daily in the morning for 16 weeks, during study period II, (SP II). All eligible participants who received atomoxetine during study period II and completed that period were re-randomized to atomoxetine or placebo in study period III (SP III).

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

Dosage and administration details:

Atomoxetine was administered at 1.0 to 1.4 mg/kg/day given orally once daily in the morning for 16 weeks

Arm title	Placebo
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Arm description:

Placebo (PLA) was packaged in the same way as active comparator to enforce double-blind study design. Placebo was given orally, daily for 16 weeks during SP II. All eligible participants who received placebo during SP II and completed that period were assigned atomoxetine in SP III.

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

Dosage and administration details:

placebo was administered orally, daily, for 16 weeks

Arm title	Healthy Participants
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Arm description:

Healthy Participants: Participants were evaluated to confirm that they did not meet criteria for Attention Deficit Hyperactivity Disorder (ADHD) or dyslexia. They received no treatment during the study.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Atomoxetine	Placebo	Healthy Participants
Started	45	44	21
Completed	36	35	19
Not completed	9	9	2
Parent/Caregiver Decision	3	3	-
Consent withdrawn by subject	1	-	-
Physician decision	3	1	1
Lost to follow-up	-	2	-
Entry Criteria Not Met	2	-	-
Protocol deviation	-	3	1

Period 2

Period 2 title	Study Period III (16-Weeks)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	ATX/ATX

Arm description:

These participants were randomized to atomoxetine in SP II and were re-randomized to atomoxetine in SP III. Atomoxetine was dosed orally once-daily in the morning 0.5 mg/kg/day for 3 days and then titrated up to a dose between 1.2 and 1.4 mg/kg/day.

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

Dosage and administration details:

Atomoxetine was administered at 1.0 to 1.4 mg/kg/day given orally once daily in the morning for 16 weeks

Arm title	ATX/PLA
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Arm description:

These participants were randomized to atomoxetine in SP II and were re-randomized to placebo in SP III. Atomoxetine was dosed orally once-daily in the morning 0.5 mg/kg/day for 3 days and then titrated up to a dose between 1.2 and 1.4 mg/kg/day.

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

Dosage and administration details:

Atomoxetine was administered at 1.0 to 1.4 mg/kg/day given orally once daily in the morning for 16 weeks

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo was administered orally, daily, for 16 weeks

Arm title	PLA/ATX
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Arm description:

These participants were randomized to placebo in SP II and were assigned to atomoxetine in SP III. Atomoxetine was dosed orally once-daily in the morning 0.5 mg/kg/day for 3 days and then titrated up to a dose between 1.2 and 1.4 mg/kg/day.

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

Dosage and administration details:

placebo was administered orally, daily, for 16 weeks

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

Dosage and administration details:

Atomoxetine was administered at 1.0 to 1.4 mg/kg/day given orally once daily in the morning for 16 weeks

Arm title	Healthy Participants
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Arm description:

Healthy Participants: Participants were evaluated to confirm that they did not meet criteria for Attention Deficit Hyperactivity Disorder (ADHD) or dyslexia. They received no treatment during the study.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	ATX/ATX	ATX/PLA	PLA/ATX
Started	18	18	35
Completed	16	17	32
Not completed	2	1	3
Consent withdrawn by subject	2	-	-
Physician decision	-	-	1
Adverse event, non-fatal	-	-	1
Parent Caregiver Decision	-	1	1

Number of subjects in period 2	Healthy Participants
Started	19
Completed	19
Not completed	0
Consent withdrawn by subject	-
Physician decision	-
Adverse event, non-fatal	-
Parent Caregiver Decision	-

Baseline characteristics

Reporting groups

Reporting group title	Atomoxetine
Reporting group description:	
Atomoxetine (ATX) 1.0 to 1.4 milligram/kilogram/day (mg/kg/day) was administered orally once daily in the morning for 16 weeks, during study period II, (SP II). All eligible participants who received atomoxetine during study period II and completed that period were re-randomized to atomoxetine or placebo in study period III (SP III).	
Reporting group title	Placebo
Reporting group description:	
Placebo (PLA) was packaged in the same way as active comparator to enforce double-blind study design. Placebo was given orally, daily for 16 weeks during SP II. All eligible participants who received placebo during SP II and completed that period were assigned atomoxetine in SP III.	
Reporting group title	Healthy Participants
Reporting group description:	
Healthy Participants: Participants were evaluated to confirm that they did not meet criteria for Attention Deficit Hyperactivity Disorder (ADHD) or dyslexia. They received no treatment during the study.	

Reporting group values	Atomoxetine	Placebo	Healthy Participants
Number of subjects	45	44	21
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	12.2	12.1	12.4
standard deviation	± 1.89	± 1.90	± 2.05
Gender categorical			
Units: Subjects			
Female	18	17	13
Male	27	27	8
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	6	2	4
Not Hispanic or Latino	39	42	17
Unknown or Not Reported	0	0	0
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	4	13	5
White	33	29	12
More than one race	0	0	0
Unknown or Not Reported	6	2	4
Region of Enrollment			
Units: Subjects			
United States	45	44	21

Reporting group values	Total		
Number of subjects	110		
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	48		
Male	62		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	12		
Not Hispanic or Latino	98		
Unknown or Not Reported	0		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	2		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	22		
White	74		
More than one race	0		
Unknown or Not Reported	12		
Region of Enrollment Units: Subjects			
United States	110		

End points

End points reporting groups

Reporting group title	Atomoxetine
Reporting group description: Atomoxetine (ATX) 1.0 to 1.4 milligram/kilogram/day (mg/kg/day) was administered orally once daily in the morning for 16 weeks, during study period II, (SP II). All eligible participants who received atomoxetine during study period II and completed that period were re-randomized to atomoxetine or placebo in study period III (SP III).	
Reporting group title	Placebo
Reporting group description: Placebo (PLA) was packaged in the same way as active comparator to enforce double-blind study design. Placebo was given orally, daily for 16 weeks during SP II. All eligible participants who received placebo during SP II and completed that period were assigned atomoxetine in SP III.	
Reporting group title	Healthy Participants
Reporting group description: Healthy Participants: Participants were evaluated to confirm that they did not meet criteria for Attention Deficit Hyperactivity Disorder (ADHD) or dyslexia. They received no treatment during the study.	
Reporting group title	ATX/ATX
Reporting group description: These participants were randomized to atomoxetine in SP II and were re-randomized to atomoxetine in SP III. Atomoxetine was dosed orally once-daily in the morning 0.5 mg/kg/day for 3 days and then titrated up to a dose between 1.2 and 1.4 mg/kg/day.	
Reporting group title	ATX/PLA
Reporting group description: These participants were randomized to atomoxetine in SP II and were re-randomized to placebo in SP III. Atomoxetine was dosed orally once-daily in the morning 0.5 mg/kg/day for 3 days and then titrated up to a dose between 1.2 and 1.4 mg/kg/day.	
Reporting group title	PLA/ATX
Reporting group description: These participants were randomized to placebo in SP II and were assigned to atomoxetine in SP III. Atomoxetine was dosed orally once-daily in the morning 0.5 mg/kg/day for 3 days and then titrated up to a dose between 1.2 and 1.4 mg/kg/day.	
Reporting group title	Healthy Participants
Reporting group description: Healthy Participants: Participants were evaluated to confirm that they did not meet criteria for Attention Deficit Hyperactivity Disorder (ADHD) or dyslexia. They received no treatment during the study.	

Primary: Change From Baseline to Endpoint in Functional Magnetic Resonance Imaging (fMRI) Activation in Participants With Dyslexia Alone (Pseudoword Rhyming and Semantic-category)

End point title	Change From Baseline to Endpoint in Functional Magnetic Resonance Imaging (fMRI) Activation in Participants With Dyslexia Alone (Pseudoword Rhyming and Semantic-category) ^{[1][2]}
End point description: Change From Baseline to Endpoint in Functional Magnetic Resonance Imaging (fMRI) Activation in Participants With Dyslexia Alone (Pseudoword Rhyming and Semantic-category). Analysis Population Description (APD): All participants who received study drug, had Dyslexia Alone and had fMRI data.	
End point type	Primary
End point timeframe: Baseline, 16 Weeks	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No inferential statistical analyses was planned for this endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13 ^[3]	10 ^[4]		
Units: scores on a scale				
arithmetic mean (standard deviation)				
Semantic-category: Left Inferior Frontal Gyrus	-0.056 (± 0.125)	-0.033 (± 0.118)		
Semantic-category: Left Interior Temporal Gyrus	-0.061 (± 0.120)	0.010 (± 0.075)		
Semantic-category: Left Medial Temporal Gyrus	-0.038 (± 0.153)	-0.006 (± 0.053)		
Semantic-category: Left Temporo-parietal Region	-0.073 (± 0.124)	-0.037 (± 0.100)		
Semantic-category: Right Inferior Frontal Gyrus	0.019 (± 0.156)	0.018 (± 0.147)		
Semantic-category: Right Interior Temporal Gyrus	0.002 (± 0.217)	0.058 (± 0.161)		
Semantic-category: Right Medial Temporal Gyrus	-0.014 (± 0.181)	0.071 (± 0.091)		
Semantic-category: Right Temporo-parietal Region	-0.015 (± 0.145)	0.076 (± 0.114)		
Pseudoword Rhyming: Left Inferior Frontal Gyrus	0.012 (± 0.200)	0.020 (± 0.147)		
Pseudoword Rhyming: Left Interior Temporal Gyrus	-0.062 (± 0.200)	-0.003 (± 0.109)		
Pseudoword Rhyming: Left Medial Temporal Gyrus	0.005 (± 0.253)	0.024 (± 0.133)		
Pseudoword Rhyming: Left Temporo-parietal Region	-0.026 (± 0.243)	-0.012 (± 0.115)		
Pseudoword Rhyming: Right Inferior Frontal Gyrus	-0.017 (± 0.304)	0.024 (± 0.187)		
Pseudoword Rhyming: Right Interior Temporal Gyrus	0.013 (± 0.266)	0.103 (± 0.174)		
Pseudoword Rhyming: Right Medial Temporal Gyrus	0.039 (± 0.250)	0.009 (± 0.098)		
Pseudoword Rhyming: Temporo-parietal Region	0.011 (± 0.296)	0.087 (± 0.170)		

Notes:

[3] - Semantic-category, Pseudoword Rhyming: n = 13

[4] - Semantic-category: n = 10

Pseudoword Rhyming: n = 09

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline to Endpoint in fMRI Activation in Participants With Dyslexia Alone (Stroop Attention Tasks)

End point title	Change From Baseline to Endpoint in fMRI Activation in Participants With Dyslexia Alone (Stroop Attention Tasks) ^{[5][6]}
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End point description:

Change From Baseline to Endpoint in fMRI Activation in Participants With Dyslexia Alone (Stroop Attention Tasks). APD: Stroop Tasks data were not collected.

End point type	Primary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No inferential statistical analyses was planned for this endpoint.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[7]	0 ^[8]		
Units: scores on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[7] - Stroop Tasks data were not collected.

[8] - Stroop Tasks data were not collected.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline to Endpoint in fMRI Activation in Participants With ADHD or ADHD + Dyslexia (Pseudoword Rhyming and Semantic-category Tasks)

End point title	Change From Baseline to Endpoint in fMRI Activation in Participants With ADHD or ADHD + Dyslexia (Pseudoword Rhyming and Semantic-category Tasks) ^{[9][10]}
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End point description:

Change From Baseline to Endpoint in fMRI Activation in Participants With ADHD or ADHD + Dyslexia (Pseudoword Rhyming and Semantic-category Tasks). APD: All participants who received study drug, had ADHD or ADHD + Dyslexia and had fMRI data.

End point type	Primary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No inferential statistical analyses was planned for this endpoint.

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11 ^[11]	12 ^[12]		
Units: scores on a scale				
arithmetic mean (standard deviation)				
ADHD+Dyslexia, SC: Left Inferior Frontal Gyrus	0.077 (± 0.085)	-0.038 (± 0.141)		

ADHD+Dyslexia, SC: Left Interior Temporal Gyrus	0.079 (\pm 0.128)	-0.1 (\pm 0.252)		
ADHD+Dyslexia, SC: Left Medial Temporal Gyrus	0.038 (\pm 0.105)	-0.037 (\pm 0.208)		
ADHD+Dyslexia, SC: Left Temporo-parietal Region	0.079 (\pm 0.065)	-0.096 (\pm 0.187)		
ADHD+Dyslexia, SC: Right Interior Frontal Gyrus	0.065 (\pm 0.095)	-0.016 (\pm 0.152)		
ADHD+Dyslexia, SC: Right Interior Temporal Gyrus	0.008 (\pm 0.150)	0.015 (\pm 0.222)		
ADHD+Dyslexia, SC: Right Medial Temporal Gyrus	-0.046 (\pm 0.169)	-0.045 (\pm 0.168)		
ADHD+Dyslexia, SC: Right Temporo-parietal Region	0.053 (\pm 0.120)	-0.035 (\pm 0.153)		
ADHD+Dyslexia, PR: Left Inferior Frontal Gyrus	0.081 (\pm 0.245)	0.005 (\pm 0.151)		
ADHD+Dyslexia, PR: Left Interior Temporal Gyrus	0.142 (\pm 0.370)	0.047 (\pm 0.202)		
ADHD+Dyslexia, PR: Left Medial Temporal Gyrus	0.091 (\pm 0.387)	0.042 (\pm 0.184)		
ADHD+Dyslexia, PR: Left Temporo-parietal Region	0.096 (\pm 0.321)	0.012 (\pm 0.184)		
ADHD+Dyslexia, PR: Right Inferior Frontal Gyrus	0.069 (\pm 0.291)	-0.006 (\pm 0.111)		
ADHD+Dyslexia, PR: Right Interior Temporal Gyrus	0.114 (\pm 0.453)	0.047 (\pm 0.164)		
ADHD+Dyslexia, PR: Right Medial Temporal Gyrus	0.080 (\pm 0.470)	0.002 (\pm 0.203)		
ADHD+Dyslexia, PR: Temporo-parietal Region	0.078 (\pm 0.308)	-0.026 (\pm 0.147)		
ADHD Only, SC: Left Inferior Frontal Gyrus	0.013 (\pm 0.166)	-0.057 (\pm 0.120)		
ADHD Only, SC: Left Interior Temporal Gyrus	-0.024 (\pm 0.083)	-0.035 (\pm 0.105)		
ADHD Only, SC: Left Medial Temporal Gyrus	-0.002 (\pm 0.168)	-0.047 (\pm 0.166)		
ADHD Only, SC: Left Temporo-parietal Region	-0.013 (\pm 0.131)	-0.064 (\pm 0.124)		
ADHD Only, SC: Right Inferior Frontal Gyrus	-0.074 (\pm 0.141)	-0.030 (\pm 0.211)		
ADHD Only, SC: Right Interior Temporal Gyrus	0.052 (\pm 0.236)	-0.100 (\pm 0.141)		
ADHD Only, SC: Right Medial Temporal Gyrus	-0.039 (\pm 0.240)	0.019 (\pm 0.211)		
ADHD Only, SC: Right Temporo-parietal Region	0.034 (\pm 0.124)	-0.101 (\pm 0.129)		
ADHD Only, PR: Left Inferior Frontal Gyrus	-0.029 (\pm 0.153)	0.101 (\pm 0.203)		
ADHD Only, PR: Left Interior Temporal Gyrus	-0.012 (\pm 0.194)	0.063 (\pm 0.240)		
ADHD Only, PR: Left Medial Temporal Gyrus	-0.030 (\pm 0.137)	0.058 (\pm 0.260)		
ADHD Only, PR: Left Temporo-parietal Region	-0.013 (\pm 0.172)	0.029 (\pm 0.195)		
ADHD Only, PR: Right Inferior Frontal Gyrus	0.005 (\pm 0.139)	0.088 (\pm 0.289)		
ADHD Only, PR: Right Interior Temporal Gyrus	-0.003 (\pm 0.226)	0.043 (\pm 0.246)		
ADHD Only, PR: Right Medial Temporal Gyrus	0.007 (\pm 0.116)	-0.011 (\pm 0.402)		
ADHD Only, PR: Temporo-parietal Region	-0.016 (\pm 0.204)	0.046 (\pm 0.149)		

Notes:

[11] - ADHD+Dyslexia, Semantic-category (SC): n=10, Pseudoword Rhyming (PR): n=9;
ADHD Only, SC, PR: n=11

[12] - ADHD+Dyslexia, Semantic-category (SC): n=12, Pseudoword Rhyming (PR): n=11; ADHD Only,
SC, PR: n=8

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline to Endpoint in fMRI Activation in Participants With ADHD or ADHD + Dyslexia (Stroop Tasks)

End point title	Change From Baseline to Endpoint in fMRI Activation in Participants With ADHD or ADHD + Dyslexia (Stroop Tasks) ^{[13][14]}
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End point description:

Change From Baseline to Endpoint in fMRI Activation in Participants With ADHD or ADHD + Dyslexia (Stroop Tasks). Stroop Tasks data were not collected.

End point type	Primary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No inferential statistical analyses was planned for this endpoint.

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[15]	0 ^[16]		
Units: scores on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[15] - Stroop Tasks data were not collected.

[16] - Stroop Tasks data were not collected.

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline to Endpoint in Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Parent Version (ADHDRS) Total Score in the ADHD or ADHD + Dyslexia

End point title	Change from Baseline to Endpoint in Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Parent Version (ADHDRS) Total Score in the ADHD or ADHD + Dyslexia ^{[17][18]}
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End point description:

The ADHDRS-IV-Parent is an 18-item scale with 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD. Each item is scored on a 0 to 3 scale: 0=none (never or rarely); 1=mild (sometimes); 2=moderate (often); 3=severe (very often). Total scores range from 0-54. Higher scores indicate higher impairment and lower scores indicate no impairment. LS mean was calculated using a restricted maximum likelihood (REML)-based, MMRM analysis which includes treatment, baseline, visit, treatment-by-visit interaction, and baseline-by-visit interaction. All randomized participants who

received at least one dose of study drug and had evaluable baseline and post baseline ADHDRS-IV-Parent: Inv measurements.

End point type	Primary
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End point timeframe:

Baseline, 16 weeks

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No inferential statistical analyses was planned for this endpoint.

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	23		
Units: units on a scale				
least squares mean (standard error)				
ADHD + Dyslexia	-11.04 (± 2.518)	-7.53 (± 2.155)		
ADHD Alone	-13.85 (± 2.323)	-1.63 (± 2.588)		

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline to Endpoint in Woodcock Johnson Tests of Achievement (WJ III) Word Attack Total Score in Participants with Dyslexia Alone

End point title	Change from Baseline to Endpoint in Woodcock Johnson Tests of Achievement (WJ III) Word Attack Total Score in Participants with Dyslexia Alone ^{[19][20]}
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End point description:

WJ III (Woodcock et al. 2001) has 2 parallel forms (A & B) alternating 2 batteries of tests—Standard & Extended. Standard tests (1 -12) have a broad set of scores. Extended tests (13 -22) have a more in-depth diagnostic assessment of academic strengths & weaknesses. Tests administered were 1, 2, 7, 9, 13, 17, & 20. Standard score scale is a mean (M) of 100 & a standard deviation (SD) of 15. WJ III ACH has extended standard scores which is a greater range of standard scores. Each individual test scores range from 0 to over 200 where 69 & below is very low & 131 and above is very superior. Higher scores indicate better reading skills. Least Square (LS) Mean was analyzed using last observation carried forward (LOCF), fixed-effects analysis of covariate (ANCOVA) models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received at least one dose of study drug and had evaluable baseline and post baseline WJ III measurements.

End point type	Primary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No inferential statistical analyses was planned for this endpoint.

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: units on a scale				
least squares mean (standard error)	-3.57 (± 4.84)	2.92 (± 4.75)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in Basic Reading Skills Cluster WJ III in Participants with Dyslexia Alone

End point title	Change from Baseline to Endpoint in Basic Reading Skills Cluster WJ III in Participants with Dyslexia Alone ^[21]
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End point description:

WJ III (Woodcock et al. 2001) has 2 parallel forms (A & B) alternating 2 batteries of tests—Standard & Extended. Standard score scale is a mean (M) of 100 & a standard deviation (SD) of 15. Basic Reading Skills is an aggregate measure of sight vocabulary, phonics, & structural analysis. It is a combination of Test 1, Letter-Word Identification, which measures the participant's word identification skills. It is the average (arithmetic mean) of tests 1 & 13. Scores for each individual test range from 0 to over 200 where 69 & below is very low and 131 & above is very superior. Higher scores indicate better reading skills. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received at least 1 dose of study drug & had evaluable baseline and post baseline WJ III measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: units on a scale				
least squares mean (standard error)	-2.81 (± 3.87)	2.25 (± 3.85)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in BADD-A Total Score in Participants With ADHD or ADHD + Dyslexia

End point title	Change From Baseline to Endpoint in BADD-A Total Score in Participants With ADHD or ADHD + Dyslexia ^[22]
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End point description:

The BADD-A is used to assess impairment in executive functions related to ADHD. These include 1) Organizing, prioritizing, and activating to work; 2) Focusing, sustaining and shifting attention to tasks;

3) Regulating alertness, sustaining effort, and processing speed; 4) Managing frustration and modulating emotions; 5) Utilizing working memory and accessing recall (Brown 2001). Scores range from 0-120. The higher the score the more severe the attention-deficit disorder (ADD). 0-39 equate to, "ADD possible but not likely". 40-54 equate to, "ADD probable but not certain". 55-120 equate to, "ADD highly probable". LS mean was calculated using a REML-based, MMRM analysis which includes treatment, baseline, visit, treatment-by-visit interaction, and baseline-by-visit interaction. APD: All randomized participants who received at least one dose of study drug and had evaluable baseline and post baseline BADD-A measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	22		
Units: units on a scale				
least squares mean (standard error)				
ADHD + Dyslexia	-6.91 (± 4.689)	-4.29 (± 4.128)		
ADHD Alone	-9.05 (± 5.515)	-1.85 (± 6.695)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in WJ III Individual Test Scores in Participants With Dyslexia Alone

End point title	Change From Baseline to Endpoint in WJ III Individual Test Scores in Participants With Dyslexia Alone ^[23]
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End point description:

WJ III (Woodcock et al. 2001) has two parallel forms (A and B) alternating two batteries of tests—Standard and Extended. Standard tests (1 -12) have a broad set of scores. Extended tests (13 - 22) have a more in-depth diagnostic assessment of academic strengths and weaknesses. Tests administered were 1, 2, 7, 9, 13, 17, and 20. The standard score scale is a mean (M) of 100 and a standard deviation (SD) of 15. The WJ III ACH has extended standard scores, which is a greater range of standard scores. Scores for each individual test range from 0 to over 200 where 69 and below is very low and 131 and above is very superior. Higher scores indicate better reading skills. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who had a WJ III baseline and post-baseline

End point type	Secondary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: units on a scale				
least squares mean (standard error)				
Letter Word Identification	0.88 (± 1.12)	2.77 (± 1.10)		
Word Attack Score	0.48 (± 1.71)	2.53 (± 1.68)		
Reading Vocabulary Score	1.04 (± 1.81)	-1.73 (± 1.75)		
Reading Fluency Score	0.13 (± 1.59)	-1.06 (± 1.53)		
Reading Comprehension Score	2.38 (± 1.81)	-1.03 (± 1.74)		
Spelling Score	0.89 (± 1.50)	-0.36 (± 1.48)		
Spelling of Sounds Score	3.11 (± 1.48)	3.59 (± 1.43)		
Basic Reading Skills Score	0.99 (± 1.15)	2.13 (± 1.15)		
Passage Comprehension	2.80 (± 2.03)	-0.20 (± 1.96)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in WJ III Individual Test Scores in Participants With ADHD + Dyslexia

End point title	Change From Baseline to Endpoint in WJ III Individual Test Scores in Participants With ADHD + Dyslexia ^[24]
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End point description:

WJ III (Woodcock et al. 2001) has two parallel forms (A and B) alternating two batteries of tests—Standard and Extended. Standard tests (1 -12) have a broad set of scores. Extended tests (13 - 22) have a more in-depth diagnostic assessment of academic strengths and weaknesses. Tests administered were 1, 2, 7, 9, 13, 17, and 20. The standard score scale is a mean (M) of 100 and a standard deviation (SD) of 15. The WJ III ACH has extended standard scores, which is a greater range of standard scores. Scores for each individual test range from 0 to over 200 where 69 and below is very low and 131 and above is very superior. Higher scores indicate better reading skills. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who had a baseline and post-baseline WJ III

End point type	Secondary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: units on a scale				
least squares mean (standard error)				
Reading Fluency	-3.41 (± 2.16)	2.61 (± 2.06)		
Reading Comprehension	2.02 (± 1.63)	0.80 (± 1.56)		
Letter Word Identification	1.71 (± 1.75)	-0.90 (± 1.69)		
Word Attack Score	2.65 (± 1.13)	0.71 (± 1.07)		
Reading Vocabulary	0.69 (± 1.89)	2.80 (± 1.77)		

Spelling	-1.36 (± 2.25)	-2.59 (± 2.19)		
Spelling of Sounds	8.42 (± 1.76)	5.02 (± 1.67)		
Basic Reading Skills	2.53 (± 1.05)	-0.21 (± 1.01)		
Passage Comprehension Score	2.65 (± 1.71)	-1.01 (± 1.65)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in WJ III Individual Test Scores in Participants With ADHD Alone

End point title	Change From Baseline to Endpoint in WJ III Individual Test Scores in Participants With ADHD Alone ^[25]
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End point description:

WJ III (Woodcock et al. 2001) has two parallel forms (A and B) alternating two batteries of tests—Standard and Extended. Standard tests (1 -12) have a broad set of scores. Extended tests (13 - 22) have a more in-depth diagnostic assessment of academic strengths and weaknesses. Tests administered were 1, 2, 7, 9, 13, 17, and 20. The standard score scale is a mean (M) of 100 and a standard deviation (SD) of 15. The WJ III ACH has extended standard scores, which is a greater range of standard scores. Scores for each individual test range from 0 to over 200 where 69 and below is very low and 131 and above is very superior. Higher scores indicate better reading skills. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. All randomized participants who had a baseline and post-baseline WJ III measurement.

End point type	Secondary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: units on a scale				
least squares mean (standard error)				
Reading Fluency	-2.70 (± 1.58)	-4.98 (± 1.81)		
Reading Comprehension	-2.92 (± 2.39)	-1.40 (± 2.77)		
Letter Word Identification	2.60 (± 1.77)	0.46 (± 2.08)		
Word Attack Score	-1.60 (± 1.56)	0.08 (± 1.78)		
Reading Vocabulary	-1.15 (± 2.65)	-1.48 (± 3.23)		
Spelling	4.30 (± 1.20)	3.62 (± 1.39)		
Spelling of Sounds	5.90 (± 3.51)	0.57 (± 4.04)		
Basic Reading Skills	0.86 (± 1.42)	0.48 (± 1.65)		
Passage Comprehension Score	-4.10 (± 2.36)	-1.80 (± 2.70)		

Statistical analyses

Secondary: Change from Baseline to Endpoint in Comprehensive Test of Phonological Processing (CTOPP) Composite Scores in Participants with Dyslexia Alone

End point title	Change from Baseline to Endpoint in Comprehensive Test of Phonological Processing (CTOPP) Composite Scores in Participants with Dyslexia Alone ^[26]
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End point description:

The CTOPP assesses phonological awareness, phonological memory, and rapid naming and is appropriate for ages 7 to 24. The test contains six core subtests. The composite scores are 1) Phonological Awareness, comprised of the standard scores of the Elision and Blending Words; 2) Phonological Memory, comprised of standard scores for Memory for Digits and Non-word Repetition; and 3) Rapid Naming, comprised of standard scores for Rapid Digit Naming and Rapid Letter Naming. Standard scores range from 1-20, and composite scores range from 35-165. Higher scores are better and lower scores are poor. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. All randomized participants who received at least one dose of study drug and had evaluable baseline and post baseline CTOPP measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 weeks

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: units on a scale				
arithmetic mean (standard deviation)				
Phonological Awareness	4.01 (± 4.81)	2.69 (± 1.91)		
Phonological Memory	5.62 (± 1.82)	0.62 (± 1.75)		
Rapid Naming Score	0.19 (± 2.31)	-1.00 (± 2.23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in CTOPP Composite Score in Participants with ADHD + Dyslexia

End point title	Change from Baseline to Endpoint in CTOPP Composite Score in Participants with ADHD + Dyslexia ^[27]
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End point description:

The CTOPP assesses phonological awareness, phonological memory, and rapid naming and is appropriate for ages 7 to 24. The test contains six core subtests. The composite scores are 1) Phonological Awareness, comprised of the standard scores of the Elision and Blending Words; 2) Phonological Memory, comprised of standard scores for Memory for Digits and Non-word Repetition; and 3) Rapid Naming, comprised of standard scores for Rapid Digit Naming and Rapid Letter Naming. Standard scores range from 1-20, and composite scores range from 35-165. Higher scores are better and lower scores are poor. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. All randomized participants who received at least one dose of study drug and had evaluable baseline and post baseline CTOPP measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 weeks

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	15		
Units: units on a scale				
arithmetic mean (standard deviation)				
Phonological Awareness	4.60 (± 1.74)	1.35 (± 1.66)		
Phonological Memory	2.33 (± 2.49)	3.43 (± 2.39)		
Rapid Naming Score	-0.71 (± 2.46)	0.21 (± 2.29)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in CTOPP Composite Score in Participants with ADHD Alone

End point title	Change from Baseline to Endpoint in CTOPP Composite Score in Participants with ADHD Alone ^[28]
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End point description:

The CTOPP assesses phonological awareness, phonological memory, and rapid naming and is appropriate for ages 7 to 24. The test contains six core subtests. The composite scores are 1) Phonological Awareness, comprised of the standard scores of the Elision and Blending Words; 2) Phonological Memory, comprised of standard scores for Memory for Digits and Non-word Repetition; and 3) Rapid Naming, comprised of standard scores for Rapid Digit Naming and Rapid Letter Naming. Standard scores range from 1-20, and composite scores range from 35-165. Higher scores are better and lower scores are poor. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received at least one dose of study drug and had evaluable baseline and post baseline CTOPP measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 weeks

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	9		
Units: units on a scale				
arithmetic mean (standard deviation)				
Phonological Awareness	3.66 (± 2.10)	7.00 (± 2.57)		
Phonological Memory	3.70 (± 2.61)	3.48 (± 2.98)		
Rapid Naming Score	2.36 (± 3.01)	1.63 (± 3.47)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in Gray Oral Reading Tests-4 (GORT-4) in Participants with Dyslexia Alone

End point title	Change from Baseline to Endpoint in Gray Oral Reading Tests-4 (GORT-4) in Participants with Dyslexia Alone ^[29]
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End point description:

The GORT-4 is a norm-referenced test of oral reading rate, accuracy, fluency, and comprehension valid for individuals aged 6 to 18 years old. The test has two parallel forms, Form A and Form B, that are administered in an alternating fashion (e.g. Week 0-Form A, Week 16-Form B, Week 32-Form A.) with each containing 14 separate stories and 5 multiple-choice comprehension questions for each story. GORT-4 yields the following scores: rate, accuracy, fluency, comprehension, and overall reading ability. Standard scores range from 1-20. Higher scores indicate better reading skills. Lower scores indicate poor reading skills. LS mean was analyzed using LOCF, fixed-effects ANCOVA models of with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received at least one dose of study drug and had evaluable baseline and post baseline GORT-4 measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 weeks

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: units on a scale				
least squares mean (standard error)				
Oral Reading Rate	0.24 (± 0.27)	-0.44 (± 0.27)		
Accuracy	-0.10 (± 0.46)	-0.72 (± 0.47)		
Fluency	-0.17 (± 0.42)	-0.65 (± 0.42)		
Reading Comprehension	0.89 (± 0.77)	-0.29 (± 0.77)		
Oral Reading Quotient	2.30 (± 2.69)	-2.66 (± 2.72)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in GORT-4 in Participants with ADHD + Dyslexia

End point title	Change from Baseline to Endpoint in GORT-4 in Participants with ADHD + Dyslexia ^[30]
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End point description:

The GORT-4 is a norm-referenced test of oral reading rate, accuracy, fluency, and comprehension valid for individuals aged 6 to 18 years old. The test has two parallel forms, Form A and Form B, that are administered in an alternating fashion (e.g. Week 0-Form A, Week 16-Form B, Week 32-Form A.) with each containing 14 separate stories and 5 multiple-choice comprehension questions for each story. GORT-4 yields the following scores: rate, accuracy, fluency, comprehension, and overall reading ability. Standard scores range from 1-20. Higher scores indicate better reading skills. Lower scores indicate poor reading skills. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms of treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received at least one dose of study drug and had evaluable baseline and post baseline GORT-4 measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 weeks

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	15		
Units: units on a scale				
least squares mean (standard error)				
Oral Reading Rate	-0.59 (± 0.40)	-0.45 (± 0.37)		
Accuracy	-1.77 (± 0.53)	-1.02 (± 0.47)		
Fluency	-1.66 (± 0.34)	-0.81 (± 0.31)		
Reading Comprehension	-2.46 (± 0.67)	-1.55 (± 0.62)		
Oral Reading Quotient	-14.01 (± 4.10)	-12.23 (± 3.40)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in GORT-4 in Participants with ADHD Alone

End point title	Change from Baseline to Endpoint in GORT-4 in Participants with ADHD Alone ^[31]
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End point description:

The GORT-4 is a norm-referenced test of oral reading rate, accuracy, fluency, and comprehension valid for individuals aged 6 to 18 years old. The test has two parallel forms, Form A and Form B, that are administered in an alternating fashion (e.g. Week 0-Form A, Week 16-Form B, Week 32-Form A.) with each containing 14 separate stories and 5 multiple-choice comprehension questions for each story. GORT-4 yields the following scores: rate, accuracy, fluency, comprehension, and overall reading ability. Standard scores range from 1-20. Higher scores indicate better reading skills. Lower scores indicate poor reading skills. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms of treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received at least one dose of study drug and had evaluable baseline and post baseline GORT-4 measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 weeks

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	9		
Units: units on a scale				
least squares mean (standard error)				
Oral Reading Rate	0.80 (± 0.42)	0.97 (± 0.48)		
Accuracy	0.46 (± 0.35)	-0.17 (± 0.40)		
Fluency	0.72 (± 0.35)	0.94 (± 0.40)		
Reading Comprehension	-0.96 (± 0.59)	0.79 (± 0.70)		
Oral Reading Quotient	-0.74 (± 2.12)	5.63 (± 2.46)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint Test of Word Reading Efficiency (TOWRE) Total Score in Participants with Dyslexia Alone

End point title	Change from Baseline to Endpoint Test of Word Reading Efficiency (TOWRE) Total Score in Participants with Dyslexia Alone ^[32]
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End point description:

The TOWRE is a measure of an individual's ability to pronounce printed words accurately and fluently and is appropriate for individuals aged 6 to 24 years old. The TOWRE contains two subtests: Sight Word Efficiency (SWE) which assesses the number of real printed words that can be accurately identified within 45 seconds and Phonemic Decoding Efficiency (PDE) which measures the number of pronounceable printed non-words that can be accurately decoded within 45 seconds. The total standard score ranges from 35-165. Higher scores indicate higher reading proficiency and lower scores indicate lower reading proficiency. LS mean was calculated using a REML-based, MMRM analysis which includes treatment, baseline, visit, treatment-by-visit interaction, and baseline-by-visit interaction. APD: All randomized participants who received at least one dose of study drug and had evaluable baseline and post baseline TOWRE measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	12		
Units: units on a scale				
least squares mean (standard error)	2.21 (± 1.345)	-0.17 (± 1.471)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in TOWRE Total Score in Participants with ADHD or ADHD + Dyslexia

End point title	Change from Baseline to Endpoint in TOWRE Total Score in Participants with ADHD or ADHD + Dyslexia ^[33]
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End point description:

The TOWRE is a measure of an individual's ability to pronounce printed words accurately and fluently and is appropriate for individuals aged 6 to 24 years old. The TOWRE contains two subtests: Sight Word Efficiency (SWE) which assesses the number of real printed words that can be accurately identified within 45 seconds and Phonemic Decoding Efficiency (PDE) which measures the number of pronounceable printed non-words that can be accurately decoded within 45 seconds. The total standard score ranges from 35-165. Higher scores indicate higher reading proficiency and lower scores indicate lower reading proficiency. LS mean was calculated using a REML-based, MMRM analysis which includes treatment, baseline, visit, treatment-by-visit interaction, and baseline-by-visit interaction. APD: All randomized participants who received at least one dose of study drug and had evaluable baseline and post baseline TOWRE measurements

End point type	Secondary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	28		
Units: units on a scale				
least squares mean (standard error)				
ADHD + Dyslexia	0.59 (± 1.435)	1.18 (± 1.231)		
ADHD Alone	4.98 (± 1.611)	4.69 (± 1.844)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in Working Memory Test Battery for Children (WMTB-C) in Participants with Dyslexia Alone

End point title	Change from Baseline to Endpoint in Working Memory Test Battery for Children (WMTB-C) in Participants with Dyslexia Alone ^[34]
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End point description:

WMTB-C is assessment of working memory capacities, consisting of 9 subtests (Trials Correct Scores

[Range from 55-145], Higher scores are better, Lower scores are poor) reflecting 3 main components of working memory: central executive (CE) control/regulation of working memory (Backward Digit Recall, Listening Recall, Counting Recall); phonological loop (PL) responsible for holding verbal information for short periods (Digit Recall, Word List Matching, Word List Recall, Non-word List Recall); and visuo-spatial sketchpad (VSSP) which holds information in visual and spatial form (Block Recall, Mazes Memory). LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received at least one dose of study drug and had evaluable baseline and post baseline WMTB-C measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	13		
Units: units on a scale				
least squares mean (standard error)				
Digit Recall Score	0.74 (± 1.25)	0.94 (± 1.26)		
Word List Matching Score	0.34 (± 2.15)	0.97 (± 2.12)		
Word List Recall Score	0.61 (± 0.81)	0.50 (± 0.83)		
Nonword List Recall Score	-0.10 (± 0.68)	0.17 (± 0.69)		
Block Recall Score	0.59 (± 1.23)	0.82 (± 1.25)		
Mazes Memory Score	-1.05 (± 1.87)	-2.96 (± 1.91)		
Listening Recall Score	1.41 (± 0.82)	-0.52 (± 0.84)		
Counting Recall Score	1.83 (± 0.85)	0.18 (± 0.88)		
Backward Digit Recall Score	-0.28 (± 1.52)	0.65 (± 1.55)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint WMTB-C in Participants with ADHD + Dyslexia

End point title	Change from Baseline to Endpoint WMTB-C in Participants with ADHD + Dyslexia ^[35]
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End point description:

WMTB-C is assessment of working memory capacities, consisting of 9 subtests (Trials Correct Scores [Range from 55-145], Higher scores are better, Lower scores are poor) reflecting 3 main components of working memory: central executive (CE) control/regulation of working memory (Backward Digit Recall, Listening Recall, Counting Recall); phonological loop (PL) responsible for holding verbal information for short periods (Digit Recall, Word List Matching, Word List Recall, Non-word List Recall); and visuo-spatial sketchpad (VSSP) which holds information in visual and spatial form (Block Recall, Mazes Memory). LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received at least one dose of study drug and had evaluable baseline and post baseline WMTB-C measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	16		
Units: units on a scale				
least squares mean (standard error)				
Digit Recall	-0.64 (± 1.04)	1.03 (± 0.93)		
Word List Matching	-0.02 (± 1.90)	-0.78 (± 1.72)		
Word List Recall	-0.78 (± 0.77)	0.80 (± 0.70)		
NonWord	0.12 (± 0.32)	1.12 (± 0.29)		
Block Recall	-1.71 (± 0.83)	0.75 (± 0.77)		
Mazes Memory Score	3.08 (± 1.34)	-1.01 (± 1.22)		
Listening Recall	-0.48 (± 0.75)	2.16 (± 0.68)		
Counting Recall	-2.26 (± 1.36)	-1.61 (± 1.21)		
Backward Digit Recall	-0.31 (± 0.82)	1.76 (± 0.74)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint WMTB-C in Participants with ADHD Alone

End point title	Change from Baseline to Endpoint WMTB-C in Participants with ADHD Alone ^[36]
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End point description:

WMTB-C is assessment of working memory capacities, consisting of 9 subtests (Trials Correct Scores [Range from 55-145], Higher scores are better, Lower scores are poor) reflecting 3 main components of working memory: central executive (CE) control/regulation of working memory (Backward Digit Recall, Listening Recall, Counting Recall); phonological loop (PL) responsible for holding verbal information for short periods (Digit Recall, Word List Matching, Word List Recall, Non-word List Recall); and visuo-spatial sketchpad (VSSP) which holds information in visual and spatial form (Block Recall, Mazes Memory). LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received at least one dose of study drug and had evaluable baseline and post baseline WMTB-C measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	10		
Units: units on a scale				
least squares mean (standard error)				
Digit Recall	2.70 (± 1.76)	0.94 (± 1.93)		
Word List Matching	-0.79 (± 1.61)	2.03 (± 1.84)		
Word List Recall	1.50 (± 1.06)	1.17 (± 1.18)		
NonWord	1.41 (± 0.82)	-0.13 (± 0.90)		
Block Recall	1.03 (± 1.36)	0.44 (± 1.67)		
Mazes Memory Score	2.70 (± 1.61)	0.16 (± 1.73)		
Listening Recall	1.53 (± 1.06)	1.57 (± 1.18)		
Counting Recall	0.31 (± 1.02)	-1.02 (± 1.14)		
Backward Digit Recall	1.82 (± 1.23)	2.15 (± 1.32)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in BADD-A Total Score in Participants With Dyslexia Alone

End point title	Change From Baseline to Endpoint in BADD-A Total Score in Participants With Dyslexia Alone ^[37]
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End point description:

The BADD-A is used to assess impairment in executive functions related to ADHD. These include 1) Organizing, prioritizing, and activating to work; 2) Focusing, sustaining and shifting attention to tasks; 3) Regulating alertness, sustaining effort, and processing speed; 4) Managing frustration and modulating emotions; 5) Utilizing working memory and accessing recall (Brown 2001). Scores range from 0-120. The higher the score the more severe the ADD. Scores of 0-39 equate to "ADD possible but not likely". Scores of 40-54 equate to "ADD probable but not certain". Scores of 55-120 equate to "ADD highly probable". LS mean was calculated using a REML-based, MMRM analysis which includes treatment, baseline, visit, treatment-by-visit interaction, and baseline-by-visit interaction. APD: All randomized participants who received at least one dose of study drug and had evaluable baseline and post baseline BADD-A measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	13		
Units: units on a scale				
least squares mean (standard error)	-7.22 (± 4.756)	-2.82 (± 5.022)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in ADHDRS-IV Total Score in Participants with Dyslexia Alone

End point title	Change from Baseline to Endpoint in ADHDRS-IV Total Score in Participants with Dyslexia Alone ^[38]
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End point description:

The ADHDRS-IV-Parent is an 18-item scale with 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD. Each item is scored on a 0 to 3 scale: 0=none (never or rarely); 1=mild (sometimes); 2=moderate (often); 3=severe (very often). Total scores range from 0-54. Higher scores indicate higher impairment and lower scores indicate no impairment. LS mean was calculated using a REML-based, MMRM analysis which includes treatment, baseline, visit, treatment-by-visit interaction, and baseline-by-visit interaction. APD: All randomized participants who received at least one dose of study drug and had evaluable baseline and post baseline ADHDRS-IV-Parent: Inv measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: units on a scale				
least squares mean (standard error)	-1.88 (± 1.441)	-2.51 (± 1.492)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in WJ III Individual Scores in Participants With Dyslexia Alone

End point title	Change From Baseline to Endpoint in WJ III Individual Scores in Participants With Dyslexia Alone ^[39]
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End point description:

WJ III (Woodcock et al. 2001) has two parallel forms (A and B) alternating two batteries of tests—Standard and Extended. Standard tests (1 -12) have a broad set of scores. Extended tests (13 - 22) have a more in-depth diagnostic assessment of academic strengths and weaknesses. Tests administered were 1, 2, 7, 9, 13, 17, and 20. The standard score scale is a mean (M) of 100 and a standard deviation (SD) of 15. The WJ III ACH has extended standard scores, which is a greater range of standard scores. Scores for each individual test range from 0 to over 200 where 69 and below is very low and 131 and above is very superior. Higher scores indicate better reading skills. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for gender, baseline score, and age. APD: All randomized participants who received atomoxetine in both phases and had evaluable baseline and post baseline WJ III measurements. No participants by design were on placebo for both study

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[39] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: units on a scale				
least squares mean (standard error)				
Reading Fluency	8.96 (± 3.63)			
Reading Comprehension	0.24 (± 1.56)			
Letter Word Identification	2.12 (± 1.67)			
Spelling	-1.81 (± 2.87)			
Spelling of Sounds	4.67 (± 4.82)			
Basic Reading Skills	3.41 (± 1.72)			
Passage Comprehension Score	2.17 (± 5.68)			
Word Attack Score	5.37 (± 4.71)			
Reading Vocabulary Score	-2.28 (± 2.18)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in WJ III Individual Scores in Participants With ADHD + Dyslexia

End point title	Change From Baseline to Endpoint in WJ III Individual Scores in Participants With ADHD + Dyslexia ^[40]
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End point description:

WJ III (Woodcock et al. 2001) has two parallel forms (A & B) alternating 2 batteries of tests—Standard & Extended. Standard tests (1 -12) have broad set of scores. Extended tests (13 -22) have more in-depth diagnostic assessment of academic strengths and weaknesses. Tests administered were 1, 2, 7, 9, 13, 17, & 20. Standard score scale is a mean (M) of 100 & a SD of 15. The WJ III ACH has extended standard scores, which is a greater range of standard scores. Scores for each individual test range 0 to over 200 where 69 & below is very low & 131 and above is very superior. Higher scores indicate better reading skills. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline score, age, & baseline score by treatment interaction. APD: All randomized participants who received atomoxetine in both phases & had evaluable baseline, post baseline WJ III measurements. No participants by design were on placebo for both II & III period

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: units on a scale				
least squares mean (standard error)				
Letter Word Identification	2.40 (± 3.30)			
Word Attack Score	-0.78 (± 0.21)			
Reading Vocabulary	0.71 (± 1.16)			
Reading Fluency	2.24 (± 0.27)			
Reading Comprehension	2.61 (± 1.31)			
Spelling	1.29 (± 3.68)			
Spelling of Sounds	-1.79 (± 1.03)			
Basic Reading Skills	0.70 (± 0.04)			
Passage Comprehension Score	3.58 (± 2.01)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in WJ III Individual Scores in Participants With ADHD Alone

End point title	Change From Baseline to Endpoint in WJ III Individual Scores in Participants With ADHD Alone ^[41]
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End point description:

WJ III (Woodcock et al. 2001) has 2 parallel forms (A & B) alternating 2 batteries of tests—Standard & Extended. Standard tests (1 -12) have a broad set of scores. Extended tests (13 -22) have a more in-depth diagnostic assessment of academic strengths and weaknesses. Tests administered were 1, 2, 7, 9, 13, 17, and 20. Standard score scale is mean (M) of 100 & SD of 15. WJ III ACH has extended standard scores, which is a greater range of standard scores. Scores for each individual test range from 0 to over 200 where 69 & below is very low & 131 and above is very superior. Higher scores indicate better reading skills. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline score, age, baseline score by treatment interaction. APD: All randomized participants who received atomoxetine in both phases & evaluable baseline, post baseline CTOPP measurements. No participants by design were on placebo for study periods II & III.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[41] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: units on a scale				
least squares mean (standard error)				
Letter Word Identification	-1.89 (± 0.39)			
Word Attack Score	-1.87 (± 1.73)			
Reading Vocabulary	5.88 (± 3.40)			
Reading Fluency	2.93 (± 3.82)			

Reading Comprehension	4.77 (\pm 2.39)			
Spelling	4.04 (\pm 2.79)			
Spelling of Sounds	6.80 (\pm 2.79)			
Basic Reading Skills	-2.44 (\pm 0.77)			
Passage Comprehension Score	-3.16 (\pm 1.09)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in CTOPP Composite Scores in Participants With Dyslexia Alone

End point title	Change From Baseline to Endpoint in CTOPP Composite Scores in Participants With Dyslexia Alone ^[42]
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End point description:

The CTOPP assesses phonological awareness, phonological memory, and rapid naming and is appropriate for ages 7 to 24. The test contains six core subtests. The composite scores are 1) Phonological Awareness, comprised of the standard scores of the Elision and Blending Words; 2) Phonological Memory, comprised of standard scores for Memory for Digits and Non-word Repetition; and 3) Rapid Naming, comprised of standard scores for Rapid Digit Naming and Rapid Letter Naming. Standard scores range from 1-20, and composite scores range from 35-165. Higher scores are better and lower scores are poor. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received atomoxetine in both phases and had evaluable baseline and post baseline CTOPP measurements. No participants by design were on placebo for both study periods II and III.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[42] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: units on a scale				
least squares mean (standard error)				
Phonological Awareness	-0.41 (\pm 0.67)			
Phonological Memory	-4.63 (\pm 2.41)			
Rapid Naming Score	3.99 (\pm 4.49)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in CTOPP Composite Scores in Participants With ADHD + Dyslexia

End point title	Change From Baseline to Endpoint in CTOPP Composite Scores in Participants With ADHD + Dyslexia ^[43]
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End point description:

The CTOPP assesses phonological awareness, phonological memory, and rapid naming and is appropriate for ages 7 to 24. The test contains six core subtests. The composite scores are 1) Phonological Awareness, comprised of the standard scores of the Elision and Blending Words; 2) Phonological Memory, comprised of standard scores for Memory for Digits and Non-word Repetition; and 3) Rapid Naming, comprised of standard scores for Rapid Digit Naming and Rapid Letter Naming. Standard scores range from 1-20, and composite scores range from 35-165. Higher scores are better and lower scores are poor. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received atomoxetine in both phases and had evaluable baseline and post baseline CTOPP measurements. No participants by design were on placebo for both study periods II and III.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: units on a scale				
least squares mean (standard error)				
Phonological Awareness	12.69 (± 1.89)			
Phonological Memory	3.40 (± 2.27)			
Rapid Naming Score	4.72 (± 3.47)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in CTOPP Composite Scores in Participants With ADHD Alone

End point title	Change From Baseline to Endpoint in CTOPP Composite Scores in Participants With ADHD Alone ^[44]
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End point description:

The CTOPP assesses phonological awareness, phonological memory, and rapid naming and is appropriate for ages 7 to 24. The test contains six core subtests. The composite scores are 1) Phonological Awareness, comprised of the standard scores of the Elision and Blending Words; 2) Phonological Memory, comprised of standard scores for Memory for Digits and Non-word Repetition; and 3) Rapid Naming, comprised of standard scores for Rapid Digit Naming and Rapid Letter Naming. Standard scores range from 1-20, and composite scores range from 35-165. Higher scores are better and lower scores are poor. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received atomoxetine in both phases and had evaluable baseline and post baseline CTOPP measurements. No participants by design were on placebo for both study periods II and III.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[44] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: units on a scale				
least squares mean (standard error)				
Phonological Awareness	5.90 (± 6.17)			
Phonological Memory	5.61 (± 2.30)			
Rapid Naming Score	2.67 (± 0.32)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in GORT-4 in Participants with Dyslexia Alone

End point title	Change from Baseline to Endpoint in GORT-4 in Participants with Dyslexia Alone ^[45]
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End point description:

The GORT-4 is a norm-referenced test of oral reading rate, accuracy, fluency, and comprehension valid for individuals aged 6 to 18 years old. The test has two parallel forms, Form A and Form B, that are administered in an alternating fashion (e.g. Week 0-Form A, Week 16-Form B, Week 32-Form A.) with each containing 14 separate stories and 5 multiple-choice comprehension questions for each story. GORT-4 yields the following scores: rate, accuracy, fluency, comprehension, and overall reading ability. Standard scores range from 1-20. Higher scores indicate better reading skills. Lower scores indicate poor reading skills. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received atomoxetine in both phases and had evaluable baseline and post baseline GORT-4 measurements. No participants by design were on placebo for both study periods II and III.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[45] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: units on a scale				
least squares mean (standard error)				
Oral Reading Rate	0.63 (± 0.79)			
Accuracy	-1.93 (± 0.47)			
Fluency	-0.66 (± 0.45)			
Reading Comprehension	-0.23 (± 2.86)			

Oral Reading Quotient	-9.53 (\pm 14.45)			
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Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in GORT-4 in Participants with ADHD + Dyslexia

End point title	Change from Baseline to Endpoint in GORT-4 in Participants with ADHD + Dyslexia ^[46]
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End point description:

The GORT-4 is a norm-referenced test of oral reading rate, accuracy, fluency, and comprehension valid for individuals aged 6 to 18 years old. The test has two parallel forms, Form A and Form B, that are administered in an alternating fashion (e.g. Week 0-Form A, Week 16-Form B, Week 32-Form A.) with each containing 14 separate stories and 5 multiple-choice comprehension questions for each story. GORT-4 yields the following scores: rate, accuracy, fluency, comprehension, and overall reading ability. Standard scores range from 1-20. Higher scores indicate better reading skills. Lower scores indicate poor reading skills. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received atomoxetine in both phases and had evaluable baseline and post baseline GORT-4 measurements. No participants by design were on placebo for both study periods II and III.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[46] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: units on a scale				
least squares mean (standard error)				
Oral Reading Rate	0.22 (\pm 0.25)			
Accuracy	0.17 (\pm 0.02)			
Fluency	-0.28 (\pm 0.34)			
Reading Comprehension	-0.61 (\pm 0.31)			
Oral Reading Quotient	-2.23 (\pm 1.89)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in GORT-4 in Participants with ADHD Alone

End point title	Change from Baseline to Endpoint in GORT-4 in Participants
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End point description:

The GORT-4 is a norm-referenced test of oral reading rate, accuracy, fluency, and comprehension valid for individuals aged 6 to 18 years old. The test has two parallel forms, Form A and Form B, that are administered in an alternating fashion (e.g. Week 0-Form A, Week 16-Form B, Week 32-Form A.) with each containing 14 separate stories and 5 multiple-choice comprehension questions for each story. GORT-4 yields the following scores: rate, accuracy, fluency, comprehension, and overall reading ability. Standard scores range from 1-20. Higher scores indicate better reading skills. Lower scores indicate poor reading skills. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received atomoxetine in both phases and had evaluable baseline and post baseline GORT-4 measurements. No participants by design were on placebo for both study periods II and III.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[47] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: units on a scale				
least squares mean (standard error)				
Oral Reading Rate	0.05 (± 0.63)			
Accuracy	-1.44 (± 0.45)			
Fluency	-0.20 (± 0.22)			
Reading Comprehension	-0.02 (± 1.07)			
Oral Reading Quotient	-1.37 (± 4.86)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in Participants in TOWRE Total Score with Dyslexia Alone

End point title	Change from Baseline to Endpoint in Participants in TOWRE Total Score with Dyslexia Alone ^[48]
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End point description:

The TOWRE is a measure of an individual's ability to pronounce printed words accurately and fluently and is appropriate for individuals aged 6 to 24 years old. The TOWRE contains two subtests: Sight Word Efficiency (SWE) which assesses the number of real printed words that can be accurately identified within 45 seconds and Phonemic Decoding Efficiency (PDE) which measures the number of pronounceable printed non-words that can be accurately decoded within 45 seconds. The total standard score ranges from 35-165. Higher scores indicate higher reading proficiency and lower scores indicate lower reading proficiency. LS mean was calculated using a REML-based, MMRM analysis which includes treatment, baseline, visit, treatment-by-visit interaction, and baseline-by-visit interaction. All randomized participants who received atomoxetine in both phases and had evaluable baseline and post baseline TOWRE measurements. No participants by design were on placebo for both study periods II and III.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[48] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: units on a scale				
least squares mean (standard error)	3.20 (\pm 3.04)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in Participants in TOWRE Total Score with ADHD or ADHD + Dyslexia

End point title	Change from Baseline to Endpoint in Participants in TOWRE Total Score with ADHD or ADHD + Dyslexia ^[49]
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End point description:

The TOWRE is a measure of an individual's ability to pronounce printed words accurately and fluently and is appropriate for individuals aged 6 to 24 years old. The TOWRE contains two subtests: Sight Word Efficiency (SWE) which assesses the number of real printed words that can be accurately identified within 45 seconds and Phonemic Decoding Efficiency (PDE) which measures the number of pronounceable printed non-words that can be accurately decoded within 45 seconds. The total standard score ranges from 35-165. Higher scores indicate higher reading proficiency and lower scores indicate lower reading proficiency. LS mean was calculated using a REML-based, MMRM analysis which includes treatment, baseline, visit, treatment-by-visit interaction, and baseline-by-visit interaction. APD: All randomized participants who received atomoxetine in both phases and had evaluable baseline and post baseline TOWRE measurements. No participants by design were on placebo for both study periods II & III

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[49] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: units on a scale				
least squares mean (standard error)				
ADHD + Dyslexia	2.77 (\pm 1.99)			
ADHD Alone	6.75 (\pm 0.04)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in Participants in WMTB-C with Dyslexia Alone

End point title	Change from Baseline to Endpoint in Participants in WMTB-C with Dyslexia Alone ^[50]
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End point description:

WMTB-C is assessment of working memory capacities, consisting of 9 subtests (Trials Correct Scores [Range from 55-145], Higher scores are better, Lower scores are poor) reflecting 3 main components of working memory: central executive (CE) control/regulation of working memory (Backward Digit Recall, Listening Recall, Counting Recall); phonological loop (PL) responsible for holding verbal information for short periods (Digit Recall, Word List Matching, Word List Recall, Non-word List Recall); and visuo-spatial sketchpad (VSSP) which holds information in visual and spatial form (Block Recall, Mazes Memory). LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received atomoxetine in both phases and had evaluable baseline and post baseline WMTB-C measurements. No participants by design were on placebo for both study periods II and III.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[50] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: units on a scale				
least squares mean (standard error)				
Digit Recall Score	0.47 (± 1.00)			
Word List Matching Score	1.29 (± 2.62)			
Word List Recall Score	0.75 (± 1.65)			
Nonword List Recall Score	-0.96 (± 2.45)			
Block Recall Score	1.25 (± 2.51)			
Mazes Memory Score	1.91 (± 3.74)			
Listening Recall Score	4.15 (± 2.14)			
Counting Recall Score	-0.88 (± 1.39)			
Backwards Digit Recall Score	-0.64 (± 2.95)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in Participants in WMTB-C with ADHD + Dyslexia

End point title	Change from Baseline to Endpoint in Participants in WMTB-C with ADHD + Dyslexia ^[51]
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End point description:

WMTB-C is assessment of working memory capacities, consisting of 9 subtests (Trials Correct Scores [Range from 55-145], Higher scores are better, Lower scores are poor) reflecting 3 main components of working memory: central executive (CE) control/regulation of working memory (Backward Digit Recall,

Listening Recall, Counting Recall)); phonological loop (PL) responsible for holding verbal information for short periods (Digit Recall, Word List Matching, Word List Recall, Non-word List Recall); and visuo-spatial sketchpad (VSSP) which holds information in visual and spatial form (Block Recall, Mazes Memory). LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who had received atomoxetine in both phases and had evaluable baseline and post baseline WMTB-C measurements. No participants by design were on placebo for both study periods II and III.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[51] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: units on a scale				
least squares mean (standard error)				
Digit Recall Score	0.06 (± 0.07)			
Word List Matching Score	-4.12 (± 1.25)			
Word List Recall Score	3.05 (± 1.51)			
Nonword List Recall Score	1.78 (± 0.42)			
Block Recall Score	0.56 (± 1.13)			
Mazes Memory Score	-0.22 (± 2.73)			
Listening Recall Score	0.73 (± 3.37)			
Counting Recall Score	-0.55 (± 2.47)			
Backward Digit Recall Score	0.05 (± 2.95)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in Participants in WMTB-C with ADHD Alone

End point title	Change from Baseline to Endpoint in Participants in WMTB-C with ADHD Alone ^[52]
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End point description:

WMTB-C is assessment of working memory capacities, consisting of 9 subtests (Trials Correct Scores [Range from 55-145], Higher scores are better, Lower scores are poor) reflecting 3 main components of working memory: central executive (CE) control/regulation of working memory (Backward Digit Recall, Listening Recall, Counting Recall); phonological loop (PL) responsible for holding verbal information for short periods (Digit Recall, Word List Matching, Word List Recall, Non-word List Recall); and visuo-spatial sketchpad (VSSP) which holds information in visual and spatial form (Block Recall, Mazes Memory). LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who had received atomoxetine in both phases and had evaluable baseline and post baseline WMTB-C measurements. No participants by design were on placebo for both study periods II and III.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[52] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: units on a scale				
least squares mean (standard error)				
Digit Recall Score	3.75 (± 0.93)			
Word List Matching Score	-3.37 (± 0.37)			
Word List Recall Score	1.25 (± 0.49)			
Nonword List Recall Score	1.12 (± 0.60)			
Block Recall Score	3.65 (± 3.48)			
Mazes Memory Score	-1.09 (± 1.43)			
Listening Recall Score	4.24 (± 1.96)			
Counting Recall Score	-3.05 (± 1.67)			
Backward Digit Recall Score	-0.45 (± 0.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in BADD-A Total Score in Participants With Dyslexia Alone

End point title	Change from Baseline to Endpoint in BADD-A Total Score in Participants With Dyslexia Alone ^[53]
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End point description:

The BADD-A is used to assess impairment in executive functions related to ADHD. These include 1) Organizing, prioritizing, and activating to work; 2) Focusing, sustaining and shifting attention to tasks; 3) Regulating alertness, sustaining effort, and processing speed; 4) Managing frustration and modulating emotions; 5) Utilizing working memory and accessing recall (Brown 2001). Scores range from 0-120. The higher the score the more severe the ADD. Scores of 0-39 equate to "ADD possible but not likely". Scores of 40-54 equate to "ADD probable but not certain". Scores of 55-120 equate to "ADD highly probable". LS Mean was calculated using ANCOVA model with terms for gender, baseline score, and age. APD: All randomized participants who received atomoxetine in both phases and had evaluable baseline and post baseline BADD-A measurements. No participants by design were on placebo for both study periods II and III.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[53] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: units on a scale				
least squares mean (standard error)	-10.07 (\pm 6.70)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in BADD-A Total Score in Participants With ADHD or ADHD + Dyslexia

End point title	Change from Baseline to Endpoint in BADD-A Total Score in Participants With ADHD or ADHD + Dyslexia ^[54]
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End point description:

The BADD-A is used to assess impairment in executive functions related to ADHD. These include 1) Organizing, prioritizing, and activating to work; 2) Focusing, sustaining and shifting attention to tasks; 3) Regulating alertness, sustaining effort, and processing speed; 4) Managing frustration and modulating emotions; 5) Utilizing working memory and accessing recall (Brown 2001). Scores range from 0-120. The higher the score the more severe the ADD. Scores of 0-39 equate to "ADD possible but not likely". Scores of 40-54 equate to "ADD probable but not certain". Scores of 55-120 equate to "ADD highly probable". LS Mean was calculated using ANCOVA model with terms for gender, baseline score, and age. APD: All randomized participants who received atomoxetine in both phases and had evaluable baseline and post baseline BADD-A measurements. No participants by design were on placebo for both study periods II and III.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[54] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: units on a scale				
least squares mean (standard error)				
ADHD + Dyslexia	-9.44 (\pm 7.43)			
ADHD Alone	-9.33 (\pm 5.04)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in ADHDRS-IV-Parent: Inv Total Score in Participants With Dyslexia Alone

End point title	Change From Baseline to Endpoint in ADHDRS-IV-Parent: Inv
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End point description:

The ADHDRS-IV-Parent is an 18-item scale with 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD. Each item is scored on a 0 to 3 scale: 0=none (never or rarely); 1=mild (sometimes); 2=moderate (often); 3=severe (very often). Total scores range from 0-54. Higher scores indicate higher impairment and lower scores indicate no impairment. LS Mean was calculated using ANCOVA model with terms for gender, baseline score, and age. APD: All randomized participants who received atomoxetine in both phases and had evaluable baseline and post baseline ADHDRS-IV-Parent: Inv measurements. No participants by design were on placebo for both study periods II and III.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[55] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: units on a scale				
least squares mean (standard error)	12.60 (± 8.17)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in ADHDRS-IV-Parent: Inv Total Score in Participants With ADHD or ADHD +Dyslexia^[56]

End point title	Change From Baseline to Endpoint in ADHDRS-IV-Parent: Inv Total Score in Participants With ADHD or ADHD +Dyslexia ^[56]
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End point description:

The ADHDRS-IV-Parent is an 18-item scale with 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD. Each item is scored on a 0 to 3 scale: 0=none (never or rarely); 1=mild (sometimes); 2=moderate (often); 3=severe (very often). Total scores range from 0-54. Higher scores indicate higher impairment and lower scores indicate no impairment. LS Mean was calculated using ANCOVA model with terms for gender, baseline score, and age. APD: All randomized participants who received atomoxetine in both phases and had evaluable baseline and post baseline ADHDRS-IV-Parent: Inv measurements. No participants by design were on placebo for both study periods II and III.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[56] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: units on a scale				
least squares mean (standard error)				
ADHD + Dyslexia	-12.96 (\pm 2.44)			
ADHD Alone	-18.76 (\pm 5.89)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in fMRI Activation in Participants With Dyslexia Alone (Pseudoword Rhyming, Semantic-category)

End point title	Change From Baseline to Endpoint in fMRI Activation in Participants With Dyslexia Alone (Pseudoword Rhyming, Semantic-category)
End point description:	
For this trial, Lilly contracted an academic institution to process the fMRI data. However, there are contractual delays limiting the timing, and Lilly does not have access to the processed fMRI data at this time. APD: For this outcome measure, there were no data collected beyond 16 weeks.	
End point type	Secondary
End point timeframe:	
From Week 16, Up to Week 32	

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[57]	0 ^[58]		
Units: participants				
Semantic Category Tasks				
Pseudoword Rhyming Tasks				

Notes:

[57] - No data collected beyond 16 weeks

[58] - No data collected beyond 16 weeks

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in fMRI Activation in Participants With Dyslexia Alone (Stroop Tasks)

End point title	Change From Baseline to Endpoint in fMRI Activation in Participants With Dyslexia Alone (Stroop Tasks)
End point description:	
For this trial, Lilly contracted an academic institution to process the fMRI data. However, there are contractual delays limiting the timing, and Lilly does not have access to the processed fMRI data at this time. APD: Stroop Tasks data were not collected.	

End point type	Secondary
End point timeframe:	
From Week 16, Up to 32 Weeks	

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[59]	0 ^[60]		
Units: participants				

Notes:

[59] - Stroop Tasks data were not collected.

[60] - Stroop Tasks data were not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in fMRI Activation in Participants With ADHD or ADHD + Dyslexia (Pseudoword Rhyming and Semantic-category Tasks)

End point title	Change From Baseline to Endpoint in fMRI Activation in Participants With ADHD or ADHD + Dyslexia (Pseudoword Rhyming and Semantic-category Tasks)
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End point description:

APD: For this outcome measure, there were no data collected beyond 16 weeks

End point type	Secondary
End point timeframe:	
From Week 16, Up to Week 32	

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[61]	0 ^[62]		
Units: participants				
Semantic Category Tasks				
Pseudoword Rhyming Tasks				

Notes:

[61] - No data collected beyond 16 weeks

[62] - No data collected beyond 16 weeks

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in fMRI Activation in Participants With ADHD or ADHD + Dyslexia (Stroop Tasks)

End point title	Change From Baseline to Endpoint in fMRI Activation in Participants With ADHD or ADHD + Dyslexia (Stroop Tasks)
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End point description:

For this trial, Lilly contracted an academic institution to process the fMRI data. However, there are contractual delays limiting the timing, and Lilly does not have access to the processed fMRI data at this time. APD: Stroop Tasks data were not collected.

End point type	Secondary
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End point timeframe:

From Week 16, Up to Week 32

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[63]	0 ^[64]		
Units: participants				

Notes:

[63] - Stroop Tasks data were not collected.

[64] - Stroop Tasks data were not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in WJ III Individual Scores in Participants With Dyslexia Alone

End point title	Change From Baseline to Endpoint in WJ III Individual Scores in Participants With Dyslexia Alone
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End point description:

WJ III (Woodcock et al. 2001) has 2 parallel forms (A & B) alternating 2 batteries of tests—Standard & Extended. Standard tests (1 -12) have a broad set of scores. Extended tests (13 -22) have in-depth diagnostic assessment of academic strength & weakness. Tests administered were 1, 2, 7, 9, 13, 17, & 20. Standard score scale is mean (M) of 100 & standard deviation (SD) of 15. WJ III ACH has standard scores, which is greater range of standard scores. Scores for each individual test range from 0 to over 200 where 69 & below is very low & 131 & above is very superior. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baselinescore, age, & baselinescore by treatment interaction. APD: All participants who received atleast 1 dose of study drug & had evaluable baseline, post baseline WJIII measurements. Objectives for this portion of trial centered around participants already exposed to ATX for 16 weeks & therefore no data for PLA/ATX.

End point type	Secondary
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End point timeframe:

From Week 16, Up to 32 Weeks

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: units on a scale				
least squares mean (standard error)				
Word Attack Score	2.79 (± 2.68)	-1.01 (± 2.10)		
Letter Word Identification	2.92 (± 2.45)	-4.08 (± 2.02)		
Reading Fluency	11.03 (± 3.14)	-1.53 (± 2.61)		
Reading Comprehension	4.52 (± 2.60)	-6.86 (± 2.16)		
Spelling	-2.90 (± 3.73)	-1.72 (± 3.00)		

Spelling of Sounds	3.33 (± 3.11)	0.30 (± 2.59)		
Basic Reading Skills	2.87 (± 1.44)	-3.80 (± 1.19)		
Passage Comprehension Score	4.51 (± 3.30)	-6.92 (± 2.74)		
Reading Vocabulary Score	3.02 (± 2.04)	-4.84 (± 1.78)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in WJ III Individual Scores in Participants With ADHD + Dyslexia

End point title	Change From Baseline to Endpoint in WJ III Individual Scores in Participants With ADHD + Dyslexia
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End point description:

WJ III (Woodcock et al. 2001) has 2 parallel forms (A & B) alternating 2 batteries of tests—Standard & Extended. Standard tests (1 -12) have a broad set of scores. Extended tests (13 -22) have in-depth diagnostic assessment of academic strength & weakness. Tests administered were 1, 2, 7, 9, 13, 17, & 20. Standard score scale is mean (M) of 100 & standard deviation (SD) of 15. WJ III ACH has standard scores, which is greater range of standard scores. Scores for each individual test range from 0 to over 200 where 69 & below is very low & 131 & above is very superior. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baselinescore, age, & baselinescore by treatment interaction. APD: All participants who received atleast 1 dose of study drug & had evaluable baseline, post baseline WJIII measurements. Objectives for this portion of trial centered around participants already exposed to ATX for 16 weeks & therefore no data for PLA/ATX.

End point type	Secondary
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End point timeframe:

From Week 16, Up to Week 32

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: units on a scale				
least squares mean (standard error)				
Word Attack Score	-2.65 (± 1.81)	-2.62 (± 1.63)		
Letter Word Identification	0.50 (± 3.19)	-1.07 (± 3.00)		
Reading Vocabulary Score	0.64 (± 2.17)	-4.08 (± 2.08)		
Reading Fluency	5.46 (± 2.77)	6.21 (± 2.84)		
Reading Comprehension	0.86 (± 2.25)	-2.49 (± 2.07)		
Spelling	0.45 (± 2.46)	0.86 (± 2.32)		
Spelling of Sounds	-10.17 (± 3.40)	-3.52 (± 3.23)		
Basic Reading Skills	-1.29 (± 1.06)	-2.17 (± 1.00)		
Passage Comprehension Score	0.15 (± 2.06)	0.52 (± 1.85)		

Statistical analyses

Secondary: Change From Baseline to Endpoint in WJ III Individual Scores in Participants With ADHD Alone

End point title	Change From Baseline to Endpoint in WJ III Individual Scores in Participants With ADHD Alone
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End point description:

WJ III (Woodcock et al. 2001) has 2 parallel forms (A & B) alternating 2 batteries of tests—Standard & Extended. Standard tests (1 -12) have a broad set of scores. Extended tests (13 -22) have in-depth diagnostic assessment of academic strength & weakness. Tests administered were 1, 2, 7, 9, 13, 17, & 20. Standard score scale is mean (M) of 100 & standard deviation (SD) of 15. WJ III ACH has standard scores, which is greater range of standard scores. Scores for each individual test range from 0 to over 200 where 69 & below is very low & 131 & above is very superior. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baselinescore, age, & baselinescore by treatment interaction. APD: All participants who received atleast 1 dose of study drug & had evaluable baseline, post baseline WJIII measurements. Objectives for this portion of trial centered around participants already exposed to ATX for 16 weeks & therefore no data for PLA/ATX.

End point type	Secondary
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End point timeframe:

From Week 16, Up to Week 32

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: units on a scale				
least squares mean (standard error)				
Word Attack Score	-1.56 (± 2.06)	-0.58 (± 1.85)		
Letter Word Identification	-3.89 (± 4.46)	-1.61 (± 4.01)		
Reading Vocabulary Score	5.15 (± 5.51)	-3.62 (± 4.26)		
Reading Fluency	13.05 (± 2.32)	4.88 (± 1.11)		
Reading Comprehension	3.86 (± 2.94)	3.26 (± 2.67)		
Spelling	2.07 (± 4.66)	1.15 (± 3.81)		
Spelling of Sounds	-2.65 (± 3.02)	2.65 (± 2.90)		
Basic Reading Skills	-2.70 (± 3.56)	-1.97 (± 3.17)		
Passage Comprehension Score	6.86 (± 3.42)	2.31 (± 3.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in CTOPP Composite Scores in Participants with Dyslexia Alone

End point title	Change from Baseline to Endpoint in CTOPP Composite Scores in Participants with Dyslexia Alone
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End point description:

The CTOPP assesses phonological awareness, phonological memory, and rapid naming and is appropriate for ages 7 to 24. Test contains six core subtests. The composite scores are 1) Phonological Awareness, comprised of the standard scores of the Elision and Blending Words; 2) Phonological Memory, comprised of standard scores for Memory for Digits and Non-word Repetition; and 3) Rapid Naming, comprised of standard scores for Rapid Digit Naming and Rapid Letter Naming. Standard scores

range from 1-20, and composite scores range from 35-165. Higher scores are better and lower scores are poor. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All participants who received at least one dose of study drug and had evaluable baseline and post baseline CTOPP measurements. The objectives for this portion of the trial centered around participants already exposed to ATX for 16 weeks and therefore no data for PLA/ATX

End point type	Secondary
End point timeframe:	
From Week 16, Up to Week 32	

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: units on a scale				
least squares mean (standard error)				
Phonological Awareness	-1.19 (± 4.03)	2.06 (± 2.82)		
Phonological Memory	-6.96 (± 3.71)	-1.76 (± 3.23)		
Rapid Naming Score	7.24 (± 5.91)	-2.42 (± 4.82)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in CTOPP Composite Scores in Participants with ADHD + Dyslexia

End point title	Change from Baseline to Endpoint in CTOPP Composite Scores in Participants with ADHD + Dyslexia
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End point description:

The CTOPP assesses phonological awareness, phonological memory, and rapid naming and is appropriate for ages 7 to 24. Test contains six core subtests. The composite scores are 1) Phonological Awareness, comprised of the standard scores of the Elision and Blending Words; 2) Phonological Memory, comprised of standard scores for Memory for Digits and Non-word Repetition; and 3) Rapid Naming, comprised of standard scores for Rapid Digit Naming and Rapid Letter Naming. Standard scores range from 1-20, and composite scores range from 35-165. Higher scores are better and lower scores are poor. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All participants who received at least one dose of study drug and had evaluable baseline and post baseline CTOPP measurements. The objectives for this portion of the trial centered around participants already exposed to ATX for 16 weeks and therefore no data for PLA/ATX

End point type	Secondary
End point timeframe:	
From Week 16, Up to Week 32	

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: units on a scale				
least squares mean (standard error)				
Phonological Awareness	3.54 (± 1.51)	5.29 (± 1.42)		
Phonological Memory	-2.65 (± 3.34)	0.12 (± 2.88)		
Rapid Naming Score	2.65 (± 2.02)	1.21 (± 1.64)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in CTOPP Composite Scores in Participants with ADHD Alone

End point title	Change from Baseline to Endpoint in CTOPP Composite Scores in Participants with ADHD Alone
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End point description:

The CTOPP assesses phonological awareness, phonological memory, and rapid naming and is appropriate for ages 7 to 24. The test contains six core subtests. Composite scores are 1) Phonological Awareness, comprised of the standard scores of the Elision and Blending Words; 2) Phonological Memory, comprised of standard scores for Memory for Digits and Non-word Repetition; and 3) Rapid Naming, comprised of standard scores for Rapid Digit Naming and Rapid Letter Naming. Standard scores range from 1-20, and composite scores range from 35-165. Higher scores are better and lower scores are poor. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All participants who received at least one dose of study drug and had evaluable baseline and post baseline CTOPP measurements. The objectives for this portion of the trial centered around participants already exposed to ATX for 16 weeks and therefore no data for PLA/ATX

End point type	Secondary
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End point timeframe:

From Week 16, Up to Week 32

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: units on a scale				
least squares mean (standard error)				
Phonological Awareness	-0.33 (± 2.89)	9.67 (± 2.61)		
Phonological Memory	3.59 (± 3.37)	0.84 (± 3.58)		
Rapid Naming Score	1.53 (± 2.36)	3.51 (± 2.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint TOWRE Total Score in Participants with Dyslexia Alone

End point title	Change from Baseline to Endpoint TOWRE Total Score in Participants with Dyslexia Alone
End point description: TOWRE is a measure of an individual's ability to pronounce printed words accurately & fluently, is appropriate for individuals aged 6 to 24 years old. The TOWRE contains 2 subtests: Sight Word Efficiency (SWE) which assesses no. of real printed words that can be accurately identified within 45 seconds & Phonemic Decoding Efficiency (PDE) which measures the no. of pronounceable printed non-words that can be accurately decoded within 45 seconds. Total standard score ranges from 35-165. Higher scores indicate higher & lower scores indicate lower reading proficiency. LS mean was calculated using a REML-based, MMRM analysis which includes treatment, baseline, visit, treatment-by-visit interaction, baseline-by-visit interaction. APD: All participants who received at least 1 dose of study drug & had evaluable baseline, post baseline TOWRE measurements. Objectives for this portion of the trial centered around participants already exposed to ATX for 16 weeks & therefore no data for PLA/ATX.	
End point type	Secondary
End point timeframe: From Week 16, Up to Week 32	

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: units on a scale				
least squares mean (standard error)	-0.17 (± 1.808)	4.17 (± 1.808)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in TOWRE Total Score in Participants with ADHD or ADHD + Dyslexia

End point title	Change from Baseline to Endpoint in TOWRE Total Score in Participants with ADHD or ADHD + Dyslexia
End point description: TOWRE is a measure of an individual's ability to pronounce printed words accurately & fluently, is appropriate for individuals aged 6 to 24 years old. The TOWRE contains 2 subtests: Sight Word Efficiency (SWE) which assesses no. of real printed words that can be accurately identified within 45 seconds & Phonemic Decoding Efficiency (PDE) which measures the no. of pronounceable printed non-words that can be accurately decoded within 45 seconds. Total standard score ranges from 35-165. Higher scores indicate higher & lower scores indicate lower reading proficiency. LS mean was calculated using a REML-based, MMRM analysis which includes treatment, baseline, visit, treatment-by-visit interaction, baseline-by-visit interaction. APD: All participants who received at least 1 dose of study drug & had evaluable baseline, post baseline TOWRE measurements. Objectives for this portion of the trial centered around participants already exposed to ATX for 16 weeks & therefore no data for PLA/ATX.	
End point type	Secondary
End point timeframe: From Week 16, Up to Week 32	

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	11		
Units: units on a scale				
least squares mean (standard error)				
ADHD + Dyslexia	3.74 (± 1.261)	1.38 (± 1.151)		
ADHD Alone	2.03 (± 4.179)	1.37 (± 4.179)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in GORT-4 in Participants with Dyslexia Alone

End point title	Change from Baseline to Endpoint in GORT-4 in Participants with Dyslexia Alone
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End point description:

The GORT-4 is a norm-referenced test of oral reading rate, accuracy, fluency, and comprehension valid for individuals aged 6 to 18 years old. Test has 2 parallel forms, Form A & B, that are administered in an alternating fashion (e.g. Week 0-Form A, Week 16-Form B, Week 32-Form A.) with each containing 14 separate stories & 5 multiple-choice comprehension questions for each story. GORT-4 yields scores: rate, accuracy, fluency, comprehension, & overall reading ability. Standard scores range from 1-20. Higher scores indicate better reading skills. Lower scores indicate poor reading skills. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All participants who received at least 1 dose of study drug and had evaluable baseline and post baseline GORT-4 measurements. The objectives for this portion of trial centered around participants already exposed to ATX for 16 weeks & therefore no data for PLA/ATX

End point type	Secondary
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End point timeframe:

From Week 16, Up to Week 32

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: units on a scale				
least squares mean (standard error)				
Oral Reading Rate	0.27 (± 0.43)	-0.64 (± 0.36)		
Accuracy	0.40 (± 0.62)	-0.69 (± 0.48)		
Fluency	0.52 (± 0.67)	-0.64 (± 0.49)		
Reading Comprehension	0.06 (± 1.40)	-0.76 (± 1.20)		
Oral Reading Quotient	-3.04 (± 10.51)	-4.91 (± 8.62)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in GORT-4 in Participants with ADHD+ Dyslexia

End point title	Change from Baseline to Endpoint in GORT-4 in Participants with ADHD+ Dyslexia
End point description: The GORT-4 is a norm-referenced test of oral reading rate, accuracy, fluency, and comprehension valid for individuals aged 6 to 18 years old. Test has 2 parallel forms, Form A & B, that are administered in an alternating fashion (e.g. Week 0-Form A, Week 16-Form B, Week 32-Form A.) with each containing 14 separate stories & 5 multiple-choice comprehension questions for each story. GORT-4 yields scores: rate, accuracy, fluency, comprehension, & overall reading ability. Standard scores range from 1-20. Higher scores indicate better reading skills. Lower scores indicate poor reading skills. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All participants who received at least 1 dose of study drug and had evaluable baseline and post baseline GORT-4 measurements. The objectives for this portion of trial centered around participants already exposed to ATX for 16 weeks & therefore no data for PLA/ATX.	
End point type	Secondary
End point timeframe: From Week 16, Up to Week 32	

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: units on a scale				
least squares mean (standard error)				
Oral Reading Rate	0.37 (± 0.73)	0.31 (± 0.66)		
Accuracy	0.07 (± 0.84)	0.45 (± 0.68)		
Fluency	0.33 (± 1.15)	0.52 (± 1.08)		
Reading Comprehension	1.75 (± 1.42)	3.64 (± 1.29)		
Oral Reading Quotient	7.16 (± 4.57)	12.92 (± 4.32)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in GORT-4 in Participants with ADHD Alone

End point title	Change from Baseline to Endpoint in GORT-4 in Participants with ADHD Alone
End point description: The GORT-4 is a norm-referenced test of oral reading rate, accuracy, fluency, and comprehension valid for individuals aged 6 to 18 years old. The test has 2 parallel forms, Form A & B, that are administered in an alternating fashion (e.g. Week 0-Form A, Week 16-Form B, Week 32-Form A.) with each containing 14 separate stories and 5 multiple-choice comprehension questions for each story. GORT-4 yields scores: rate, accuracy, fluency, comprehension, and overall reading ability. Standard scores range from 1-20. Higher scores indicate better reading skills. Lower scores indicate poor reading skills. LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All participants who received at least 1 dose of study drug & had evaluable baseline, post baseline GORT-4 measurements. Objectives for this portion of trial centered around participants already exposed to ATX for 16 weeks & therefore no data for PLA/ATX	
End point type	Secondary

End point timeframe:
From Week 16, Up to Week 32

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: units on a scale				
least squares mean (standard error)				
Oral Reading Rate	0.36 (± 0.99)	-0.35 (± 0.70)		
Accuracy	-1.29 (± 1.00)	0.15 (± 0.82)		
Fluency	-0.54 (± 0.76)	-0.38 (± 0.57)		
Reading Comprehension	3.46 (± 1.05)	-0.04 (± 0.75)		
Oral Reading Quotient	8.27 (± 8.94)	-3.13 (± 5.38)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in WMTB-C in Participants with Dyslexia Alone

End point title	Change from Baseline to Endpoint in WMTB-C in Participants with Dyslexia Alone
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End point description:

WMTB-C is assessment of working memory capacities, consisting of 9 subtests (Trials Correct Scores [Range from 55-145], Higher scores are better, Lower scores are poor) reflecting 3 main components of working memory: central executive (CE) control/regulation of working memory (Backward Digit Recall, Listening Recall, Counting Recall); phonological loop (PL) responsible for holding verbal info for short periods (Digit Recall, Word List Matching, Word List Recall, Non-word List Recall); & visuo-spatial sketchpad (VSSP) which holds info in visual & spatial form (Block Recall, Mazes Memory). LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received at least 1 dose of study drug & had baseline & post baseline WMTB-C measurements. Objectives for this portion of trial centered around participants already exposed to ATX for 16 weeks & therefore no data for PLA/ATX are given.

End point type	Secondary
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End point timeframe:

From Week 16, Up to Week 32

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: units on a scale				
least squares mean (standard error)				
Digit Recall Score	-1.77 (± 1.78)	0.45 (± 1.48)		
Word List Matching Score	3.98 (± 4.14)	1.84 (± 2.99)		
Word List Recall Score	-0.68 (± 2.56)	-1.90 (± 2.27)		
Nonword List Recall Score	2.25 (± 0.71)	-0.40 (± 0.55)		

Block Recall Score	1.57 (± 1.55)	-1.73 (± 1.07)		
Mazes Memory Score	6.90 (± 3.29)	1.27 (± 2.76)		
Listening Recall Score	3.44 (± 1.11)	-1.23 (± 0.95)		
Counting Recall Score	-2.05 (± 2.23)	-2.21 (± 1.87)		
Backward Digit Recall Score	2.74 (± 4.47)	2.49 (± 2.21)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint WMTB-C in Participants with ADHD + Dyslexia

End point title	Change from Baseline to Endpoint WMTB-C in Participants with ADHD + Dyslexia
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End point description:

WMTB-C is assessment of working memory capacities, consisting of 9 subtests (Trials Correct Scores [Range from 55-145], Higher scores are better, Lower scores are poor) reflecting 3 main components of working memory: central executive (CE) control/regulation of working memory (Backward Digit Recall, Listening Recall, Counting Recall); phonological loop (PL) responsible for holding verbal info for short periods (Digit Recall, Word List Matching, Word List Recall, Non-word List Recall); and visuo-spatial sketchpad (VSSP) which holds info in visual and spatial form (Block Recall, Mazes Memory). LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received at least 1 dose of study drug & had baseline, post baseline WMTB-C measurements. Objectives for this portion of trial centered around participants already exposed to ATX for 16 weeks & therefore no data for PLA/ATX are given

End point type	Secondary
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End point timeframe:

From Week 16, Up to Week 32

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: units on a scale				
least squares mean (standard error)				
Digit Recall Score	-1.25 (± 0.63)	1.83 (± 0.59)		
Word List Matching Score	-4.48 (± 1.74)	-4.40 (± 1.60)		
Word List Recall Score	2.34 (± 0.66)	2.28 (± 0.61)		
NonWord List Recall	2.17 (± 1.00)	0.64 (± 1.57)		
Block Recall Score	-1.71 (± 2.57)	3.81 (± 1.89)		
Mazes Memory Score	-2.82 (± 2.69)	1.28 (± 2.55)		
Listening Recall Score	1.93 (± 1.80)	0.49 (± 1.45)		
Counting Recall Score	1.34 (± 2.52)	-0.89 (± 2.46)		
Backward Recall Score	0.76 (± 2.03)	-0.14 (± 1.94)		

Statistical analyses

Secondary: Change from Baseline to Endpoint WMTB-C in Participants with ADHD Alone

End point title	Change from Baseline to Endpoint WMTB-C in Participants with ADHD Alone
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End point description:

WMTB-C is assessment of working memory capacities, consisting of 9 subtests (Trials Correct Scores [Range from 55-145], Higher scores are better, Lower scores are poor) reflecting 3 main components of working memory: central executive (CE) control/regulation of working memory (Backward Digit Recall, Listening Recall, Counting Recall); phonological loop (PL) responsible for holding verbal information for short periods (Digit Recall, Word List Matching, Word List Recall, Non-word List Recall); & visuo-spatial sketchpad (VSSP) which holds info in visual & spatial form (Block Recall, Mazes Memory). LS mean was analyzed using LOCF, fixed-effects ANCOVA models with terms for treatment, gender, baseline, age, treatment*baseline. APD: All randomized participants who received atleast 1 dose of study drug & had baseline, post baseline WMTB-C measurements. Objectives for this portion of trial centered around participants already exposed to ATX for 16weeks & therefore no data for PLA/ATX are given

End point type	Secondary
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End point timeframe:

From Week 16, Up to Week 32

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: units on a scale				
least squares mean (standard error)				
Digit Recall Score	2.56 (± 2.92)	-0.97 (± 2.19)		
Word List Matching Score	-1.22 (± 3.84)	-1.71 (± 3.48)		
Word List Recall Score	-1.23 (± 1.41)	1.71 (± 1.22)		
NonWord List Recall	-1.29 (± 1.02)	-1.12 (± 0.87)		
Block Recall Score	-1.14 (± 1.96)	0.59 (± 1.72)		
Mazes Memory Score	1.11 (± 2.35)	-2.51 (± 2.00)		
Listening Recall Score	-1.12 (± 3.23)	-0.09 (± 2.94)		
Counting Recall Score	-0.03 (± 4.53)	-2.90 (± 3.75)		
Backward Recall Score	-0.68 (± 2.03)	-0.46 (± 1.83)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in BADD-A Total Score in Participants With Dyslexia Alone

End point title	Change From Baseline to Endpoint in BADD-A Total Score in Participants With Dyslexia Alone
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End point description:

The BADD-A is used to assess impairment in executive functions related to ADHD. These include 1) Organizing, prioritizing, & activating to work 2) Focusing, sustaining and shifting attention to tasks 3) Regulating alertness, sustaining effort, & processing speed; 4) Managing frustration & modulating emotions; 5) Utilizing working memory & accessing recall (Brown 2001). Scores range from 0-120. Higher score, more severe ADD. Scores of 0-39 = "ADD possible but not likely". Scores of 40-54 = "ADD

probable but not certain". Scores of 55-120 = "ADD highly probable". LS mean calculated using a REML-based, MMRM analysis which includes treatment, baseline, visit, treatment-by-visit interaction, & baseline-by-visit interaction. APD: All randomized participants who received atleast 1 dose of study drug and had baseline and post baseline BADD-A measurements. The objectives for this portion of trial centered around participants already exposed to ATX for 16 weeks, so no data for PLA/ATX are given

End point type	Secondary
End point timeframe:	
From Week 16, Up to Week 32	

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: units on a scale				
least squares mean (standard error)	-6.96 (± 5.240)	7.13 (± 5.240)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in BADD-A Total Score in Participants With ADHD or ADHD + Dyslexia

End point title	Change From Baseline to Endpoint in BADD-A Total Score in Participants With ADHD or ADHD + Dyslexia
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End point description:

BADD-A is used to assess impairment in executive functions related to ADHD. These include 1) Organizing, prioritizing, & activating to work; 2) Focusing, sustaining & shifting attention to tasks; 3) Regulating alertness, sustaining effort, & processing speed; 4) Managing frustration & modulating emotions; 5) Utilizing working memory & accessing recall (Brown 2001). Scores range from 0-120. The higher score, more severe ADD. Scores of 0-39 equate to "ADD possible but not likely". Scores of 40-54 equate to "ADD probable but not certain". Scores of 55-120 equate to "ADD highly probable". LS mean was calculated using REML-based, MMRM analysis which includes treatment, baseline, visit, treatmentbyvisit interaction, & baselinebyvisit interaction. APD: All randomized participants who received atleast 1dose ofdrug & had baseline, postbaseline BADD-A measurements. Objectives for this portion of trial centered around participants already exposed to ATX for16weeks & no data for PLA/ATX are given

End point type	Secondary
End point timeframe:	
From Week 16, Up to Week 32	

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10 ^[65]	11 ^[66]		
Units: units on a scale				
least squares mean (standard error)				
ADHD + Dyslexia	-0.90 (± 8.646)	14.59 (± 7.892)		
ADHD Alone	1.01 (± 4.416)	3.69 (± 4.461)		

Notes:

[65] - ADHD + Dyslexia, ADHD Alone: n = 5

[66] - ADHD + Dyslexia: n = 6

ADHD Alone: n = 5

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in ADHDRS-IV Total Score in Participants with Dyslexia Alone

End point title	Change from Baseline to Endpoint in ADHDRS-IV Total Score in Participants with Dyslexia Alone
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End point description:

The ADHDRS-IV-Parent is an 18-item scale with 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD. Each item is scored on a 0 to 3 scale: 0=none (never or rarely); 1=mild (sometimes); 2=moderate (often); 3=severe (very often). Total scores range from 0-54. Higher scores indicate higher impairment and lower scores indicate no impairment. LS mean was calculated using a REML-based, MMRM analysis which includes treatment, baseline, visit, treatment-by-visit interaction, and baseline-by-visit interaction. APD: All randomized participants who received at least one dose of study drug and had baseline and post baseline ADHDRS-IV measurements. The objectives for this portion of the trial centered around participants already exposed to ATX for 16 weeks and therefore no data for PLA/ATX are given.

End point type	Secondary
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End point timeframe:

From Week 16, Up to Week 32

End point values	ATX/ATX	ATX/PLA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	18		
Units: units on a scale				
least squares mean (standard error)	3.02 (± 2.537)	0.27 (± 1.457)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in ADHDRS-IV-Parent: Inv Total Score in Participants with ADHD or ADHD + Dyslexia

End point title	Change from Baseline to Endpoint in ADHDRS-IV-Parent: Inv Total Score in Participants with ADHD or ADHD + Dyslexia
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End point description:

The ADHDRS-IV-Parent is an 18-item scale with 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD. Each item is scored on a 0 to 3 scale: 0=none (never or rarely); 1=mild (sometimes); 2=moderate (often); 3=severe (very often). Total scores range from 0-54. Higher scores indicate higher impairment and lower scores indicate no impairment. LS mean was calculated using a REML-based, MMRM analysis which includes treatment, baseline, visit, treatment-by-visit interaction, and baseline-by-visit interaction. APD: All randomized participants who received at least one dose of study drug and had baseline and post baseline ADHDRS-IV measurements. The objectives for this

portion of the trial centered around participants already exposed to ATX for 16 weeks and therefore no data for PLA/ATX are given.

End point type	Secondary
End point timeframe:	
From Week 16, Up to Week 32	

End point values	ATX/ATX	PLA/ATX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10 ^[67]	32 ^[68]		
Units: units on a scale				
least squares mean (standard error)				
ADHD + Dyslexia	-0.32 (± 3.991)	-6.38 (± 1.946)		
ADHD alone	-6.29 (± 2.546)	-8.83 (± 1.561)		

Notes:

[67] - ADHD + Dyslexia, ADHD alone: n = 5

[68] - ADHD + Dyslexia: n = 19

ADHD alone: n = 13

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants with Treatment Emergent Adverse Events (TEAE) in Participants with Dyslexia

End point title	The Number of Participants with Treatment Emergent Adverse Events (TEAE) in Participants with Dyslexia ^[69]
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End point description:

The number of participants who experienced one or more treatment emergent adverse events (TEAEs) and who had Dyslexia A summary of other non-serious adverse events and all serious adverse events, regardless of causality, is located in the Reported Adverse Events Section. APD: All randomized participants who received at least one dose of study drug.

End point type	Secondary
End point timeframe:	
16 Weeks	

Notes:

[69] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	15		
Units: participants	13	11		

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants with TEAE in Participants with ADHD or ADHD+Dyslexia.

End point title	The Number of Participants with TEAE in Participants with ADHD or ADHD+Dyslexia. ^[70]
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End point description:

The number of participants who experienced one or more TEAEs and who had ADHD and ADHD+Dyslexia. A summary of other non-serious adverse events and all serious adverse events, regardless of causality, is located in the Reported Adverse Events Section. APD: All randomized participants who received at least one dose of study drug.

End point type	Secondary
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End point timeframe:

16 Weeks

Notes:

[70] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	29		
Units: participants				
ADHD + Dyslexia	12	14		
ADHD alone	12	8		

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants with TEAE in Participants with Dyslexia

End point title	The Number of Participants with TEAE in Participants with Dyslexia
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End point description:

The number of participants with at least one TEAE and had Dyslexia. A summary of other non-serious adverse events and all serious adverse events, regardless of causality, is located in the Reported Adverse Events Section. APD: All randomized participants who received at least one dose of study drug.

End point type	Secondary
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End point timeframe:

From 16 Weeks Up to Week 32

End point values	ATX/ATX	ATX/PLA	PLA/ATX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	6	12	
Units: participants	3	2	8	

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants With TEAE in Participants With ADHD or ADHD+Dyslexia.

End point title	The Number of Participants With TEAE in Participants With ADHD or ADHD+Dyslexia.
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End point description:

The number of participants who experienced one or more TEAEs with ADHD and ADHD + Dyslexia. A summary of other non-serious adverse events and all serious adverse events, regardless of causality, is located in the Reported Adverse Events Section. APD: All randomized participants who received at least one dose of study drug.

End point type	Secondary
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End point timeframe:

From Week 16 Up to Week 32

End point values	ATX/ATX	ATX/PLA	PLA/ATX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	12	18	
Units: participants				
ADHD + Dyslexia	2	2	10	
ADHD Alone	3	4	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events

End point title	Number of Participants with Adverse Events ^[71]
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End point description:

Number of participants who had at least one adverse event. A summary of other non-serious adverse events and all serious adverse events, regardless of causality, is located in the Reported Adverse Events Section. APD: All randomized participants who received at least one dose of study drug.

End point type	Secondary
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End point timeframe:

32 Weeks

Notes:

[71] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Atomoxetine	Placebo	ATX/ATX	ATX/PLA
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	44	18	18
Units: participants	35	31	8	8

End point values	PLA/ATX			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: participants	25			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in WJ III Individual Scores in Healthy Participants

End point title	Change From Baseline to Endpoint in WJ III Individual Scores in Healthy Participants ^[72]
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End point description:

WJ III (Woodcock et al. 2001) has two parallel forms (A and B) alternating two batteries of tests—Standard and Extended. Standard tests (1 -12) have a broad set of scores. Extended tests (13 - 22) have a more in-depth diagnostic assessment of academic strengths and weaknesses. Tests administered were 1, 2, 7, 9, 13, 17, and 20. The standard score scale is a mean (M) of 100 and a standard deviation (SD) of 15. The WJ III ACH has extended standard scores, which is a greater range of standard scores. Scores for each individual test range from 0 to over 200 where 69 and below is very low and 131 and above is very superior. Higher scores indicate better reading skills. APD: All healthy participants who had evaluable baseline and post baseline WJ III measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[72] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Healthy Participants			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
arithmetic mean (standard deviation)				
Letter Word Identification	-3.42 (± 5.18)			
Word Attack Score	-2.74 (± 6.54)			

Reading Vocabulary	-0.63 (± 7.87)			
Reading Fluency	5.37 (± 10.45)			
Reading Comprehension	-1.84 (± 6.98)			
Spelling	2.21 (± 5.70)			
Spelling of Sounds	-2.16 (± 18.35)			
Basic Reading Skills	-3.58 (± 5.10)			
Passage Comprehension	-2.11 (± 7.89)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in CTOPP Composite Scores in Healthy Participants

End point title	Change From Baseline to Endpoint in CTOPP Composite Scores in Healthy Participants ^[73]
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End point description:

The CTOPP assesses phonological awareness, phonological memory, and rapid naming and is appropriate for ages 7 to 24. The test contains six core subtests. The composite scores are 1) Phonological Awareness, comprised of the standard scores of the Elision and Blending Words; 2) Phonological Memory, comprised of standard scores for Memory for Digits and Non-word Repetition; and 3) Rapid Naming, comprised of standard scores for Rapid Digit Naming and Rapid Letter Naming. Standard scores range from 1-20, and composite scores range from 35-165. Higher scores are better and lower scores are poor. APD: All healthy participants who had evaluable baseline and post baseline CTOPP measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[73] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Healthy Participants			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
arithmetic mean (standard deviation)				
Phonological Awareness	3.63 (± 11.12)			
Phonological Memory	2.05 (± 3.88)			
Rapid Naming Score	0.63 (± 10.75)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in GORT-4 in Healthy Participants

End point title	Change from Baseline to Endpoint in GORT-4 in Healthy Participants ^[74]
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End point description:

The GORT-4 is a norm-referenced test of oral reading rate, accuracy, fluency, and comprehension valid for individuals aged 6 to 18 years old. The test has two parallel forms, Form A and Form B, that are administered in an alternating fashion (e.g. Week 0-Form A, Week 16-Form B, Week 32-Form A.) with each containing 14 separate stories and 5 multiple-choice comprehension questions for each story. GORT-4 yields the following scores: rate, accuracy, fluency, comprehension, and overall reading ability. Standard scores range from 1-20. Higher scores indicate better reading skills. Lower scores indicate poor reading skills. APD: All healthy participants who had evaluable baseline and post baseline GORT-4 measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 weeks

Notes:

[74] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Healthy Participants			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
arithmetic mean (standard deviation)				
Oral Reading Rate	0.74 (± 1.52)			
Accuracy	0.68 (± 2.60)			
Fluency	0.74 (± 1.97)			
Reading Comprehension	-0.16 (± 2.95)			
Oral Reading Quotient	-3.42 (± 24.58)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint TOWRE Total Score in Healthy Participants

End point title	Change from Baseline to Endpoint TOWRE Total Score in Healthy Participants ^[75]
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End point description:

The TOWRE is a measure of an individual's ability to pronounce printed words accurately and fluently and is appropriate for individuals aged 6 to 24 years old. The TOWRE contains two subtests: Sight Word Efficiency (SWE) which assesses the number of real printed words that can be accurately identified within 45 seconds and Phonemic Decoding Efficiency (PDE) which measures the number of pronounceable printed non-words that can be accurately decoded within 45 seconds. The total standard score ranges from 35-165. Higher scores indicate higher reading proficiency and lower scores indicate lower reading proficiency. LS mean was calculated using a REML-based, MMRM analyses which includes diagnostic group, visit, and diagnostic group-by-visit interaction. APD: All healthy participants who had evaluable baseline and post baseline TOWRE measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[75] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Healthy Participants			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
least squares mean (standard error)	0.20 (\pm 1.487)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in WMTB-C in Healthy Participants

End point title	Change from Baseline to Endpoint in WMTB-C in Healthy Participants ^[76]
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End point description:

WMTB-C is assessment of working memory capacities, consisting of 9 subtests (Trials Correct Scores [Range from 55-145], Higher scores are better, Lower scores are poor) reflecting 3 main components of working memory: central executive (CE) control/regulation of working memory (Backward Digit Recall, Listening Recall, Counting Recall); phonological loop (PL) responsible for holding verbal information for short periods (Digit Recall, Word List Matching, Word List Recall, Non-word List Recall); and visuo-spatial sketchpad (VSSP) which holds information in visual and spatial form (Block Recall, Mazes Memory).
APD: All healthy participants who had evaluable baseline and post baseline WMTB-C measurements.

End point type	Secondary
End point timeframe:	
Baseline, 16 Weeks	

Notes:

[76] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Healthy Participants			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
arithmetic mean (standard deviation)				
Digit Recall Score	2.47 (\pm 4.50)			
Word List Matching Score	-0.95 (\pm 5.38)			
Word List Recall Score	1.79 (\pm 2.53)			
Nonword List Recall Score	0.58 (\pm 4.31)			
Block Recall Score	1.63 (\pm 4.83)			
Mazes Memory Score	1.11 (\pm 7.72)			
Listening Recall Score	-0.58 (\pm 3.61)			
Counting Recall Score	0.37 (\pm 3.44)			
Backward Digit Recall Score	2.95 (\pm 4.17)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in BADD-A Total Score in Healthy Participants

End point title	Change From Baseline to Endpoint in BADD-A Total Score in Healthy Participants ^[77]
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End point description:

The BADD-A is used to assess impairment in executive functions related to ADHD. These include 1) Organizing, prioritizing, and activating to work; 2) Focusing, sustaining and shifting attention to tasks; 3) Regulating alertness, sustaining effort, and processing speed; 4) Managing frustration and modulating emotions; 5) Utilizing working memory and accessing recall (Brown 2001). Scores range from 0-120. The higher the score the more severe the ADD. Scores of 0-39 equate to "ADD possible but not likely". Scores of 40-54 equate to "ADD probable but not certain". Scores of 55-120 equate to "ADD highly probable". LS mean was calculated using a REML-based, MMRM analysis which includes the effects of diagnostic group, visit, and diagnostic group-by-visit interaction. APD: All participants who had evaluable baseline and post baseline BADD-A measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[77] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Healthy Participants			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
least squares mean (standard error)	1.42 (\pm 3.572)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in ADHDRS-IV Total Score in Healthy Participants

End point title	Change from Baseline to Endpoint in ADHDRS-IV Total Score in Healthy Participants ^[78]
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End point description:

The ADHDRS-IV-Parent is an 18-item scale with 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD. Each item is scored on a 0 to 3 scale: 0=none (never or rarely); 1=mild (sometimes); 2=moderate (often); 3=severe (very often). Total scores range from 0-54. Higher scores indicate higher impairment and lower scores indicate no impairment. LS mean was calculated using a REML-based, MMRM analysis which includes diagnostic group, visit, and diagnostic group-by-visit

interaction. APD: All healthy participants who had evaluable baseline and post baseline ADHDRS-IV measurements.

End point type	Secondary
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End point timeframe:

Baseline, 16 Weeks

Notes:

[78] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Healthy Participants			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
least squares mean (standard error)	0.15 (\pm 1.055)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in WJ III Individual Scores in Healthy Participants

End point title	Change From Baseline to Endpoint in WJ III Individual Scores in Healthy Participants ^[79]
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End point description:

WJ III (Woodcock et al. 2001) has two parallel forms (A and B) alternating two batteries of tests—Standard and Extended. Standard tests (1 -12) have a broad set of scores. Extended tests (13 - 22) have a more in-depth diagnostic assessment of academic strengths and weaknesses. Tests administered were 1, 2, 7, 9, 13, 17, and 20. The standard score scale is a mean (M) of 100 and a standard deviation (SD) of 15. The WJ III ACH has extended standard scores, which is a greater range of standard scores. Scores for each individual test range from 0 to over 200 where 69 and below is very low and 131 and above is very superior. Higher scores indicate better reading skills. APD: All healthy participants who had baseline and post-baseline WJ III measurements.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

Notes:

[79] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Healthy Participants			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
arithmetic mean (standard deviation)				
Letter Word Identification	-0.37 (\pm 5.45)			
Word Attack Score	-3.58 (\pm 7.23)			
Reading Vocabulary	0.79 (\pm 7.79)			
Reading Comprehension	0.47 (\pm 7.99)			

Reading Fluency	7.84 (\pm 11.69)			
Spelling	1.95 (\pm 4.49)			
Spelling of Sounds	3.63 (\pm 18.94)			
Basic Reading Skills Score	-2.00 (\pm 5.35)			
Passage Comprehension	0.05 (\pm 9.34)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in CTOPP Composite Scores in Healthy Participants

End point title	Change from Baseline to Endpoint in CTOPP Composite Scores in Healthy Participants ^[80]
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End point description:

The CTOPP assesses phonological awareness, phonological memory, and rapid naming and is appropriate for ages 7 to 24. The test contains six core subtests. The composite scores are 1) Phonological Awareness, comprised of the standard scores of the Elision and Blending Words; 2) Phonological Memory, comprised of standard scores for Memory for Digits and Non-word Repetition; and 3) Rapid Naming, comprised of standard scores for Rapid Digit Naming and Rapid Letter Naming. Standard scores range from 1-20, and composite scores range from 35-165. Higher scores are better and lower scores are poor. APD: All healthy participants who had evaluable baseline and post baseline CTOPP measurements.

End point type	Secondary
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End point timeframe:

Baseline, 32 weeks

Notes:

[80] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is planned only for these reporting arms in the baseline period.

End point values	Healthy Participants			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
arithmetic mean (standard deviation)				
Phonological Awareness	3.63 (\pm 11.12)			
Phonological Memory	2.05 (\pm 3.88)			
Rapid Naming Score	0.63 (\pm 10.75)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in GORT-4 in Healthy Participants

End point title	Change from Baseline to Endpoint in GORT-4 in Healthy Participants
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End point description:

The GORT-4 is a norm-referenced test of oral reading rate, accuracy, fluency, and comprehension valid for individuals aged 6 to 18 years old. The test has two parallel forms, Form A and Form B, that are administered in an alternating fashion (e.g. Week 0-Form A, Week 16-Form B, Week 32-Form A.) with each containing 14 separate stories and 5 multiple-choice comprehension questions for each story. GORT-4 yields the following scores: rate, accuracy, fluency, comprehension, and overall reading ability. Standard scores range from 1-20. Higher scores indicate better reading skills. Lower scores indicate poor reading skills. APD: All healthy participants who had evaluable baseline and post baseline GORT-4 measurements.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

End point values	Healthy Participants			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
arithmetic mean (standard deviation)				
Oral Reading Rate	0.74 (± 1.52)			
Accuracy	0.68 (± 2.60)			
Fluency	0.74 (± 1.97)			
Comprehension	-0.16 (± 2.95)			
Oral Reading Quotient	-3.42 (± 24.58)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in TOWRE Total Score in Healthy Participants

End point title	Change from Baseline to Endpoint in TOWRE Total Score in Healthy Participants
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End point description:

The TOWRE is a measure of an individual's ability to pronounce printed words accurately and fluently and is appropriate for individuals aged 6 to 24 years old. The TOWRE contains two subtests: Sight Word Efficiency (SWE) which assesses the number of real printed words that can be accurately identified within 45 seconds and Phonemic Decoding Efficiency (PDE) which measures the number of pronounceable printed non-words that can be accurately decoded within 45 seconds. The total standard score ranges from 35-165. Higher scores indicate higher reading proficiency and lower scores indicate lower reading proficiency. LS mean was calculated using a REML-based, MMRM analysis which includes diagnostic group, visit, and diagnostic group-by-visit interaction. APD: All healthy participants who had evaluable baseline and post baseline TOWRE measurements.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

End point values	Healthy Participants			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
least squares mean (standard error)	4.05 (\pm 1.578)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in WMTB-C in Healthy Participants

End point title	Change from Baseline to Endpoint in WMTB-C in Healthy Participants
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End point description:

WMTB-C is assessment of working memory capacities, consisting of 9 subtests (Trials Correct Scores [Range from 55-145], Higher scores are better, Lower scores are poor) reflecting 3 main components of working memory: central executive (CE) control/regulation of working memory (Backward Digit Recall, Listening Recall, Counting Recall); phonological loop (PL) responsible for holding verbal information for short periods (Digit Recall, Word List Matching, Word List Recall, Non-word List Recall); and visuo-spatial sketchpad (VSSP) which holds information in visual and spatial form (Block Recall, Mazes Memory).
APD: All healthy participants who had evaluable baseline and post baseline WMTB-C measurements.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

End point values	Healthy Participants			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
arithmetic mean (standard deviation)				
Digit Recall Score	2.47 (\pm 4.50)			
Word List Matching Score	-0.95 (\pm 5.38)			
Word List Recall Score	1.79 (\pm 2.53)			
Nonword List Recall Score	0.58 (\pm 4.31)			
Block Recall Score	1.63 (\pm 4.83)			
Mazes Memory Score	1.11 (\pm 7.72)			
Listening Recall Score	-0.58 (\pm 3.61)			
Counting Recall Score	0.37 (\pm 3.44)			
Backwards Digit Recall Score	2.95 (\pm 4.17)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in BADD-A Total Score in Healthy Participants

End point title	Change from Baseline to Endpoint in BADD-A Total Score in Healthy Participants
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End point description:

The BADD-A is used to assess impairment in executive functions related to ADHD. These include 1) Organizing, prioritizing, and activating to work; 2) Focusing, sustaining and shifting attention to tasks; 3) Regulating alertness, sustaining effort, and processing speed; 4) Managing frustration and modulating emotions; 5) Utilizing working memory and accessing recall (Brown 2001). Scores range from 0-120. The higher the score the more severe the ADD. Scores of 0-39 equate to "ADD possible but not likely". Scores of 40-54 equate to "ADD probable but not certain". Scores of 55-120 equate to "ADD highly probable". LS mean was calculated using a REML-based, MMRM which includes the effects of diagnostic group, visit, diagnostic group-by-visit interaction. APD: All healthy participants who had evaluable baseline and post baseline BADD-A measurements.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

End point values	Healthy Participants			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
least squares mean (standard error)	5.74 (\pm 3.991)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Endpoint in ADHDRS-IV-Parent: Inv Total Score in Healthy Participants

End point title	Change From Baseline to Endpoint in ADHDRS-IV-Parent: Inv Total Score in Healthy Participants
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End point description:

The ADHDRS-IV-Parent is an 18-item scale with 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD. Each item is scored on a 0 to 3 scale: 0=none (never or rarely); 1=mild (sometimes); 2=moderate (often); 3=severe (very often). Total scores range from 0-54. Higher scores indicate higher impairment and lower scores indicate no impairment. LS mean was calculated using a REML-based, MMRM analysis which includes the effects of diagnostic group, visit, diagnostic group-by-visit interaction. APD: All healthy participants who had evaluable baseline and post baseline ADHDRS-IV measurements.

End point type	Secondary
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End point timeframe:

Baseline, 32 Weeks

End point values	Healthy Participants			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: units on a scale				
least squares mean (standard error)	1.17 (± 1.046)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline Up To 34 Weeks

Adverse event reporting additional description:

The safety population includes all randomized participants who received one dose of study drug. Healthy participants did not receive any drug. Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	Atomoxetine - Acute Phase (SPII)
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Reporting group description:

Atomoxetine 1.0 to 1.4 mg/kg was administered orally once daily in the morning for 16 weeks, during SP II. All eligible participants who received atomoxetine during SP II and completed that period were re-randomized to atomoxetine or placebo in SP III.

Reporting group title	Placebo - Acute Phase (SPII)
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Reporting group description:

Placebo was packaged in the same way as active comparator to enforce double-blind study design. Placebo was given orally, daily for 16 weeks during SP II. All eligible participants who received placebo during SP II and completed that period were assigned atomoxetine in SP III.

Reporting group title	Placebo/Atomoxetine - Rerandomization Phase (SPIII)
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Reporting group description:

These participants were randomized to placebo in SP II and were assigned to atomoxetine in SP III. Atomoxetine was dosed orally once-daily in the morning 0.5 mg/kg/day for 3 days and then titrated up to a dose between 1.2 and 1.4 mg/kg/day.

Reporting group title	Atomoxetine/Placebo - Rerandomization Phase (SPIII)
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Reporting group description:

These participants were randomized to atomoxetine in SP II and were re-randomized to placebo in SP III. Atomoxetine was dosed orally once-daily in the morning 0.5 mg/kg/day for 3 days and then titrated up to a dose between 1.2 and 1.4 mg/kg/day.

Reporting group title	Atomoxetine/Atomoxetine - Rerandomization Phase (SPIII)
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Reporting group description:

These participants were randomized to atomoxetine in SP II and were re-randomized to atomoxetine in SP III. Atomoxetine was dosed orally once-daily in the morning 0.5 mg/kg/day for 3 days and then titrated up to a dose between 1.2 and 1.4 mg/kg/day.

Serious adverse events	Atomoxetine - Acute Phase (SPII)	Placebo - Acute Phase (SPII)	Placebo/Atomoxetine - Rerandomization Phase (SPIII)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 45 (0.00%)	0 / 44 (0.00%)	0 / 35 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Atomoxetine/Placebo	Atomoxetine/Atomoxetine	
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	o - Rerandomization Phase (SPIII)	etine - Rerandomization Phase (SPIII)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Atomoxetine - Acute Phase (SPII)	Placebo - Acute Phase (SPII)	Placebo/Atomoxetine - Rerandomization Phase (SPIII)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 45 (77.78%)	31 / 44 (70.45%)	25 / 35 (71.43%)
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	15 / 45 (33.33%)	5 / 44 (11.36%)	3 / 35 (8.57%)
occurrences (all)	15	5	3
therapeutic response unexpected			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	13 / 45 (28.89%)	10 / 44 (22.73%)	5 / 35 (14.29%)
occurrences (all)	20	12	6
Social circumstances			
educational problem	Additional description: The safety population includes all randomized participants who received one dose of study drug. Healthy participants did not receive any drug.		
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 45 (2.22%)	1 / 44 (2.27%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Reproductive system and breast disorders			
dysmenorrhoea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed ^[1]	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			

cough alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3	4 / 44 (9.09%) 4	0 / 35 (0.00%) 0
oropharyngeal pain alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 44 (0.00%) 0	1 / 35 (2.86%) 1
nasal congestion alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3	2 / 44 (4.55%) 2	0 / 35 (0.00%) 0
Psychiatric disorders abnormal behaviour alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	2 / 44 (4.55%) 2	2 / 35 (5.71%) 2
attention deficit/hyperactivity disorder alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 44 (0.00%) 0	0 / 35 (0.00%) 0
emotional disorder alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3	1 / 44 (2.27%) 1	4 / 35 (11.43%) 4
initial insomnia alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	1 / 44 (2.27%) 1	2 / 35 (5.71%) 2
irritability alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3	1 / 44 (2.27%) 1	5 / 35 (14.29%) 5
personality change alternative dictionary used:			

MedDRA 19.0			
subjects affected / exposed	0 / 45 (0.00%)	0 / 44 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
nightmare			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 45 (0.00%)	3 / 44 (6.82%)	0 / 35 (0.00%)
occurrences (all)	0	3	0
mood swings			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 45 (2.22%)	0 / 44 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Investigations			
neutrophil count decreased			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 45 (0.00%)	0 / 44 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
monocyte count decreased			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 45 (0.00%)	0 / 44 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
weight decreased			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	8 / 45 (17.78%)	2 / 44 (4.55%)	9 / 35 (25.71%)
occurrences (all)	8	2	9
white blood cell count decreased			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 45 (0.00%)	0 / 44 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
animal bite			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 45 (0.00%)	0 / 44 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
contusion			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 45 (2.22%)	3 / 44 (6.82%)	0 / 35 (0.00%)
occurrences (all)	1	4	0
joint dislocation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 45 (0.00%)	0 / 44 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
disturbance in attention			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 45 (0.00%)	0 / 44 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
dizziness			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	4 / 45 (8.89%)	0 / 44 (0.00%)	1 / 35 (2.86%)
occurrences (all)	4	0	1
headache			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	12 / 45 (26.67%)	6 / 44 (13.64%)	3 / 35 (8.57%)
occurrences (all)	12	6	3
somnolence			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 45 (0.00%)	0 / 44 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
psychomotor hyperactivity			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 45 (0.00%)	0 / 44 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
abdominal discomfort			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 45 (0.00%)	4 / 44 (9.09%)	2 / 35 (5.71%)
occurrences (all)	0	4	2
abdominal pain upper			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed occurrences (all)	10 / 45 (22.22%) 10	12 / 44 (27.27%) 12	4 / 35 (11.43%) 4
constipation alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	1 / 44 (2.27%) 1	0 / 35 (0.00%) 0
nausea alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	7 / 45 (15.56%) 7	5 / 44 (11.36%) 5	1 / 35 (2.86%) 1
vomiting alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2	0 / 44 (0.00%) 0	2 / 35 (5.71%) 2
Skin and subcutaneous tissue disorders skin hyperpigmentation alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 44 (0.00%) 0	0 / 35 (0.00%) 0
Musculoskeletal and connective tissue disorders tendonitis alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 44 (0.00%) 0	0 / 35 (0.00%) 0
Infections and infestations influenza alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3	2 / 44 (4.55%) 2	0 / 35 (0.00%) 0
upper respiratory tract infection alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	2 / 44 (4.55%) 2	2 / 35 (5.71%) 2
rhinitis alternative dictionary used: MedDRA 19.0			

subjects affected / exposed occurrences (all)	4 / 45 (8.89%) 4	4 / 44 (9.09%) 4	1 / 35 (2.86%) 1
Metabolism and nutrition disorders decreased appetite alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	8 / 45 (17.78%) 8	2 / 44 (4.55%) 2	8 / 35 (22.86%) 8
increased appetite alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	3 / 44 (6.82%) 3	0 / 35 (0.00%) 0

Non-serious adverse events	Atomoxetine/Placebo - Rerandomization Phase (SPIII)	Atomoxetine/Atomoxetine - Rerandomization Phase (SPIII)	
Total subjects affected by non-serious adverse events subjects affected / exposed	8 / 18 (44.44%)	8 / 18 (44.44%)	
General disorders and administration site conditions fatigue alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 18 (0.00%) 0	
therapeutic response unexpected alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 5	2 / 18 (11.11%) 2	
Social circumstances educational problem alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	<div>Additional description: The safety population includes all randomized participants who received one dose of study drug. Healthy participants did not receive any drug.</div> <div>1 / 18 (5.56%) 1</div>		
	0 / 18 (0.00%) 0		
Reproductive system and breast disorders dysmenorrhoea alternative dictionary used: MedDRA 19.0			

subjects affected / exposed ^[1] occurrences (all)	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders cough alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	
oropharyngeal pain alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	2 / 18 (11.11%) 2	
nasal congestion alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	
Psychiatric disorders abnormal behaviour alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	
attention deficit/hyperactivity disorder alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 18 (0.00%) 0	
emotional disorder alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	
initial insomnia alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 18 (0.00%) 0	
irritability alternative dictionary used: MedDRA 19.0			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 18 (0.00%)</p> <p>0</p>	<p>0 / 18 (0.00%)</p> <p>0</p>	
<p>personality change</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 18 (5.56%)</p> <p>1</p>	<p>0 / 18 (0.00%)</p> <p>0</p>	
<p>nightmare</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 18 (0.00%)</p> <p>0</p>	<p>0 / 18 (0.00%)</p> <p>0</p>	
<p>mood swings</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 18 (5.56%)</p> <p>1</p>	<p>0 / 18 (0.00%)</p> <p>0</p>	
<p>Investigations</p> <p>neutrophil count decreased</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 18 (0.00%)</p> <p>0</p>	<p>1 / 18 (5.56%)</p> <p>1</p>	
<p>monocyte count decreased</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 18 (0.00%)</p> <p>0</p>	<p>1 / 18 (5.56%)</p> <p>1</p>	
<p>weight decreased</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 18 (0.00%)</p> <p>0</p>	<p>0 / 18 (0.00%)</p> <p>0</p>	
<p>white blood cell count decreased</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 18 (0.00%)</p> <p>0</p>	<p>1 / 18 (5.56%)</p> <p>1</p>	
<p>Injury, poisoning and procedural complications</p> <p>animal bite</p> <p>alternative dictionary used: MedDRA 19.0</p>		

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>contusion</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>joint dislocation</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 18 (0.00%)</p> <p>0</p> <p>0 / 18 (0.00%)</p> <p>0</p> <p>1 / 18 (5.56%)</p> <p>1</p>	<p>1 / 18 (5.56%)</p> <p>1</p> <p>0 / 18 (0.00%)</p> <p>0</p> <p>0 / 18 (0.00%)</p> <p>0</p>	
<p>Nervous system disorders</p> <p>disturbance in attention</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>dizziness</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>headache</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>somnolence</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>psychomotor hyperactivity</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 18 (5.56%)</p> <p>1</p> <p>0 / 18 (0.00%)</p> <p>0</p> <p>0 / 18 (0.00%)</p> <p>0</p> <p>1 / 18 (5.56%)</p> <p>1</p> <p>1 / 18 (5.56%)</p> <p>1</p>	<p>0 / 18 (0.00%)</p> <p>0</p> <p>0 / 18 (0.00%)</p> <p>0</p> <p>1 / 18 (5.56%)</p> <p>1</p> <p>0 / 18 (0.00%)</p> <p>0</p>	
<p>Gastrointestinal disorders</p> <p>abdominal discomfort</p> <p>alternative dictionary used: MedDRA 19.0</p>			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>abdominal pain upper</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>constipation</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>nausea</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>vomiting</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 18 (0.00%)</p> <p>0</p> <p>0 / 18 (0.00%)</p> <p>0</p> <p>1 / 18 (5.56%)</p> <p>1</p> <p>0 / 18 (0.00%)</p> <p>0</p> <p>1 / 18 (5.56%)</p> <p>1</p>	<p>0 / 18 (0.00%)</p> <p>0</p> <p>0 / 18 (0.00%)</p> <p>0</p> <p>0 / 18 (0.00%)</p> <p>0</p> <p>0 / 18 (0.00%)</p> <p>0</p>	
<p>Skin and subcutaneous tissue disorders</p> <p>skin hyperpigmentation</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 18 (0.00%)</p> <p>0</p>	<p>1 / 18 (5.56%)</p> <p>1</p>	
<p>Musculoskeletal and connective tissue disorders</p> <p>tendonitis</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 18 (0.00%)</p> <p>0</p>	<p>1 / 18 (5.56%)</p> <p>1</p>	
<p>Infections and infestations</p> <p>influenza</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>upper respiratory tract infection</p> <p>alternative dictionary used: MedDRA 19.0</p>	<p>0 / 18 (0.00%)</p> <p>0</p>	<p>1 / 18 (5.56%)</p> <p>1</p>	

subjects affected / exposed	1 / 18 (5.56%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
rhinitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
increased appetite			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 October 2012	<ul style="list-style-type: none">- Addition of Synopsis- Update of safety reporting- Objectives were updated to organize all objectives based on patient diagnostic criteria- Exclusion Criteria was updated to exclude subjects weighing 25 kg or less- Treatments Administered required a change as a result of the unavailability of the 2.5 mg and 5 mg capsules and a 10 mg clinical trial package which are needed for the 18 to 25 kg weight range.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported