Clinical trial results:
A Phase 4, Open-label, Multicentre, 2-Year Safety Study of Lisdexamfetamine Dimesylate in Children and Adolescents Aged 6-17 Years With Attention-Deficit/Hyperactivity Disorder (ADHD)

Summary

EudraCT number	2010-020951-30
Trial protocol	GB NL BE ES SE PL DE HU IT
Global end of trial date	30 September 2014

Results information

Result version number	v1 (current)
This version publication date	04 September 2018
First version publication date	25 April 2015

Trial information

Trial identification

Sponsor protocol code	SPD489-404

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01328756
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Shire Pharmaceutical Development Ltd.
Sponsor organisation address	Hampshire International Business Park, Chineham, Basingstoke, Hampshire, RG24 8EP, United Kingdom,
Public contact	Study Physician, Shire, 1866 8425335,
Scientific contact	Study Physician, Shire, 1866 8425335,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-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	30 September 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety of SPD489 administered as a daily morning dose (30, 50, and 70 milligram [mg]) in the treatment of children and adolescents (6-17 years of age inclusive at the time of consent in this study or a previous SPD489 study [SPD489-317 {2009-011745-94}, SPD489-325 {2008-000679-90}, or SPD489-326 {2008-000720-10}]) diagnosed with moderate to severely symptomatic Attention-Deficit/Hyperactivity Disorder (ADHD).

Protection of trial subjects:

This study was conducted in accordance with current applicable regulations, International Conference on Harmonisation (ICH) of Good Clinical Practice (GCP), the principles of the Declaration of Helsinki, as well as other applicable local ethical and legal requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 July 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 14
Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Romania: 11
Country: Number of subjects enrolled	Spain: 82
Country: Number of subjects enrolled	Sweden: 43
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	Germany: 52
Country: Number of subjects enrolled	Hungary: 63
Country: Number of subjects enrolled	Italy: 17
Worldwide total number of subjects	314
EEA total number of subjects	314

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)	170
Adolescents (12-17 years)	140
Adults (18-64 years)	4
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study SPD489-404 enrolled subjects from 3 antecedent studies (SPD489-317, SPD489-325, and SPD489-326), or directly enrolled. Of 348 subjects screened, 314 subjects were enrolled and treated.

Pre-assignment

Screening details:

At optimization period,subjects initiated SPD489 at 30 mg and dose was titrated until acceptable response(30% reduction from baseline in ADHD Rating Scale-IV total score, clinical global impression-improvement[CGI-I]score of 1 or 2 with tolerable side effects)was achieved.Maximum dose was 70 mg.Dose adjustments were done in dose maintenance period.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Lisdexamfetamine dimesylate

Arm description:

Lisdexamfetamine dimesylate (SPD489) 30, 50 and 70 mg capsules once daily orally during the 4-week dose optimization period and the 100-week maintenance period.

Arm type	Experimental
Investigational medicinal product name	Lisdexamfetamine dimesylate
Investigational medicinal product code	SPD489
Other name	Vyvanse,Venvanse, Elvanse, Tyvense
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Lisdexamfetamine dimesylate (SPD489) 30, 50 and 70 mg capsules once daily orally during the 4-week dose optimization period and the 100-week maintenance period.

Number of subjects in period 1	Lisdexamfetamine dimesylate
Started	314
Completed	191
Not completed	123
Consent withdrawn by subject	41
Adverse event	39
Unspecified	29
Lost to follow-up	5
Protocol deviation	4
Lack of efficacy	5

Baseline characteristics

Reporting groups	
Reporting group title	Lisdexamfetamine dimesylate
Reporting group description:	
Lisdexamfetamine dimesylate (SPD489) 30, 50 and 70 mg capsules once daily orally during the 4-week dose optimization period and the 100-week maintenance period.	

Reporting group values	Lisdexamfetamine dimesylate	Total	
Number of subjects	314	314	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	11.4		
standard deviation	± 2.88	-	
Gender categorical			
Units: Subjects			
Female	64	64	
Male	250	250	
Clinical Global Impressions – Severity of Illness (CGI-S) Rating			
The Clinical Global Impressions (CGI) Scale permits a global evaluation of the subject's severity and improvement over time. This assessment will help guide the clinician on dosing adjustments. The CGI has been used extensively in clinical studies of ADHD. CGI-S was a 7-point scale ranging from 1 (normal, not at all ill) to 7 (among the most extremely ill subjects), evaluated by the Investigator.			
Units: Subjects			
Normal, not all ill	0	0	
Borderline mentally ill	0	0	
Mildly ill	1	1	
Moderately ill	69	69	
Markedly ill	152	152	
Severely ill	81	81	
Among the most extremely ill subjects	11	11	
Body Weight			
Units: kilogram(s)			
arithmetic mean	46.13		
standard deviation	± 16.434	-	
Height			
Units: centimeters			
arithmetic mean	152.29		
standard deviation	± 16.633	-	
Body Mass Index (BMI)			
BMI was calculated as (weight [kilogram] per height [square meter]) at screening.			
Units: kilogram per square meter			
arithmetic mean	19.22		
standard deviation	± 3.389	-	
Attention-Deficit/Hyperactivity Disorder			

Rating Scale-IV (ADHD-RS-IV): Total Score			
ADHD-RS-IV consisted of 18 items designed to reflect current symptomatology of ADHD based on Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition – Text Revision (DSM-IV-TR) criteria, completed by the Investigator. Each item was scored from a range of 0 (reflecting no symptoms) to 3 (reflecting severe symptoms) with total scores ranging from 0-54. Higher scores depicted worse symptoms.			
Units: scores on a scale arithmetic mean standard deviation	 41.1 ± 7.03	 -	
ADHD-RS-IV: Inattention Subscale Score			
ADHD-RS-IV consisted of 18 items designed to reflect current symptomatology of ADHD based on Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition – Text Revision (DSM-IV-TR) criteria, completed by the Investigator. Each item was scored from a range of 0 (reflecting no symptoms) to 3 (reflecting severe symptoms) with total scores ranging from 0-54. The 18 items were grouped into 2 sub-scales: hyperactivity/impulsivity and inattention. Inattention subscale score consisted of odd number items 1-17 with scores ranging from 0 to 27. Higher score indicated worse symptom.			
Units: scores on a scale arithmetic mean standard deviation	 22.1 ± 3.52	 -	
ADHD-RS-IV: Hyperactivity/Impulsivity Subscore			
ADHD-RS-IV consisted of 18 items designed to reflect current symptomatology of ADHD based on DSM-IV-TR criteria, completed by the Investigator. Each item was scored from a range of 0 (reflecting no symptoms) to 3 (reflecting severe symptoms) with total scores ranging from 0-54. The 18 items were grouped into 2 sub-scales: hyperactivity/impulsivity and inattention. Hyperactivity/impulsivity subscale score consisted of even number items 2-18 with scores ranging from 0 to 27. Higher score indicated worse symptom.			
Units: scores on a scale arithmetic mean standard deviation	 19 ± 5.86	 -	

End points

End points reporting groups

Reporting group title	Lisdexamfetamine dimesylate

Reporting group description:

Lisdexamfetamine dimesylate (SPD489) 30, 50 and 70 mg capsules once daily orally during the 4-week dose optimization period and the 100-week maintenance period.

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety population (N=314) was defined as all subjects who took at least 1 dose of Lisdexamfetamine dimesylate during this study.

Subject analysis set title	Full Analysis Set (FAS) population
Subject analysis set type	Full analysis

Subject analysis set description:

Of 314 enrolled subjects, 299 subjects were included in the FAS (that is, took at least 1 dose of SPD489 and had at least 1 on-treatment post baseline efficacy assessment). One subject without post baseline efficacy data and 14 additional subjects from one site were excluded from the FAS.

Primary: Number of Subjects With all Treatment-Emergent Adverse Events (TEAEs) and Serious TEAEs

End point title	Number of Subjects With all Treatment-Emergent Adverse Events (TEAEs) and Serious TEAEs[1]

End point description:

An adverse event (AE) was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. TEAEs were defined as AEs/SAEs that started or worsened after the study drug treatment up to follow-up visit (Week 108).

End point type	Primary

End point timeframe:

Baseline (Week 0) up to follow-up visit (Week 108).

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Lisdexamfetamine dimesylate			
Subject group type	Reporting group			
Number of subjects analysed	314[2]			
Units: Subjects				
Any TEAE	282			
Serious TEAE	28			

Notes:

[2] - Safety population

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Pulse Rate at Last On-treatment Assessment (LOTA)

End point title	Change From Baseline in Pulse Rate at Last On-treatment Assessment (LOTA)[3]

End point description:

End point type	Primary

End point timeframe:

Baseline (Week 0), LOTA (Week 104)

Notes:

[3] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Lisdexamfetamine dimesylate			
Subject group type	Reporting group			
Number of subjects analysed	313[4]			
Units: beats per minute				
arithmetic mean (standard deviation)	7 (± 11.6)			

Notes:

[4] - Safety population with subjects evaluable for this outcome

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Sitting Diastolic Blood Pressure (DBP) at Last On-treatment Assessment (LOTA)

End point title	Change From Baseline in Sitting Diastolic Blood Pressure (DBP) at Last On-treatment Assessment (LOTA)[5]

End point description:

End point type	Primary

End point timeframe:

Baseline (Week 0), LOTA (Week 104)

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Lisdexamfetamine dimesylate			
Subject group type	Reporting group			
Number of subjects analysed	313[6]			
Units: mmHg				
arithmetic mean (standard deviation)	3.2 (± 9.05)			

Notes:

[6] - Safety population with subjects evaluable for this outcome

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Sitting Systolic Blood Pressure (SBP) at Last On-

treatment Assessment (LOTA)

End point title	Change From Baseline in Sitting Systolic Blood Pressure (SBP) at Last On-treatment Assessment (LOTA)[7]

End point description:

End point type	Primary

End point timeframe:

Baseline (Week 0), LOTA (Week 104)

Notes:

[7] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Lisdexamfetamine dimesylate			
Subject group type	Reporting group			
Number of subjects analysed	313[8]			
Units: mmHg				
arithmetic mean (standard deviation)	3.4 (± 10.33)			

Notes:

[8] - Safety population with subjects evaluable for this outcome

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Body Weight at Last On-treatment Assessment (LOTA)

End point title	Change From Baseline in Body Weight at Last On-treatment Assessment (LOTA)[9]

End point description:

End point type	Primary

End point timeframe:

Baseline (Week 0), LOTA (Week 104)

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Lisdexamfetamine dimesylate			
Subject group type	Reporting group			
Number of subjects analysed	313[10]			
Units: kilogram(s)				
arithmetic mean (standard deviation)	2.1 (± 5.83)			

Notes:

[10] - Safety population with subjects evaluable for this outcome

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Height at Last On-treatment Assessment (LOTA)

End point title	Change From Baseline in Height at Last On-treatment Assessment (LOTA)[11]

End point description:

End point type	Primary

End point timeframe:

Baseline (Week 0), LOTA (Week 104)

Notes:

[11] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Lisdexamfetamine dimesylate			
Subject group type	Reporting group			
Number of subjects analysed	301[12]			
Units: centimeter(s)				
arithmetic mean (standard deviation)	6.1 (± 4.9)			

Notes:

[12] - Safety population with subjects evaluable for this outcome

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Body Mass Index (BMI) at Last On-treatment Assessment (LOTA)

End point title	Change From Baseline in Body Mass Index (BMI) at Last On-treatment Assessment (LOTA)[13]

End point description:

End point type	Primary

End point timeframe:

Baseline (Week 0), LOTA (Week 104)

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Lisdexamfetamine dimesylate			
Subject group type	Reporting group			
Number of subjects analysed	313[14]			
Units: kilogram per square meter				
arithmetic mean (standard deviation)	-0.5 (± 1.72)			

Notes:

[14] - Safety population with subjects evaluable for this outcome

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Heart Rate at Last On-treatment Assessment (LOTA)

End point title	Change From Baseline in Heart Rate at Last On-treatment Assessment (LOTA)[15]

End point description:

End point type	Primary

End point timeframe:

Baseline (Week 0), LOTA (Week 104)

Notes:

[15] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Lisdexamfetamine dimesylate			
Subject group type	Reporting group			
Number of subjects analysed	303[16]			
Units: beats per minute				
arithmetic mean (standard deviation)	7.1 (± 13.51)			

Notes:

[16] - Safety population with subjects evaluable for this outcome

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in QT interval at Last On-treatment Assessment (LOTA)

End point title	Change From Baseline in QT interval at Last On-treatment Assessment (LOTA)[17]

End point description:

End point type	Primary

End point timeframe:

Baseline (Week 0), LOTA (Week 104)

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Lisdexamfetamine dimesylate			
Subject group type	Reporting group			
Number of subjects analysed	302[18]			
Units: milliseconds				
arithmetic mean (standard deviation)	-10.3 (± 23.53)			

Notes:

[18] - Safety population with subjects evaluable for this outcome

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in QT Interval Corrected Using Fridericia's Formula (QTcF) at Last On-treatment Assessment (LOTA)

End point title	Change From Baseline in QT Interval Corrected Using Fridericia's Formula (QTcF) at Last On-treatment Assessment (LOTA)[19]

End point description:

End point type	Primary

End point timeframe:

Baseline (Week 0), LOTA (Week 104)

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Lisdexamfetamine dimesylate			
Subject group type	Reporting group			
Number of subjects analysed	302[20]			
Units: milliseconds				
arithmetic mean (standard deviation)	-0.6 (± 15.24)			

Notes:

[20] - Safety population with subjects evaluable for this outcome

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Brief Psychiatric Rating Scale for Children (BPRS-C) Total Scores at Last On-treatment Assessment (LOTA)

End point title	Change From Baseline in Brief Psychiatric Rating Scale for Children (BPRS-C) Total Scores at Last On-treatment Assessment (LOTA)[21]

End point description:

The BPRS-C was designed to provide a characterization of the child and adolescent psychopathology, was used to monitor subject safety. The BPRS-C assessed 7 independent factors (3 items each), for a total of 21 items that represented behavioural disorders, depression, thinking disturbance, psychomotor excitation, withdrawal retardation, anxiety, and organicity. Each item was rated using a 7-point scale including 0 (not present), 1 (very mild), 2 (mild), 3 (moderate), 4 (moderately severe), 5 (severe), and 6 (extremely severe). Total score is the sum of each item score; range from 0 to 126. Higher score indicated worse psychology.

End point type	Primary

End point timeframe:

Baseline (Week 0), LOTA (Week 104)

Notes:

[21] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Lisdexamfetamine dimesylate			
Subject group type	Reporting group			
Number of subjects analysed	313[22]			
Units: scores on a scale				
arithmetic mean (standard deviation)	-10.3 (± 9.64)			

Notes:

[22] - Safety population with subjects evaluable for this outcome

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Attention-Deficit/Hyperactivity Disorder Rating Scale-IV (ADHD-RS-IV) Total Score at Last On-treatment Assessment (LOTA)

End point title	Change From Baseline in the Attention-Deficit/Hyperactivity Disorder Rating Scale-IV (ADHD-RS-IV) Total Score at Last On-treatment Assessment (LOTA)

End point description:

ADHD-RS-IV consisted of 18 items designed to reflect current symptomatology of ADHD based on Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition – Text Revision (DSM-IV-TR) criteria, completed by the Investigator. Each item was scored from a range of 0 (reflecting no symptoms) to 3 (reflecting severe symptoms) with total scores ranging from 0-54. Higher score indicated worse symptom.
Please find the statistical analysis in the attachment below.

End point type	Secondary

End point timeframe:

Baseline (Week 0), LOTA (Week 104)

End point values	Lisdexamfetamine dimesylate			
Subject group type	Reporting group			
Number of subjects analysed	299[23]			
Units: Scores on a scale				
arithmetic mean (standard deviation)	-25.8 (± 11.1)			

Notes:

[23] - FAS population

Attachments (see zip file)	Statistical analysis_Secondary_ADHD-RS-IV Total Sc/SPD489-

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinical Global Impression-Global Improvement (CGI-I) at Last On-treatment Assessment (LOTA)

End point title	Number of Subjects With Clinical Global Impression-Global Improvement (CGI-I) at Last On-treatment Assessment (LOTA)

End point description:

The Clinical Global Impressions (CGI) Scale permits a global evaluation of the subject's severity and improvement over time. This assessment will help guide the clinician on dosing adjustments. The CGI

has been used extensively in clinical studies of ADHD. CGI-I was a 7-point scale ranging from 1 (very much improved) to 7 (very much worse), evaluated by the Investigator.

End point type	Secondary

End point timeframe:

LOTA (Week 104)

End point values	Lisdexamfetamine dimesylate			
Subject group type	Reporting group			
Number of subjects analysed	299[24]			
Units: Subjects				
Very much improved	141			
Much improved	92			
Minimally improved	28			
No change	20			
Minimally worse	13			
Much worse	5			
Very much worse	0			

Notes:

[24] - FAS population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinical Global Impression-Severity of Illness (CGI-S) at Last On-treatment Assessment (LOTA)

End point title	Number of Subjects With Clinical Global Impression-Severity of Illness (CGI-S) at Last On-treatment Assessment (LOTA)

End point description:

The Clinical Global Impressions (CGI) Scale permits a global evaluation of the subject's severity and improvement over time. This assessment will help guide the clinician on dosing adjustments. The CGI has been used extensively in clinical studies of ADHD. CGI-S was a 7-point scale ranging from 1 (normal, not at all ill) to 7 (among the most extremely ill subjects), evaluated by the Investigator.

End point type	Secondary

End point timeframe:

LOTA (Week 104)

End point values	Lisdexamfetamine dimesylate			
Subject group type	Reporting group			
Number of subjects analysed	299[25]			
Units: Subjects				
Normal, not all ill	73			
Borderline mentally ill	97			
Mildly ill	67			
Moderately ill	39			
Markedly ill	17			

Severely ill	4			
Among the most extremely ill subjects	2			

Notes:

[25] - FAS population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline (Week 0) up to follow-up (Week 108)	
Adverse event reporting additional description:	
TEAEs were defined as AEs/SAEs that started or worsened after the study drug treatment up to follow-up visit (Week 108).	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups	
Reporting group title	Lisdexamfetamine dimesylate
Reporting group description:	
Lisdexamfetamine dimesylate (Vyvanse, SPD489) 30 to 70 mg capsule once daily orally.	

Serious adverse events	Lisdexamfetamine dimesylate		
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 314 (8.92%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	1 / 314 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Agitation postoperative			
subjects affected / exposed	1 / 314 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			
subjects affected / exposed	1 / 314 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			

subjects affected / exposed	1 / 314 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	1 / 314 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			
subjects affected / exposed	6 / 314 (1.91%)		
occurrences causally related to treatment / all	3 / 7		
deaths causally related to treatment / all	0 / 0		
Migraine			
subjects affected / exposed	1 / 314 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	1 / 314 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	1 / 314 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 314 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	1 / 314 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dental caries			
subjects affected / exposed	1 / 314 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Disbacteriosis			
subjects affected / exposed	1 / 314 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Testicular torsion			
subjects affected / exposed	1 / 314 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	1 / 314 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	1 / 314 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oppositional defiant disorder			
subjects affected / exposed	1 / 314 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Panic attack			

subjects affected / exposed	1 / 314 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Suicidal ideation				
subjects affected / exposed	1 / 314 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Appendicitis				
subjects affected / exposed	3 / 314 (0.96%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Infectious peritonitis				
subjects affected / exposed	1 / 314 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 314 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oral herpes				
subjects affected / exposed	1 / 314 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lobar pneumonia				
subjects affected / exposed	1 / 314 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mumps				
subjects affected / exposed	1 / 314 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Retroperitoneal abscess				

subjects affected / exposed	1 / 314 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	2 / 314 (0.64%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Lisdexamfetamine dimesylate		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	250 / 314 (79.62%)		
Investigations			
Weight decreased			
subjects affected / exposed	63 / 314 (20.06%)		
occurrences (all)	68		
Nervous system disorders			
Headache			
subjects affected / exposed	68 / 314 (21.66%)		
occurrences (all)	139		
General disorders and administration site conditions			
Irritability			
subjects affected / exposed	36 / 314 (11.46%)		
occurrences (all)	39		
Pyrexia			
subjects affected / exposed	32 / 314 (10.19%)		
occurrences (all)	40		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	28 / 314 (8.92%)		
occurrences (all)	34		
Vomiting			
subjects affected / exposed	27 / 314 (8.60%)		
occurrences (all)	33		
Nausea			

subjects affected / exposed	31 / 314 (9.87%)		
occurrences (all)	41		
Abdominal pain			
subjects affected / exposed	29 / 314 (9.24%)		
occurrences (all)	36		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	22 / 314 (7.01%)		
occurrences (all)	25		
Oropharyngeal pain			
subjects affected / exposed	18 / 314 (5.73%)		
occurrences (all)	24		
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	19 / 314 (6.05%)		
occurrences (all)	20		
Tic			
subjects affected / exposed	18 / 314 (5.73%)		
occurrences (all)	25		
Initial insomnia			
subjects affected / exposed	38 / 314 (12.10%)		
occurrences (all)	46		
Insomnia			
subjects affected / exposed	60 / 314 (19.11%)		
occurrences (all)	75		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	18 / 314 (5.73%)		
occurrences (all)	21		
Nasopharyngitis			
subjects affected / exposed	73 / 314 (23.25%)		
occurrences (all)	128		
Pharyngitis			
subjects affected / exposed	16 / 314 (5.10%)		
occurrences (all)	18		
Metabolism and nutrition disorders			

Decreased appetite subjects affected / exposed occurrences (all)	170 / 314 (54.14%) 213		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 November 2011	1. Emergency contact information was updated 2. Inclusion and exclusion criteria were updated primarily to simplify subject inclusion with regard to their involvement in previous SPD489 clinical studies 3. Subjects with age >=18 years, were included at screening and blood pressure criteria for subjects with >=18 years at study entry were added 4. Excluded subjects whose symptoms were well-controlled on their currently prescribed ADHD medication with acceptable tolerability 5. 12-lead ECG was added at Visit 4 6. Permitted use of oral corticosteroids was defined 7. Restriction for montelukast sodium widened to include all leukotriene antagonists 8. Ferritin was added to biochemistry panel 9. Growth sub-section was added in accordance with primary objective.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Since this study is an open-label trial, results should be interpreted with caution.

Notes: