A Phase 3, Double-blind, Placebo-controlled, Multicentre, Randomised withdrawal, Long-term Maintenance of Efficacy and Safety Study of Extended-release Guanfacine Hydrochloride in Children and Adolescents Aged 6-17 With Attention deficit/Hyperactivity Disorder

Published: 23-11-2010
Last updated: 04-05-2024

The primary objective of this study is to evaluate the long-term maintenance of efficacy of SPD503 in childrenand adolescents (6-17 years) with attention-deficit/hyperactivity disorder (ADHD) who respond to an initial open-label,short-term treatment...

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

Summary

ID

NL-OMON39353

Source
ToetsingOnline

Brief title
Study of Guanfacine Hydrochloride 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 Development Inc.

Intervention

Keyword: ADHD, Children and adolescents, Extended-release

Outcome measures

Primary outcome

The primary efficacy endpoint for each subject is treatment failure during the

double-blind

randomised-withdrawal phase (Phase 2), defined as a *50% increase (worsening) in

ADHD-RS-IV total score at 2 consecutive Phase 2 visits (Visits 14*23/ET)

relative to Visit 13

and a *2 point increase (worsening) in CGI-S score relative to CGI-S at Visit

13 at the

corresponding Phase 2 visits.

Secondary outcome

The secondary endpoints are ADHD-RS-IV total scores, CGI-S scores, CGI-I scores,

HUI-2/3, and WFIRS-P results.

Safety endpoints include results of vital signs, ECG measurements, TEAEs,

clinical

laboratory tests, and C-SSRS results.

Study description

Background summary

The SPD503 clinical program has studied the efficacy, safety, and tolerability of this product in treating symptoms
of ADHD in children and adolescents aged 6-17 through short-term, placebo-controlled studies and long-term,
open-label studies. This study will more rigorously assess the long-term maintenance of efficacy using a
placebo-controlled, randomised-withdrawal design. To date, all of the completed studies conducted as part of the
SPD503 program have enrolled subjects from the US. This study is designed to evaluate the long-term
maintenance of efficacy of SPD503 for the treatment of ADHD in children aged 6-17 years in Europe, Australia,
Canada, and the US.

Study objective

The primary objective of this study is to evaluate the long-term maintenance of efficacy of SPD503 in children
and adolescents (6-17 years) with attention-deficit/hyperactivity disorder (ADHD) who respond to an initial open-label,
short-term treatment with SPD503.

Study design

This study is a double-blind, placebo-controlled, randomised-withdrawal study to evaluate the long-term
maintenance of efficacy and safety of SPD503 in children and adolescents (6-17 years of age) diagnosed with
ADHD. The study will consist of approximately 6 periods: (1) Screening and washout; (2) 7-week open-label
optimisation; (3) 6-week open-label maintenance of optimised SPD503; (4) 26-week (6-month) double-blind,
randomised withdrawal of SPD503; (5) 2-week post-treatment taper; and (6) 1-week safety follow-up. Subjects
will be required to visit the study centre up to 25 times over approximately a 47 week period.

Intervention

The investigational medicinal product, SPD503, is an extended-release tablet formulation containing guanfacine

hydrochloride designed for once-a-day oral administration.
The sponsor will provide SPD503 in 1, 2, 3, and 4mg tablets as well as matching placebo tablets. Subjects will
take either 1 SPD503 or matching placebo tablet (if optimised to a dose of 1-4mg) or 2 SPD503 or matching
placebo tablets (if optimised to a dose of 5-7mg) each morning.
Dosing will be flexibly optimised in order to maximise the potential benefits while minimising risk of adverse
events (AEs).
Dosing in all subjects will initiate with 1mg/day, and may be increased by 1mg increments after a minimum of 1
week on the current dose to the below maximum doses based on age and weight:
* Aged 6-12 years 25.0kg and up = maximum of 4mg/day.
* Aged 13-17 years 34.0-41.4kg = maximum of 4mg/day.
* Aged 13-17 years 41.5-49.4kg = maximum of 5mg/day.
* Aged 13-17 years 49.5-58.4kg = maximum of 6mg/day.
* Aged 13-17 years 58.5-91.0kg = maximum of 7mg/day.

Study burden and risks

Patients will be screened at the start of the study.

Patients will take part in the study for at least 16 weeks (14 visits) and not longer than 42 weeks (25 visits), depending on whether the patient enters fase 2 of the study. The patient will come to the hospital about every week.
During the study the patients will be subjected to the procedures as described under question E4.
A detailed description of the patient load is included in appendix 2 of the informed consent.

Taking SPD503 may cause side effects or possible discomfort. Serious side effects, considered related to the study drug, that have been reported are seizure, low blood pressure while standing, and fainting. An overview of the risks is also described in appendix 3 of the informed consent.

Contacts

Public
Shire

Chesterbrook Boulevard 725
Wayne, Pennsylvania 19087
US
Scientific

Shire

Chesterbrook Boulevard 725
Wayne, Pennsylvania 19087
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Male or female, aged 6-17 years at the time of consent/assent at Screening/Visit 1.
2. Subject meets Diagnostic and Statistical Manual of Mental Disorders, 4th ed.-Text Revision (DSM-IV-TR®) criteria for a primary diagnosis of ADHD, combined sub-type, hyperactive/impulsive sub-type, or inattentive sub-type based on a detailed psychiatric evaluation using the Kiddie Schedule for Affective Disorders and schizophrenia-Present and Lifetime version (K-SADS-PL).
3. Subject has a minimum ADHD-RS-IV total score of 32 at Enrolment/Visit 2.
4. Subject has a minimum CGI-S score of 4 at Enrolment/Visit 2.
5. Subject is able to swallow intact tablets.

Exclusion criteria

1. Subject has a current, controlled (requiring a prohibited medication or behavioural modification program) or uncontrolled, co-morbid psychiatric diagnosis, except Oppositional Defiant Disorder (ODD), including any severe comorbid Axis II disorders or severe Axis I disorders such as Post Traumatic Stress Disorder, bipolar illness, psychosis, pervasive developmental disorder, obsessive-compulsive disorder, substance abuse disorder, or other symptomatic manifestations or lifetime history of bipolar illness, psychosis, or conduct disorder that, in the opinion of the Investigator, contraindicate SPD503 treatment or confound efficacy or safety assessments.

2. Subject has a known history or presence of structural cardiac abnormalities, serious heart rhythm abnormalities, syncope, cardiac conduction problems (e.g., clinically significant heart block), exercise-related cardiac events including syncope and pre-syncope, or clinically significant bradycardia.
3. Subject with orthostatic hypotension or a known history of controlled or uncontrolled hypertension.
4. Current use of any prohibited medication or other medications, including herbal supplements, that affect blood pressure (BP) or heart rate or that have central nervous system (CNS) effects or affect cognitive performance, such as sedating antihistamines and decongestant sympathomimetics (inhaled bronchodilators are permitted) or a history of chronic use of sedating medications (i.e., antihistamines) in violation of the protocol specified washout criteria at Enrolment/Visit 2.
5. Subject is significantly overweight based on Centre for Disease Control and Prevention Body Mass Index (BMI)-for-age gender specific charts. Significantly overweight is defined as a BMI >95th percentile.
6. Children aged 6-12 years with a body weight of <25.0kg or adolescents aged 13-17 years with a body weight of <34.0kg or >91.0kg at Screening/Visit 1.
7. Subject has a history of alcohol or other substance abuse or dependence, as defined by DSM-IV-TR (with the exception of nicotine) within the last 6 months.
8. 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 (see protocol for additional guidance).
9. History of failure to respond to an adequate trial of an *2-agonist for the treatment of ADHD
10. Children who are stable with their current medication do not take part in this study.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-10-2011
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	SPD503 (Guanfacine hydrochloride)
Generic name:	NVT

Ethics review

Approved WMO Date:	23-11-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	08-08-2011
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	02-12-2011
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	27-02-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	05-04-2012

Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	02-05-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-06-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-11-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	30-01-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-02-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	21-02-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	31-01-2014
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	EUCTR2009-018161-12-NL
ClinicalTrials.gov	NCTO1081145
CCMO	NL33970.068.10