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A single-dose study of zavegepant in healthy male volunteers

Submission date
23/03/2022

Recruitment status
No longer recruiting

Registration date
01/04/2022

Overall study status
Completed

Last Edited
15/07/2022

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Zavegepant (also known as BHV-3500) is being developed as a treatment for migraine. The aim of this study is to identify the absorption, distribution, metabolism, and excretion of radiolabeled zavegepant.

Who can participate?
Healthy men aged 30 to 60 years

What does the study involve?
Participants will be screened with blood tests, vital signs, electrocardiogram (ECG), physical examination, and completion of the Sheehan Suicidality Tracking Scale (S-STS) to determine study eligibility. If qualified, participants will return to the clinic to check in the day before dosing is planned. After fasting overnight, on the morning of Day 1, an intravenous (IV) infusion tube will be inserted into the participants' arms and they will be given a single 5 mg dose of the test drug, 14C-zavegepant solution, by IV over 15 minutes. Participants will stay in the clinic until up to 240 hours after dosing (Day 11). During this time, urine, stool and blood samples will be collected to measure the amount of radioactivity being excreted and the participants will be monitored for any adverse events. Participants will be released as a group when over 90% of the dose of radioactivity administered has been recovered or if less than 1% of the dose administered has been collected in urine and stool within two separate consecutive 24-hour periods.

What are the possible benefits and risks of participating?
There will be no benefit to the participants. The main risks will be the frequent collection of blood samples and exposure to radioactivity from the study drug. Blood sampling is a standard procedure which is unlikely to cause subjects any problems but can sometimes cause discomfort. Collecting a blood sample from a vein may cause pain, swelling, bruising, light headedness, fainting, and very rarely, clot formation, nerve damage and/or infection at the site of the needle stick. [14C]-zavegepant is the test medicine in this study and is radioactive. The radiation is used to trace where the test medicine (and its breakdown products) is in the participant's body. Participants will be exposed to a small amount of radiation that they wouldn't be exposed to if they didn't participate in the study. The amount of radiation that subjects would be exposed to

from the test medicine is slightly more than two abdominal x-rays, for example, and less than annual background radiation exposure.

Where is the study run from?
Quotient Sciences Limited (UK)

When is the study starting and how long is it expected to run for?
February 2020 to August 2020

Who is funding the study?
Biohaven Pharmaceuticals, Inc. (USA)

Who is the main contact?
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Contact information

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Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
2020-000735-41

Integrated Research Application System (IRAS)
279969

Protocol serial number
BHV3500-104

Study information

Scientific Title
BHV3500-104: a single-dose study to assess the mass balance recovery, absorption, metabolism and excretion of [14C]-zavegepant (BHV-3500) in healthy male subjects after intravenous dosing

Acronym
BHV3500-104 Human ADME Study

Study objectives
The objectives of this study are to assess the mass balance recovery after a single 15-minute intravenous (IV) infusion dose of ([14C])-zavegepant, and to provide plasma, urine, and fecal samples for metabolite profiling and structural identification.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 15/05/2020, Health and Social Care Research Ethics Committee A (HSC REC A) (ORECNI Office, Lissue Industrial Estate, West Rathdown Walk, Moira Road, Lisburn, BT28 2RF, UK; +44(0)28 95361400; RECA@hscni.net), ref: 20/NI/0055

Primary study design
Interventional

Study design
Phase I open-label single-center single-period non-randomized study

Study type(s)
Other

Health condition(s) or problem(s) studied
Migraine

Interventions
This Phase I, open-label, single-center, single-period, non-randomized study includes healthy male volunteers. After an overnight fast of 8 hours, volunteers are dosed on the morning of Day 1 with a single 5 mg dose of the test drug, 14C-zavegepant, through intravenous infusion over 15 minutes and remain resident in the clinic until up to 240 h after dosing (Day 11). It is planned that subjects will be released as a group when all subjects have achieved a mass balance cumulative recovery of >90% or if <1% of the dose administered has been collected in urine and feces within two separate, consecutive 24 h periods. Adverse events (AEs), vital signs, electrocardiogram (ECG), Sheehan Suicidality Tracking Scale (S-STS), and physical examination are also assessed.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Zavegepant; BHV-3500; formerly vazegepant

Primary outcome(s)
The rates and routes of elimination of the test medicine from the body, and the ways in which the body processes the test medicine will be assessed by taking whole blood, plasma, urine, and feces for liquid scintillation counting to measure the amount of radioactivity, and to identify breakdown products of the test medicine by liquid chromatography with radio detection and high-resolution mass spectrometry, between Days 1 and Day 11. Participants' stay may be extended an additional 2 days and they may need to continue collections of urine and faeces for a few days at home after they have left the ward.

Key secondary outcome(s)
1. The intravenous pharmacokinetics of the test medicine in plasma, feces, and urine after a single dose will be assessed by taking blood samples and urine samples for liquid chromatography with tandem mass spectrometry (LC-MS/MS assay) of the test medicine between Days 1 and Day 11
2. Adverse events (to assess tolerability of the test medicine) will be collected by asking volunteers how they are feeling from the start of the trial until follow up
3. Other safety measures (including vital signs, ECGs and laboratory safety tests) will be assessed by standard phase 1 unit monitoring at screening, from Day-1 to discharge from the ward

Completion date
28/08/2020

Eligibility

Key inclusion criteria
1. Must provide written informed consent prior to any study-related procedures
2. Healthy males
3. Age 30 to 60 years of age inclusive at the time of signing informed consent
4. Body mass index (BMI) of 18.0 to 32.0 kg/m² as measured at screening
5. Subject's score on the Sheehan Suicidality Tracking Scale (S-STS) test must be 0
6. Must be able to understand the requirements of the study, and willing and able to communicate and comply with all study procedures
7. Must have regular bowel movements (i.e. average stool production of ≥1 and ≤3 stools per day)
8. Must agree to adhere to the contraception requirements

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
Male

Total final enrolment
6

Key exclusion criteria
1. Subjects who have received any IMP in a clinical research study within the 90 days prior to Day 1
2. Subjects who are, or are immediate family members of a study site or sponsor employee
3. Subjects who have previously been administered IMP in this study
4. History of any drug or alcohol abuse in the past 2 years
5. Regular alcohol consumption >21 units per week (1 unit = ½ pint beer, or a 25 ml shot of 40% spirit, 1.5 to 2 units = 125 ml glass of wine, depending on type)
6. A confirmed positive alcohol breath test at screening or admission
7. A confirmed breath carbon monoxide reading of greater than 10 ppm at screening or admission
8. Current smokers and those who have smoked within the last 12 months and/or current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months
9. Subjects with partners who are pregnant or lactating or planning to become pregnant during

the study ore within 90 days after study drug administration
10. Radiation exposure, including that from the present study, excluding background radiation but including diagnostic x-rays and other therapeutic medical exposures, exceeding 5 mSv in the last 12 months or 10 mSv in the last 5 years. No occupationally exposed worker, as defined in the Ionising Radiation Regulations 2017, shall participate in the study
11. Subjects who do not have suitable veins for multiple venepunctures/cannulation as assessed by the investigator or delegate at screening/pre-dose
12. Clinically significant abnormal clinical chemistry, haematology or urinalysis as judged by the investigator. Subjects with Gilbert's Syndrome are allowed.
13. Confirmed positive drugs of abuse test result at screening or admission
14. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) results
15. Evidence of renal impairment at screening, as indicated by an estimated creatinine clearance of <80 mL/min using the Cockcroft-Gault equation
16. History of clinically significant cardiovascular, renal, hepatic, pulmonary, gastrointestinal, hematologic, neoplastic, endocrine, immunological, neurological or psychiatric disease or disorder, as judged by the investigator
17. History of clinically significant illness and surgery within 4 weeks prior to dosing. Subjects vomiting within 24 h pre-dose will be carefully evaluated for upcoming illness/disease. Inclusion pre-dosing is at the discretion of the investigator.
18. Significant history of seizure disorder other than a single childhood febrile seizure (e.g. epilepsy)
19. Serious adverse reaction or serious hypersensitivity to any drug or the formulation excipients
20. Presence or history of clinically significant allergy requiring treatment, as judged by the investigator. Hay fever is allowed unless it is active
21. Donation or loss of greater than 400 ml of blood within the previous 3 months
22. Subjects who are taking, or have taken, any prescribed or over-the-counter drug or herbal remedies or dietary supplements (other than up to 4 g of paracetamol per day) in the 14 days before IMP administration. Exceptions may apply on a case by case basis, if considered not to interfere with the objectives of the study, as determined by the investigator.
23. Use of any drugs known to induce or inhibit hepatic drug metabolism within 30 days prior to the first drug administration.
24. Any of the following laboratory parameters above the upper limit of normal (ULN) values at screening or baseline (Day -1): alkaline phosphatase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyl-transpeptidase, direct bilirubin, indirect bilirubin, and total bilirubin. Only abnormal values between up to 1.5 × ULN may be repeated once for confirmation of a return to normal range.
25. Any of the following abnormalities on 12-lead ECG or blood pressure at screening, confirmed by repeat:
25.1. PR (PR interval) ≥220 msec
25.2. QRS (QRS complex) ≥120 msec
25.3. QT (QT interval) ≥ 500 msec
25.4. QTcF (Fridericia's corrected QT interval) ≥450 msec
25.5. Sitting (for at least 5 min) systolic blood pressure >140 mmHg
25.6. Sitting (for at least 5 min) diastolic blood pressure >90 mmHg
26. Any of the following abnormal laboratory test values at screening or baseline (Day -1):
26.1. Haemoglobin <12.8 g/dl
26.2. Haematocrit <37%
26.3. Total white blood cell <3.0 × 10e9/l
26.4. Platelet count <100 × 10e9/l
26.5. Neutrophils <1.4 × 10e9/L and < 1.0 × 10e9/l for black/African-American subjects
26.6. Creatine kinase >3 × ULN

27. Clinically significant history of depression or suicidal thoughts within the previous 12 months prior to screening
28. Failure to satisfy the investigator of fitness to participate for any other reason

Date of first enrolment
17/07/2020

Date of final enrolment
30/07/2020

Locations

Countries of recruitment
United Kingdom

England

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Sponsor information

Organisation
Biohaven Pharmaceuticals (United States)

ROR
https://ror.org/00m2ky193

Funder(s)

Funder type
Industry

Funder Name
Biohaven Pharmaceuticals, Inc.

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available. The findings of this Phase I study will be shared with the sponsor, Biohaven Pharmaceuticals, Inc. only. As these findings are confidential due to commercial sensitivity, it is not appropriate to share the results of this study with other researchers at this time.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results		20/05/2022	15/07/2022	No	No
HRA research summary			28/06/2023	No	No