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)

Published: 01-02-2011
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Primary: The primary objective of this study is to evaluate the long-term safety of SPD489 administered as adaily morning dose (30, 50, and 70mg) in the treatment of children and adolescents (6-17 years of ageinclusive at the time of consent in this...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cognitive and attention disorders and disturbances
Study type	Interventional

Summary

ID

NL-OMON38374

Source
ToetsingOnline

Brief title
Study of LDX in children and adolescents with ADHD

Condition

- Cognitive and attention disorders and disturbances

Synonym
ADHD, attention-deficit/hyperactivity disorder

Research involving

Human

Sponsors and support

Primary sponsor: Shire
Source(s) of monetary or material Support: Shire Pharmaceutical Development Ltd.

Intervention

Keyword: 6-17 years, ADHD, Lisdexamfetamine Dimeslytate, safety study

Outcome measures

Primary outcome

The primary endpoint of this study is the long-term safety of SPD489. The

evaluation of

safety will be based on the occurrence of TEAEs, evaluation of vital signs, and

ECG results.

Additionally the effects on growth, sexual development (Tanner Staging) and

neurocognition

(via Cambridge Neuropsychological Test Automated Battery - CANTAB) will be

assessed

and psychiatric AEs such as psychosis (using the Brief Psychiatric Rating Scale

for Children

- BPRS-C) and suicidality (using the Columbia-Suicide Severity Rating Scale -

C-SSRS) will

be monitored.

The measures used to assess the primary outcomes are detailed further in

Section 9.14.

of the protocol.

Secondary outcome

Secondary endpoints of the study are listed below:

• The change from Baseline (Visit 0) in the ADHD-RS-IV total score as well as

the

Hyperactivity/Impulsivity and Inattention subscale scores at each post-baseline

visit

• The CGI-I and CGI-S at Endpoint and each post-baseline visit.

Study description

Background summary

The symptoms and subsequent impairment associated with ADHD is increasingly being
recognised as a lifetime disease. The treatment of ADHD in some children continues until or
after puberty and covers an important time in growth, physical, sexual, and cognitive
development.
As such, further research into the concept of lifetime treatment with ADHD medications and
in particular effects on growth, development, and neurocognition in addition to long-term
safety is required.
While the SPD489 clinical program has studied the efficacy, safety, and tolerability of
SPD489 in treating core symptoms of ADHD in children and adolescents aged 6-17 years and
adults aged 18-55 years, the majority of these studies have been of short duration - up to
8 weeks. A number of long-term studies have been undertaken (up to 1 year) and these have
confirmed the safety and ongoing efficacy in this patient population. Study SPD489-404 has
been designed to further evaluate the long-term effects of SPD489 in children and adolescents
over a 2-year treatment period. This study is the first opportunity to collect scientific data on

specific endpoints such as sexual development and cognition in an open-label environment.
The study will also serve to provide additional long-term safety data, since prior exposure has
been limited to 1 year of treatment. The collection of this long-term data represents an
important opportunity to better characterise the safety, efficacy and tolerability profile of
SPD489.

Study objective

Primary: The primary objective of this study is to evaluate the long-term safety of SPD489 administered as a
daily morning dose (30, 50, and 70mg) 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, SPD489-325, or
SPD489-326) diagnosed with moderately to severely symptomatic ADHD.
The evaluation of safety will be based on the occurrence of treatment-emergent adverse events (TEAEs),
evaluation of vital signs, and electrocardiogram (ECG) results. Additionally, the effects on growth, sexual
development, and neurocognition will be assessed and psychiatric adverse events (AEs) including psychosis
and suicidality will be monitored.
Secondary: The secondary objectives of this study are:
1. To assess the long-term efficacy of SPD489 using the clinician-administered ADHD-rating scale-IV
(ADHD-RS-IV) total score and hyperactivity/impulsivity and inattentiveness subscale scores.
2. To assess the long-term efficacy of SPD489 using global clinical measures of severity and improvement
as measured by the Clinical Global Impressions - Severity of Illness (CGI-S) and Clinical Global
Impressions - Global Improvement (CGI-I).

Study design

This study is a Phase 4, multicentre, open-label study designed to evaluate the safety of SPD489 administered
as a daily morning dose (30, 50, or 70mg) for 2 years. Children and adolescents (6-17 years of age inclusive
at time of consent in this study or a previous SPD489 study [SPD489-317, SPD489-325, or SPD489-326] who
have been diagnosed with ADHD will be enrolled and treated for up to 104 weeks

to evaluate the long-term
safety and efficacy of SPD489.
The study will have 3 phases: (1) screening and washout; (2) a 104-week treatment phase inclusive of a
4-week dose optimisation period and a 100-week maintenance period; and (3) a safety follow-up visit (28-30
days after the last dose of investigational product). Subjects will be required to visit the site up to 16 times
over a 109-114 week period.

Intervention

At visit 0 the patients will receive the study drug in a dose of 30mg. This can be increased weekly with 20mg until an optimal dose is reached (maximum 70mg per day). This during a period of 4 weeks. The dosage can also be decreased with 20mg, with a minimul of 30mg per day.

These 4 weeks are followed by a period of 100 weeks (maintenance period).

Study burden and risks

A physicial exam will be done 3 times. During most visit the blood pressure, temperature, weight and height will be measured. The patient will complete a questionnaire 6 times. The ECG will be done 5 times.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

For subjects who participated in another SPD489 study (SPD489-317, SPD489-325 and/or SPD489-326):
1. Subject is a male or female aged 6-17 years inclusive at the time of consent for the previous SPD489 study.
2. Subject participated in SPD489-317, completed 9 weeks of treatment, and completed the 1-week posttreatment safety follow-up visit.
For subjects who have not participated in another SPD489 study:
3. Subject is a male or female aged 6-17 years inclusive at the time of consent.
4. Subject must meet DSM IV TR criteria for a primary diagnosis of ADHD based on a detailed psychiatric evaluation.
For all subjects:
5. Subject has a Baseline (Visit 0) ADHD-RS-IV total score >=28.
6. Subject, who is female of childbearing potential (FOCP), must have a negative serum beta Human Chorionic Gonadotropin (HCG) pregnancy test at Screening (Visit -1) and a negative urine pregnancy test at Baseline (Visit 0), be non-lactating, and agree to comply with any applicable contraceptive requirements of the protocol.
7. Subject*s parent or legally authorised representative (LAR) must provide signature of informed consent, and there must be documentation of assent (if applicable) by the subject indicating that the subject is aware of the investigational nature of the study and the required procedures and restrictions in accordance with the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Guideline E6 and applicable regulations, before completing any study-related procedures.
8. Subject and parent/LAR are willing and able to comply with all the testing and requirements defined in this protocol, including oversight of morning dosing. Specifically, the parent/LAR must be available upon awakening, at approximately 7:00AM, to dispense the dose of Investigational Product for the duration of the study.
9. Subject aged 6-17 years has blood pressure measurements within the 95th percentile for age, sex, and height at Screening (Visit -1) and Baseline (Visit 0). Subject aged >=18 years has a systolic blood pressure <=139mmHg and a diastolic blood pressure <=89mmHg at Screening (Visit -1) and Baseline (Visit 0).
10. Subject is functioning at an age-appropriate level intellectually, as deemed by the study

Investigator.
11. Subject is able to swallow a capsule.

Exclusion criteria

For subjects who participated in another SPD489 study:
1. Subject was terminated from a previous SPD489 study (SPD489-325 or SPD489-326) for protocol non-adherence and/or subject non-compliance and/or experienced a medication-related SAE or AE resulting in termination from the previous study.
2. Subject experienced any clinically significant AEs in a prior SPD489 study (SPD489-317, SPD489-325, or SPD489-326) that, in the opinion of the Investigator, would preclude further exposure to SPD489.
For all subjects:
3. Subject*s symptoms are well-controlled on their currently prescribed ADHD medication with acceptable tolerability.
4. Subject has a positive urine drug result at Screening (Visit -1), with the exception of the subject*s current ADHD therapy.
5. Subject has a current, controlled (requiring a restricted medication) or uncontrolled, comorbid psychiatric diagnosis with significant symptoms such as any severe comorbid Axis II disorder or severe Axis I disorder (such as Post Traumatic Stress Disorder, psychosis, bipolar illness, pervasive developmental disorder, severe obsessive compulsive disorder, severe depressive or severe anxiety disorder) or other symptomatic manifestations, such as agitated states, marked anxiety, or tension that, in the opinion of the examining clinician, will contraindicate treatment with SPD489 or confound efficacy or safety assessments. Comorbid psychiatric diagnoses will be established using the K-SADS-PL and additional modules if warranted by the results of the initial interview. Participation in behavioural therapy is permitted.
6. Subject has taken another Investigational Product or taken part in a clinical study with the exception of a prior SPD489 study within 30 days prior to Screening (Visit -1).
7. Subject weighs <22.7kg (50lbs) or is significantly underweight based on World Health Organization Body Mass Index (BMI)-for-age sex-specific charts at Screening (Visit -1). Significantly underweight is defined as a BMI <3rd percentile for this study.
8. Subject is significantly overweight based on World Health Organization Body Mass Index (BMI)-for-age sex-specific charts at Screening (Visit -1). Significantly overweight is defined as a BMI >97th percentile for this study.
9. Subject has a conduct disorder. Oppositional defiant disorder is not exclusionary.
10. Subject has a concurrent chronic or acute illness (such as severe allergic rhinitis or an infectious process requiring antibiotics), disability, or other condition that might confound the results of safety assessments conducted in the study or that might increase risk to the subject. Similarly, the subject will be excluded if he or she has any additional condition(s) that, in the Investigator*s opinion, would prohibit the subject from completing the study or would not be in the best interest of the subject. The additional condition(s) would include any significant illness or unstable medical condition that could lead to difficulty complying with the protocol. Mild, stable asthma is not exclusionary.
11. Subject is currently considered a suicide risk in the opinion of the Investigator, has

previously made a suicide attempt, or has a prior history of, or is currently demonstrating active suicidal ideation. Subjects with intermittent passive suicidal ideation are not necessarily excluded based on the assessment of the Investigator.
12. Subject has glaucoma.
13. Subject has current abnormal thyroid function, defined as abnormal thyroid stimulating hormone (TSH) and thyroxine (T4) at Screening (Visit -1). Treatment with a stable dose of thyroid medication for at least 3 months is permitted.
14. Subject has any clinically significant ECG abnormality at Screening (Visit -1) or Baseline (Visit 0)
15. Subject has any clinically significant laboratory abnormalities at Screening (Visit -1) or Baseline (Visit 0) if repeated.
16. Subject has a documented allergy, hypersensitivity, or intolerance to any active ingredient or excipients in SPD489.
17. Subject has a recent history (within the past 6 months) of suspected substance abuse or dependence disorder (excluding nicotine) in accordance with DSM-IV-TR* criteria.
18. Subject has a history of seizures (other than infantile febrile seizures), a chronic or current tic disorder, a current diagnosis of Tourette*s Disorder, or a known family history of Tourette*s Disorder. Subject has a history of tics that is judged by the Investigator to be exclusionary.
19. Subject has a known history of symptomatic cardiovascular or cerebrovascular disease, advanced arteriosclerosis, structural cardiac abnormality, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems that may place them at increased vulnerability to the sympathomimetic effects of a stimulant drug.
20. Subject has a known family history of sudden cardiac death or ventricular arrhythmia.
21. Subject is taking any medication that is excluded.
22. Subject has a medical condition, other than ADHD, that requires treatment with medications that have central nervous system effects and/or affect performance. Stable use of anticholinergic or theophylline bronchodilator inhalers is not exclusionary.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-09-2011
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	/
Generic name:	Lysdexamfetamine dimesylate

Ethics review

Approved WMO Date:	01-02-2011
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-07-2011
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	19-10-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	21-11-2011
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	18-06-2012

Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	10-07-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-08-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2010-020951-30-NL
CCMO	NL34862.068.10