



Clinical trial results:

A phase III, randomized, double blind, multicenter, parallel group, placebo and active controlled, dose optimization safety and efficacy study of Lisdexamfetamine Dimesylate (LDX) in children and adolescent aged 6-17 with attention-deficit/hyperactivity disorder (ADHD)

Summary

EudraCT number	2008-000679-90
Trial protocol	GB DE FR ES NL SE BE IT HU
Global end of trial date	16 March 2011

Results information

Result version number	v1 (current)
This version publication date	21 June 2018
First version publication date	07 June 2015

Trial information

Trial identification

Sponsor protocol code	SPD489-325
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00763971
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Shire
Sponsor organisation address	Hampshire International Business Park, Chineham, Basingstoke, Hampshire, United Kingdom, RG24 8EP
Public contact	Study Physician, Shire Development LLC, +1 866 842 5335,
Scientific contact	Study Physician, Shire Development LLC, +1 866 842 5335,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-000553-PIP01-09
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	16 March 2011
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	16 March 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy of SPD489 administered as a daily morning dose (30, 50, and 70mg/day) compared to placebo over the course of 7 weeks. This study enrolled children and adolescents (6-17 years of age, inclusive) diagnosed with moderately symptomatic ADHD. The primary measure of efficacy was the clinician-administered ADHD Rating Scale-IV (ADHD-RS-IV).

Protection of trial subjects:

It was the responsibility of the Investigator to obtain written Informed Consent and assent, where applicable, from study subjects. The subject's informed consent was mandatory for study participation and was obtained in writing.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 November 2008
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	9 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Poland: 10
Country: Number of subjects enrolled	Spain: 41
Country: Number of subjects enrolled	Sweden: 52
Country: Number of subjects enrolled	United Kingdom: 27
Country: Number of subjects enrolled	Belgium: 11
Country: Number of subjects enrolled	France: 30
Country: Number of subjects enrolled	Germany: 107
Country: Number of subjects enrolled	Hungary: 32
Country: Number of subjects enrolled	Italy: 25
Worldwide total number of subjects	336
EEA total number of subjects	336

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)	197
Adolescents (12-17 years)	139
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited to participate at 48 sites in the European Union.

Pre-assignment

Screening details:

Subjects were screened for eligibility over a period of 42 days.

Period 1

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

Blinding implementation details:

The test product, reference product, and placebo were overencapsulated and appeared identical.

Arms

Are arms mutually exclusive?	Yes
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Arm title	Lisdexamfetamine Dimesylate
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Arm description:

Lisdexamfetamine Dimesylate was administered orally once-daily at approximately 7:00AM for 7 weeks (4-week dose optimization period and a 3-week dose maintenance period).

Arm type	Experimental
Investigational medicinal product name	Lisdexamfetamine Dimesylate
Investigational medicinal product code	
Other name	LDX, Vyvanse, SPD489
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 30, 50, or 70mg capsule orally once-daily at approximately 7:00AM for 7 weeks (4-week dose optimization period and a 3-week dose maintenance period).

Arm title	Methylphenidate Hydrochloride
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Arm description:

Methylphenidate Hydrochloride was administered orally once-daily at approximately 7:00AM for 7 weeks (4-week dose optimization period and a 3-week dose maintenance period).

Arm type	Active comparator
Investigational medicinal product name	Methylphenidate Hydrochloride
Investigational medicinal product code	
Other name	Concerta, OROS MPH
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One 18, 36, or 54mg tablet orally once-daily at approximately 7:00AM for 7 weeks (4-week dose optimization period and a 3-week dose maintenance period); 54mg is the maximum approved dose of CONCERTA in Europe.

Arm title	Placebo
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Arm description:

Placebo was administered orally once-daily at approximately 7:00AM for 7 weeks.

Arm type	Placebo
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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 once-daily at approximately 7:00AM for 7 weeks.

Number of subjects in period 1	Lisdexamfetamine Dimesylate	Methylphenidate Hydrochloride	Placebo
Started	113	112	111
Completed	80	74	42
Not completed	33	38	69
Randomization error	-	-	1
Subject wanted dose reduction	-	1	-
Unable to swallow capsule	2	1	1
'Exclusion criteria met '	1	-	-
Adverse event	5	2	4
Participation in 489-326 required	1	-	-
Medical monitor decision	-	-	1
Sponsor decision	1	-	-
'Lack of availability '	-	1	-
Withdrawal by subject	4	5	5
Protocol violation	3	3	2
Personal reason	3	-	-
Moved to another country	-	1	-
Lost to follow-up	-	1	-
Performed final visit on phone	-	1	-
Lack of efficacy	11	22	54
Due to holiday season	2	-	1

Baseline characteristics

Reporting groups

Reporting group title	Lisdexamfetamine Dimesylate
Reporting group description: Lisdexamfetamine Dimesylate was administered orally once-daily at approximately 7:00AM for 7 weeks (4-week dose optimization period and a 3-week dose maintenance period).	
Reporting group title	Methylphenidate Hydrochloride
Reporting group description: Methylphenidate Hydrochloride was administered orally once-daily at approximately 7:00AM for 7 weeks (4-week dose optimization period and a 3-week dose maintenance period).	
Reporting group title	Placebo
Reporting group description: Placebo was administered orally once-daily at approximately 7:00AM for 7 weeks.	

Reporting group values	Lisdexamfetamine Dimesylate	Methylphenidate Hydrochloride	Placebo
Number of subjects	113	112	111
Age categorical Units: Subjects			
6-12 years	79	81	80
13-17 years	34	31	31
Age continuous Units: years			
arithmetic mean	10.8	10.8	11
standard deviation	± 2.87	± 2.63	± 2.81
Gender categorical Units: Subjects			
Female	24	21	19
Male	89	91	92
Region of enrollment Units: Subjects			
France	10	9	11
Hungary	11	10	11
Spain	13	14	14
Poland	3	4	3
Belgium	4	3	4
Netherlands	1	0	0
Germany	36	36	35
United Kingdom	8	10	9
Italy	9	9	7
Sweden	18	17	17

Reporting group values	Total		
Number of subjects	336		
Age categorical Units: Subjects			
6-12 years	240		
13-17 years	96		

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	64		
Male	272		
Region of enrollment Units: Subjects			
France	30		
Hungary	32		
Spain	41		
Poland	10		
Belgium	11		
Netherlands	1		
Germany	107		
United Kingdom	27		
Italy	25		
Sweden	52		

End points

End points reporting groups

Reporting group title	Lisdexamfetamine Dimesylate
Reporting group description: Lisdexamfetamine Dimesylate was administered orally once-daily at approximately 7:00AM for 7 weeks (4-week dose optimization period and a 3-week dose maintenance period).	
Reporting group title	Methylphenidate Hydrochloride
Reporting group description: Methylphenidate Hydrochloride was administered orally once-daily at approximately 7:00AM for 7 weeks (4-week dose optimization period and a 3-week dose maintenance period).	
Reporting group title	Placebo
Reporting group description: Placebo was administered orally once-daily at approximately 7:00AM for 7 weeks.	

Primary: Change From Baseline in Attention Deficit Hyperactivity Disorder Rating Scale-fourth Edition (ADHD-RS-IV) Total Score at up to 7 Weeks

End point title	Change From Baseline in Attention Deficit Hyperactivity Disorder Rating Scale-fourth Edition (ADHD-RS-IV) Total Score at up to 7 Weeks
End point description: The ADHD-RS-IV consists of 18 items scored on a 4-point scale ranging from 0 (no symptoms) to 3 (severe symptoms) with total score ranging from 0 to 54. A decrease in score indicates an improvement in ADHD symptomology. This end point analysed the Full Analysis set (FAS), defined as all subjects who were randomized and who took at least 1 dose of investigational product.	
End point type	Primary
End point timeframe: Baseline and up to 7 weeks	

End point values	Lisdexamfetamine Dimesylate	Methylphenidate Hydrochloride	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	98	103	104	
Units: scores on a scale				
least squares mean (standard error)	-24.3 (± 1.16)	-18.7 (± 1.14)	-5.7 (± 1.13)	

Statistical analyses

Statistical analysis title	Analysis of ADHD-RS-IV Total Score-LDX
Comparison groups	Placebo v Lisdexamfetamine Dimesylate

Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in least squares means
Point estimate	-18.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.5
upper limit	-15.7

Statistical analysis title	Analysis of ADHD-RS-IV Total Score-MPH
Comparison groups	Placebo v Methylphenidate Hydrochloride
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in least squares means
Point estimate	-13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.9
upper limit	-10.2

Secondary: Percent of Subjects With Improvement on Clinical Global Impression-Improvement (CGI-I) Scores

End point title	Percent of Subjects With Improvement on Clinical Global Impression-Improvement (CGI-I) Scores
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End point description:

The CGI-I consists of a 7-point scale ranging from 1 (very much improved) to 7 (very much worse). Improvement is defined as a score of 1 (very much improved) or 2 (much improved) on the scale. The end point analysed the FAS, defined as all subjects who were randomized and who took at least 1 dose of investigational product.

End point type	Secondary
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End point timeframe:

Up to 7 weeks

End point values	Lisdexamfetamine Dimesylate	Methylphenidate Hydrochloride	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	100	104	104	
Units: percent of subjects				
number (not applicable)	78	60.6	14.4	

Statistical analyses

Statistical analysis title	Analysis of CGI-I-LDX
Comparison groups	Placebo v Lisdexamfetamine Dimesylate
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentages
Point estimate	63.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	53
upper limit	74.1

Statistical analysis title	Analysis of CGI-I-MPH
Comparison groups	Placebo v Methylphenidate Hydrochloride
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentages
Point estimate	46.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	34.6
upper limit	57.7

Secondary: Change From Baseline in Conner's Parent Rating Scale - Revised (CPRS-R) Total Score at up to 7 Weeks

End point title	Change From Baseline in Conner's Parent Rating Scale - Revised (CPRS-R) Total Score at up to 7 Weeks
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End point description:

The CPRS-R consists of 27 questions graded on a scale from 0 (not true at all) to 3 (very much true) with a total score ranging from 0 to 81. Higher scores are indicative of increased ADHD. This scale allows parents to respond on the basis of the child's behavior and help assess ADHD and evaluate problem behavior.

This end point analysed the FAS, defined as all subjects who were randomized and who took at least 1 dose of investigational product.

End point type	Secondary
End point timeframe:	
Baseline and up to 7 weeks	

End point values	Lisdexamfetamine Dimesylate	Methylphenidate Hydrochloride	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96	99	100	
Units: scores on a scale				
least squares mean (standard error)	-24.5 (± 1.7)	-18.4 (± 1.69)	-3.2 (± 1.69)	

Statistical analyses

Statistical analysis title	Analysis of CPRS-R Total Score-LDX
Comparison groups	Lisdexamfetamine Dimesylate v Placebo
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in least squares means
Point estimate	-21.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.5
upper limit	-17

Statistical analysis title	Analysis of CPRS-R Total Score-MPH
Comparison groups	Placebo v Methylphenidate Hydrochloride
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in least squares means
Point estimate	-15.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.3
upper limit	-10.9

Secondary: Health Utilities Index-2 (HUI-2) Scores at up to 7 Weeks

End point title	Health Utilities Index-2 (HUI-2) Scores at up to 7 Weeks
End point description:	
<p>The HUI-2 is used to describe health status and to obtain utility scores by collecting data using one or more questionnaires in formats selected to match the specific study design criteria. Scoring ranges from 0.00 (dead) to 1.00 (perfect health). Higher scores represent better health status.</p> <p>This end point analysed the FAS, defined as all subjects who were randomized and who took at least 1 dose of investigational product.</p>	
End point type	Secondary
End point timeframe:	
Baseline and up to 7 weeks	

End point values	Lisdexamfetamine Dimesylate	Methylphenidate Hydrochloride	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	98	103	97	
Units: scores on a scale				
arithmetic mean (standard deviation)				
Baseline	0.811 (± 0.1451)	0.822 (± 0.1377)	0.806 (± 0.146)	
Up to 7 weeks	0.878 (± 0.1322)	0.887 (± 0.1151)	0.843 (± 0.1431)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Child Health and Illness Profile, Child Edition: Parent Report Form (CHIP-CE:PRF) Global T-score at up to 7 Weeks

End point title	Change From Baseline in the Child Health and Illness Profile, Child Edition: Parent Report Form (CHIP-CE:PRF) Global T-score at up to 7 Weeks
End point description:	
<p>The CHIP-CE:PRF evaluates health-related quality of life. It is composed of 5 domains (satisfaction, comfort, resilience, avoidance, and achievement) consisting of a total of 76 items. The global score is an average of the scores for the 5 domains. The majority of items assess frequency of events using a 5-point response format. There is no range for a total score. Raw scale scores are used to generate T-scores. Higher scores indicate better health.</p> <p>This end point analysed the FAS, defined as all subjects who were randomized and who took at least 1 dose of investigational product.</p>	
End point type	Secondary

End point timeframe:

Baseline and up to 7 weeks

End point values	Lisdexamfetamine Dimesylate	Methylphenidate Hydrochloride	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	75	80	
Units: T-scores				
least squares mean (standard error)	8.6 (\pm 1.08)	7.1 (\pm 1.1)	-0.2 (\pm 1.07)	

Statistical analyses

Statistical analysis title	Analysis of CHIP-CE:PRF Global T-score-LDX
Comparison groups	Placebo v Lisdexamfetamine Dimesylate
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in least squares means
Point estimate	8.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.1
upper limit	11.5

Statistical analysis title	Analysis of CHIP-CE:PRF Global T-score-MPH
Comparison groups	Placebo v Methylphenidate Hydrochloride
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in least squares means
Point estimate	7.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.6
upper limit	10

Secondary: Change From Baseline in Weiss Functional Impairment Rating Scale - Parent Report (WFIRS-P) Global Score at up to 7 Weeks

End point title	Change From Baseline in Weiss Functional Impairment Rating Scale - Parent Report (WFIRS-P) Global Score at up to 7 Weeks
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End point description:

The WFIRS-P is a 50-item scale with each item scored from 0 (never/not at all) to 3 (very often/very much). Mean scores range from 0 to 3. Higher scores indicate greater functional impairment. This end point analysed the FAS, defined as all subjects who were randomized and who took at least 1 dose of investigational product.

End point type	Secondary
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End point timeframe:

Baseline and up to 7 weeks

End point values	Lisdexamfetamine Dimesylate	Methylphenidate Hydrochloride	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	83	87	
Units: scores on a scale				
least squares mean (standard error)	-0.3 (± 0.04)	-0.3 (± 0.04)	0 (± 0.04)	

Statistical analyses

Statistical analysis title	Analysis of WFIRS-P Global Score-LDX
Comparison groups	Lisdexamfetamine Dimesylate v Placebo
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in least squares means
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	-0.2

Statistical analysis title	Analysis of WFIRS-P Global Score-MPH
Comparison groups	Placebo v Methylphenidate Hydrochloride

Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference in least squares means
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	-0.1

Secondary: Change From Baseline in Brief Psychiatric Rating Scale for Children (BPRS-C) Total Score at up to 7 Weeks

End point title	Change From Baseline in Brief Psychiatric Rating Scale for Children (BPRS-C) Total Score at up to 7 Weeks
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End point description:

The BPRS-C characterizes psychopathology. A total of 21 items are rated on a scale from 0 (not present) to 6 (extremely severe) with a total score ranging from 0 to 126. A decrease in score indicates a reduction in psychopathology.

This end point analysed the Safety Population, defined as all subjects who took at least 1 dose of investigational product.

End point type	Secondary
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End point timeframe:

Baseline and up to 7 weeks

End point values	Lisdexamfetamine Dimesylate	Methylphenidate Hydrochloride	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	21	22	
Units: scores on a scale				
arithmetic mean (standard deviation)	-9.15 (± 11.264)	-9.71 (± 6.936)	-2.59 (± 7.436)	

Statistical analyses

No statistical analyses for this end point

Secondary: Columbia-Suicide Severity Rating Scale (C-SSRS)

End point title	Columbia-Suicide Severity Rating Scale (C-SSRS)
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End point description:

The C-SSRS is a 19-item semi-structured interview designed to capture suicide-related thoughts and behaviors.

This end point analysed the Safety Population, defined as all subjects who took at least 1 dose of investigational product.

End point type	Secondary
End point timeframe:	
Up to 7 weeks	

End point values	Lisdexamfetamine Dimesylate	Methylphenidate Hydrochloride	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	29	27	
Units: subjects				
Suicidal ideation	1	0	0	
Non-suicidal self injurious behavior	1	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

56 days

Adverse event reporting additional description:

Adverse events are reported for the Safety population, defined as all subjects who took at least 1 dose of investigational product.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	11.1
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Reporting groups

Reporting group title	Lisdexamfetamine Dimesylate
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Reporting group description:

Lisdexamfetamine Dimesylate was administered orally once-daily at approximately 7:00AM for 7 weeks (4-week dose optimization period and a 3-week dose maintenance period).

Reporting group title	Methylphenidate Hydrochloride
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Reporting group description:

Methylphenidate Hydrochloride was administered orally once-daily at approximately 7:00AM for 7 weeks (4-week dose optimization period and a 3-week dose maintenance period).

Reporting group title	Placebo
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Reporting group description:

Placebo was administered orally once-daily at approximately 7:00AM for 7 weeks.

Serious adverse events	Lisdexamfetamine Dimesylate	Methylphenidate Hydrochloride	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 111 (2.70%)	2 / 111 (1.80%)	3 / 110 (2.73%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 111 (0.00%)	0 / 111 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 111 (0.00%)	1 / 111 (0.90%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hematoma			

subjects affected / exposed	0 / 111 (0.00%)	0 / 111 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 111 (0.90%)	1 / 111 (0.90%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	0 / 111 (0.00%)	0 / 111 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastroesophageal reflux disease			
subjects affected / exposed	1 / 111 (0.90%)	0 / 111 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 111 (0.90%)	0 / 111 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Lisdexamfetamine Dimesylate	Methylphenidate Hydrochloride	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	80 / 111 (72.07%)	72 / 111 (64.86%)	63 / 110 (57.27%)
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	3 / 111 (2.70%)	1 / 111 (0.90%)	1 / 110 (0.91%)
occurrences (all)	7	1	1
Weight decreased			
subjects affected / exposed	15 / 111 (13.51%)	5 / 111 (4.50%)	0 / 110 (0.00%)
occurrences (all)	15	5	0

Injury, poisoning and procedural complications			
Joint sprain			
subjects affected / exposed	0 / 111 (0.00%)	4 / 111 (3.60%)	1 / 110 (0.91%)
occurrences (all)	0	4	1
Wrong drug administered			
subjects affected / exposed	4 / 111 (3.60%)	2 / 111 (1.80%)	1 / 110 (0.91%)
occurrences (all)	4	2	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 111 (3.60%)	2 / 111 (1.80%)	1 / 110 (0.91%)
occurrences (all)	4	2	1
Headache			
subjects affected / exposed	16 / 111 (14.41%)	22 / 111 (19.82%)	22 / 110 (20.00%)
occurrences (all)	21	30	27
Migraine			
subjects affected / exposed	3 / 111 (2.70%)	1 / 111 (0.90%)	0 / 110 (0.00%)
occurrences (all)	4	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 111 (4.50%)	1 / 111 (0.90%)	3 / 110 (2.73%)
occurrences (all)	5	1	3
Irritability			
subjects affected / exposed	4 / 111 (3.60%)	4 / 111 (3.60%)	0 / 110 (0.00%)
occurrences (all)	6	5	0
Pyrexia			
subjects affected / exposed	3 / 111 (2.70%)	5 / 111 (4.50%)	0 / 110 (0.00%)
occurrences (all)	3	5	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	6 / 111 (5.41%)	4 / 111 (3.60%)	6 / 110 (5.45%)
occurrences (all)	6	4	10
Abdominal upper pain			
subjects affected / exposed	8 / 111 (7.21%)	9 / 111 (8.11%)	6 / 110 (5.45%)
occurrences (all)	15	10	9
Diarrhea			

subjects affected / exposed occurrences (all)	5 / 111 (4.50%) 8	2 / 111 (1.80%) 2	3 / 110 (2.73%) 3
Nausea subjects affected / exposed occurrences (all)	12 / 111 (10.81%) 14	8 / 111 (7.21%) 8	3 / 110 (2.73%) 4
Vomiting subjects affected / exposed occurrences (all)	4 / 111 (3.60%) 5	4 / 111 (3.60%) 4	1 / 110 (0.91%) 1
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	3 / 111 (2.70%) 3	8 / 111 (7.21%) 8	0 / 110 (0.00%) 0
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all)	1 / 111 (0.90%) 1	0 / 111 (0.00%) 0	3 / 110 (2.73%) 4
Psychiatric disorders Aggression subjects affected / exposed occurrences (all)	4 / 111 (3.60%) 4	3 / 111 (2.70%) 3	1 / 110 (0.91%) 1
Initial insomnia subjects affected / exposed occurrences (all)	3 / 111 (2.70%) 3	7 / 111 (6.31%) 7	1 / 110 (0.91%) 1
Insomnia subjects affected / exposed occurrences (all)	16 / 111 (14.41%) 16	9 / 111 (8.11%) 9	0 / 110 (0.00%) 0
Sleep disorder subjects affected / exposed occurrences (all)	6 / 111 (5.41%) 6	2 / 111 (1.80%) 2	1 / 110 (0.91%) 1
Tic subjects affected / exposed occurrences (all)	2 / 111 (1.80%) 2	3 / 111 (2.70%) 4	2 / 110 (1.82%) 2
Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all)	4 / 111 (3.60%) 4	3 / 111 (2.70%) 3	1 / 110 (0.91%) 1

Influenza			
subjects affected / exposed	0 / 111 (0.00%)	3 / 111 (2.70%)	0 / 110 (0.00%)
occurrences (all)	0	3	0
Nasopharyngitis			
subjects affected / exposed	8 / 111 (7.21%)	14 / 111 (12.61%)	8 / 110 (7.27%)
occurrences (all)	9	14	9
Upper respiratory tract infection			
subjects affected / exposed	3 / 111 (2.70%)	1 / 111 (0.90%)	2 / 110 (1.82%)
occurrences (all)	3	1	2
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	12 / 111 (10.81%)	6 / 111 (5.41%)	2 / 110 (1.82%)
occurrences (all)	13	8	2
Decreased appetite			
subjects affected / exposed	28 / 111 (25.23%)	17 / 111 (15.32%)	3 / 110 (2.73%)
occurrences (all)	31	21	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported