A Multicenter, Long-Term Open-Label Safety Study of Adjunctive Troriluzole in Subjects with Obsessive Compulsive Disorder

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

Summary

ID

NL-OMON52032

Source
ToetsingOnline

Brief title
Troriluzole Long Term Safety Study in Subjects with OCD

Condition

- Psychiatric and behavioural symptoms NEC

Synonym
Obsessive Compulsive Disorder, OCD

Research involving
Human

Sponsors and support

Primary sponsor: Biohaven Pharmaceuticals Inc.

Source(s) of monetary or material Support: Biohaven Pharmaceuticals;Inc.

Intervention

Keyword: Obsessive Compulsive Disorder, Troriluzole

Outcome measures

Primary outcome

Safety and tolerability are assessed using the frequency of unique subjects with: SAE; AEs leading to discontinuation; AEs judged to be related to study medication; and clinically significant laboratory abnormalities that are observed from baseline to week 48.

Secondary outcome

Not applicable

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

The primary objective of the study is to evaluate the long term safety and tolerability of troriluzole as adjunctive therapy in subjects with OCD who have had an inadequate response to standard of care (SOC) treatment for OCD and as defined in the parent protocols (BHV4157-302 and BHV4157-303).

Study design

BHV4157-209 is a Phase 2b/3, multicenter, 48-week open-label safety study designed to assess safety and tolerability of troriluzole as adjunctive therapy in subjects with OCD with the option for an additional 48-week treatment extension.
The expected duration of study participation for each subject is up to 96 weeks, including:
• Open label Phase 48 weeks
• Extension Phase 48 weeks
• Posttreatment safety period 2 weeks

Subjects will receive open label troriluzole at a dose of 200 mg QD for the first two (2) weeks and will then be increased to 280 mg QD for the duration of the study.
Subjects in the Open-Label Phase will undergo visits at Weeks 2, 4, 8, 12, 24, 36, and 48. Subjects who complete the Open-Label Phase and are continuing into the Extension Phase will have their first visit 12 weeks after the week 48 visit at Week 60. Thereafter, subjects will undergo visits every 12 weeks at weeks 72, 84 and 96.. All subjects will undergo a post study drug termination visit two weeks after the last dose of study drug.

Intervention

Subjects will receive troriluzole 200 mg for the first two weeks and then will be increased to 280 mg 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. Informed Consent:
a. Signed informed consent form prior to the initiation of any protocol required procedures.
2. Age and Sex:
a. Male and female outpatient subjects between the ages of 18 - 65 upon entry into BHV4157-302 or BHV4157-303.
3.Target Population:
a. Eligible subjects who complete study BHV4157-302 or BHV4157-303 and for whom the investigator believes open-label treatment offers an acceptable risk-benefit profile.
b.Determined by the investigator to be medically stable at the final visit of BHV4157-302 or BHV4157-303, as assessed by medical history, physical

examination, laboratory test results, and electrocardiogram testing.
c. Minimum of 6 years of education or equivalent to complete necessary scales and understand consent forms;
d. Subjects must have adequate hearing, vision, and language skills to perform neuropsychiatric testing and interviews as specified in the protocol;
e. Subjects must be able to understand and agree to comply with the prescribed dosage regimens and procedures; report for regularly scheduled office visits; and reliably communicate with study personnel about AEs and concomitant medications;
f. Women of child bearing potential (WOCBP) and fertile men (including those vasectomized for less than 6 months) with female partners who are WOCBP (not having undergone bilateral tubal occlusion procedure and not post- menopausal) must agree to use highly effective birth control, including two methods of contraception, for the duration of the study.
g. The two methods should include:
i. one barrier method (e.g. diaphragm with spermicide, condom with spermicidal gel, intrauterine devices, 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 (Section 5.5);
h. Women of childbearing potential must have a negative serum pregnancy test throughout the study
i. 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)
j. No clinically significant abnormality on the medical or laboratory evaluation. A subject with a clinical abnormality or laboratory parameters outside the reference range may be included only if the investigator considers that the finding is not clinically significant and will not introduce additional risk factors and will not interfere with the study procedure

Exclusion criteria

1. Target Disease Exceptions
a.Subjects who did not successfully complete randomization phase in BHV4157-302/BHV4157-303 study
b.Current or prior history 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 OCD diagnosis are allowed,but primary diagnosis of hoarding disorder is excluded);current diagnosis of Tourette's disorder

c.Any eating disorder within last 12 months
d.Primary active major depressive episode or primary active anxiety disorder within past 6 months
e.Acute suicidality or suicide attempt or self injurious behavior in last 12 months
f. Any positive Columbia Suicide Severity Rating Scale response to questions 1-5 at baseline(final visit of BHV4157-302/BHV4157-303) unless,after evaluation of subject at Week 10 visit,investigator believes subject should continue in study and that open-label treatment offers acceptable risk-benefit profile
g.Patients who plan to receive non-biological or biological investigational agent in while enrolled in trial
h.History of psychosurgery,Deep Brain Stimulation or Electroconvulsive Therapy
2.Medical History Exclusions:
a.History of substance use disorder(drug or alcohol) in last 12 months,with exception of tobacco,as defined by DSM-5 criteria
bPositive urine drug screening (UDS) for cannabis (both medical and recreational use of cannabis are prohibited):, amphetamines (including MDMA/ecstasy), cocaine, barbiturate, PCP, and/or opiates at study entry.
c.Prior or current general medical condition that may confound ability to interpret safety and efficacy results as determined by Investigator
d.Clinical history of stroke,seizure disorder,traumatic brain injury with ongoing sequelae
e.Patients with history of Type I or Type II insulin-dependent diabetes mellitus
f.Active liver disease or history of hepatic intolerance to medications that,in investigator's judgment, is medically significant
g.Any unstable cardiovascular(includes uncontrolled hypertension),pulmonary,gastrointestinal, or hepatic disease at study entry
h.End-stage cardiovascular disease(e.g.,Congestive Heart Failure New York Heart Association Class III or IV or unstable angina)
i.History of chronic pulmonary disease or chronic pulmonary symptoms; well controlled asthma is allowed per investigator's clinical judgement;
j.Immunocompromised subjects.Subjects taking systemic immunosuppressive agent may be entered in trial only if they are on stable dose,have no clinically relevant immunosuppression,and have white blood count within normal limits
k.History of medically significant gastrointestinal illnesses including:
i.Current diagnosis of active,peptic ulceration or gastrointestinal bleeding and/orchronic inflammatory bowel disease at study entry;
ii.History of any gastrointestinal surgery that impacts absorption of study drug;
iii.Chronic or frequent episodes of loose stools
l.History or evidence of any medical,neurological or psychological condition that would expose subject to undue risk of significant AE or interfere with assessments of safety and efficacy during course of trial
as determined by investigator's clinical judgment
m.Women who are pregnant or breastfeeding
3. Physical and Laboratory Test Findings
a.Uncontrolled hypertension at study entry (e.g., repeated diastolic

measurements >= 96 mmHg);
b.Hepatic test abnormalities at study entry (last visit of BHV4157-302 & BHV4157-303). If any abnormalities are present after review of Baseline (last visit of BHV4157-302 & BHV4157-303) labs they may be repeated after discussion with Biohaven Medical Monitor:
i.Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT) or GGT > 3 times the upper limit of normal; or
ii.Total bilirubin > 2 times the upper limit of normal (ULN); unless subject has documented history of Gilbert*s Syndrome in which case subject may be enrolled if total bilirubin is less than 5 mg/dL, assuming all other criteria are fulfilled.
d.Creatinine >= 2 mg/dL at study entry. If any abnormalities are present after review of Baseline (the last visit of BHV4157-302 & BHV4157-303) labs they may be repeated after discussion with Biohaven Medical Monitor.
e.Hematologic abnormalities at study entry.
i. Hemoglobin < 10 g/dL; or
ii. WBC < 3.0 x 103/mm3; or iii. Platelet count < 100,000/mm3. iv. Neutrophils, Absolute < 1500/mm3
f.QTcF (Fridericia) interval >= 470 msec during study period or uncontrolled arrhythmia or frequent premature ventricular contraction (PVCs) (> 5/minute) or Mobitz Type II second or third degree atrioventricular (AV) block or left bundle branch block, or right bundle branch block with a QRS duration >= 150 msec or intraventricular conduction defect with a QRS duration >= 150 msec or evidence of acute or sub-acute myocardial infarction or ischemia or other ECG findings that, in the investigator*s opinion, would preclude participation in the study.
4. Prohibited Treatments and/or Therapies
a. Previous treatment with riluzole
b. Patients who would likely require prohibited concomitant therapy after study entry
c. Herbal medication and supplement use during the course of study is prohibited
d. Transcranial Magnetic Stimulation is prohibited during study
e. Subjects who are participating in any other clinical research study.
5. The use of the following medications is prohibited during the study:
a.Medical or recreational marijuana;
b.Cannabidiol (CBD) oil
c.Tricyclic antidepressants (with the exception of clomipramine);
d.Monoamine-oxidase (MAO) inhibitors
e.Other medications, as stated in section 5.4 of protocol

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	15-02-2022
Enrollment:	8
Type:	Anticipated

Medical products/devices used

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

Ethics review

Approved WMO Date:	21-10-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-11-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-02-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-03-2022

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-07-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-08-2022
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:	20-07-2023
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	EUCTR2020-004654-30-NL
ClinicalTrials.gov	NCT04708834
CCMO	NL77805.018.21