A Randomized, Double-Blind, Placebo-Controlled Trial of Adjunctive Troriluzole in Obsessive Compulsive Disorder

Published: 01-06-2021
Last updated: 04-04-2024

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Ethical review	Approved WMO
Status	Pending
Health condition type	Psychiatric and behavioural symptoms NEC
Study type	Interventional

Summary

ID

NL-OMON52232

Source
ToetsingOnline

Brief title
A research study investigating troriluzole as a possible treatment for OCD

Condition

- Psychiatric and behavioural symptoms NEC

Synonym
Obsessive Compulsive Disorder, OCD

Research involving
Human

Sponsors and support

Primary sponsor: Accelsiors CRO and Consultancy Services Ltd
Source(s) of monetary or material Support: Biohaven Pharmaceuticals;Inc.

Intervention

Keyword: Obsessive Compulsive Disorder, Troriluzole

Outcome measures

Primary outcome

Improvement in obsessive-compulsive symptomatology is assessed using the Y-BOCS change from baseline in the total score.

Secondary outcome

• Safety and tolerability are assessed using the frequency of unique subjects with: SAEs; AEs leading to discontinuation; AEs judged to be related to study medication; and clinically significant laboratory abnormalities that are observed during the double-blind phase;

• Improvement in functional disability is assessed using the change in the Sheehan Disability Scale (SDS) total score from baseline;

• Improvement in global clinical condition is assessed using the change in the CGI-S score from baseline

Study description

Background summary

Biohaven Pharmaceuticals, Inc. is developing a new drug, troriluzole, for the treatment of Obsessive-Compulsive Disorder (OCD) as well as for other neurologic and psychiatric disorders. Troriluzole is a tripeptide prodrug of the glutamate modulating agent riluzole that has been optimized for improved bioavailability, pharmacokinetics and dosing. The proposed study in OCD is based on recent preclinical, clinical and neuroimaging studies that implicate glutamatergic hyperactivity in the pathogenesis of OCD. Additionally, preliminary efficacy findings from BHV4157-202, a proof-of-concept study, indicate, troriluzole 200 mg, administered once daily as adjunctive therapy in subjects with OCD who had an inadequate response to SOC treatment showed

numerically greater improvement versus placebo in the total Y-BOCS score in the randomization phase. Biohaven hypothesizes that the pleiotropic effects of riluzole (e.g., glutamate modulation) may target mechanisms underlying pathologic brain function that is associated with OCD, and thus provide symptomatic benefit in patients suffering from Obsessive Compulsive Disorder (OCD).
The proposed study is based on recent preclinical, clinical, genetic and neuroimaging studies that implicate glutamatergic hyperactivity in the pathogenesis of OCD. In multiple published clinical case studies, the use of agents that modulate brain glutamate have been suggested to have efficacy in patients with refractory OCD.

Study objective

2.1 Primary
The primary objective of the study is to evaluate the efficacy of troriluzole as adjunctive therapy compared to placebo in subjects with OCD who have had an inadequate response to their current OCD treatment based on the change in their Y-BOCS score.
2.2 Secondary
• To assess the safety and tolerability of troriluzole, relative to placebo, in subjects with OCD;
• Evaluate the efficacy of troriluzole compared to placebo on functional disability as measured by the Sheehan Disability Scale (SDS);
• Evaluate the efficacy of troriluzole compared to placebo on global clinical condition as measured by the Clinical Global Impression- Severity Scale (CGI-S);

Study design

BHV4157-303 is a Phase III, multicenter, randomized, double-blind, 2-arm placebo- controlled parallel-group study designed to assess safety, tolerability, and efficacy of troriluzole as adjunctive therapy in a population of subjects with OCD who have had an inadequate response to standard of care treatment.
The expected duration of study participation for each subject is up to 18 weeks, including:
• Screening phase up to 6 weeks
• Treatment period 10 weeks
Post-treatment safety period: subjects will have a follow-up safety visit two weeks after discontinuing study drug or if eligible, will participate in the Open Label Extension Study, BHV4157-209

Intervention

Subjects who are stable on SOC medication and having an inadequate response (as

defined above) will be randomized to additionally receive placebo (QD) or troriluzole in ration 1:1. Subjects will receive either placebo or troriluzole 200mg for the first two weeks and then will be increased to 280 mg (or matching placebo) for the duration of the study.

Study burden and risks

Analysis of the available data with troriluzole from in-vitro studies, preclinical studies (in rats and monkeys), and clinical studies in healthy subjects as well as patients with OCD, GAD, SCA, and AD, supports a favorable benefit-risk profile. Therefore, it is considered that the benefits of evaluating troriluzole as a potential treatment for OCD outweigh the risks.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1.Primary diagnosis of OCD as per Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition as confirmed by the MINI at Screening; The duration of the subject's illness must be >= 1 year;

2.Subjects must be currently experiencing non-response or inadequate response to their current SOC medication defined as: Subjects Y-BOCS total score must be >= 22 at Screening and Baseline, reflecting moderate or severe OCD symptoms.

3.Subjects must currently be on an SSRI (with the exception of fluvoxamine, see Section 1.1.3), or clomipramine, venlafaxine or desvenlafaxine monotherapy treatment for an adequate duration and at an adequate dose defined as in clinical trial protocol

4.Subjects must be on stable doses of other psychotropic medication (with exclusions specified below) for at least 12 weeks prior to screening;

5.CGI-S score of >= 4 at screening and baseline;

6.Women of child bearing potential (WOCBP) and fertile men (including those vasectomized for less than 6 months) with female partners whoare WOCBP (not having undergone bilateral tubal occlusion procedure and not postmenopausal) must agree to use highly effective birth control, including two methods of contraception, for the duration of the study (i.e., beginning 30 days prior to Baseline and extending to 30 days for women and 90 days for men after the last dose of study drug). The
two methods of contraception should include:

i.One barrier method (e.g. diaphragm with spermicide, condom with spermicidal gel, cervical cap)*

ii.One other method that could include hormonal contraceptives (e.g. combined estrogen and progesterone containing, or progesterone only with oral, vaginal, injectable, or transdermal route of administration), intrauterine device, or intrauterine hormone releasing system used for at least 4 weeks prior to sexual intercourse

7.WOCBP must have a negative serum pregnancy test at screening and a negative urine pregnancy test within approximately 24 hours prior to dosing at Baseline

8.It is required that men who are sexually active with WOCBP agree to use two methods of contraception for the duration of the study (beginning at first treatment and extending to 90 days after the last dose of study drug).

Exclusion criteria

1.Subjects with a history of more than two (2) previous failed or inadequate treatment classes SSRIs, clomipramine, venlafaxine, or desvenlafaxine, given for an adequate duration at an adequate dose as defined by the criteria taken from the MGH-TRQ-OCD .

2.Subjects should be excluded at screening or baseline if any medical or psychiatric condition other than OCD, as specified in the inclusion criteria, could predominantly explain or contribute significantly to the subjects' symptoms or that could confound assessment of OCD symptoms;

3.Current or prior history, per DSM-5 criteria, of bipolar I or II disorder, schizophrenia or other psychotic disorders, schizoaffective disorder, autism or autistic spectrum disorders, borderline personality disorder, antisocial personality disorder, body dysmorphic disorder, hoarding disorder (symptoms of hoarding disorder as part of the OCD diagnosis are allowed, but a primary diagnosis of hoarding disorder is excluded); a current diagnosis of Tourette's disorder is also excluded;

4.Any eating disorder within the last 12 months;

5.Primary active major depressive episode or primary active anxiety disorder within the past 6 months.

6.Acute suicidality or suicide attempt or self-injurious behavior in the last 12 months.

7.Any positive ("yes") C-SSRS response to questions 1-5 in last 6 months at screening and/or Since the Last Visit (before dosing) at the baseline visit;

9.Subjects who may have received a non-biological investigational agent in any clinical trial within 30 days or a biological agent within 90 days prior to screening;

10.History of psychosurgery, Deep Brain Stimulation (DBS) or Electroconvulsive Therapy (ECT).

11.History of substance use disorder (drug or alcohol) in the last 12 months, with the exception of tobacco, as defined by DSM-5 criteria;

12.Positive urine drug screening for cannabis (both medical and recreational use of cannabis are prohibited; subjects will be expected to refrain from use during the period of the study), amphetamines (including MDMA/ecstasy), cocaine, barbiturate, PCP, and/or opiates at screening.

13. Women who are pregnant or brestfeeding

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:	Pending
Start date (anticipated):	13-09-2021
Enrollment:	14
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Troriluzole
Generic name:	Troriluzole

Ethics review

Approved WMO Date:	01-06-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-09-2021

Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-12-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-02-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-06-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-06-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-11-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-12-2022
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

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	EUCTR2020-004653-69-NL
ClinicalTrials.gov	NCT04693351
CCMO	NL76918.018.21