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A study in healthy male volunteers to assess how the radiolabelled test medicine is taken up and broken down by the body

Submission date 10/11/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 11/11/2022	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 17/03/2025	**Condition category** Not Specified	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
The Sponsor is developing the test medicine, pelabresib, for the potential treatment of myelofibrosis, a type of blood cancer, and other blood disorders. Blood cancers affect the production and function of blood cells meaning too many or too few blood cells may be produced. This healthy volunteer study will try to identify how the test medicine is taken up and broken down by the body when given by the mouth in the form of radioactive suspension. To help investigate this, the test medicine is 'radiolabelled' meaning the test medicine has a radioactive component (Carbon-14) to help track where the medicine is in the body. The safety and tolerability of the test medicine is also being studied.

Who can participate?
Healthy males aged 35 to 65 years inclusive

What does the study involve?
The study consists of one part, involving a single cohort of 8 volunteers. Volunteers receive a single oral dose of the radiolabelled test medicine in the fasted state. Volunteers enter the clinical unit on Day -1 (the day before their dose) and are discharged on Day 19 (432 hours after their dose). Volunteers' blood, urine and faeces are taken throughout the study for analysis of the test medicine and for their safety. Volunteers are expected to be involved in this study for approximately 8 weeks from screening to discharge.

What are the possible risks and benefits of participating?
Participants get no medical benefit from taking part in the study. However, development of a treatment for myelofibrosis and other blood disorders may benefit the population as a whole. It is considered that the risk/benefit evaluation in this study supports the use of healthy volunteers. Full information on possible side effects is provided to volunteers in the Participant Information Sheet and Informed Consent Form. Volunteers are closely monitored during the study and safety assessments are performed regularly.

Where is the study run from?
Constellation Pharmaceuticals, Inc. (A fully owned subsidiary of MorphoSys U.S. Inc., United States)

When is the study starting and how long is it expected to run for?
November 2022 until December 2022

Who is funding the study?
Constellation Pharmaceuticals, Inc. (A fully owned subsidiary of MorphoSys U.S. Inc.)

Who is the main contact?
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Contact information

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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

Integrated Research Application System (IRAS)
1006147

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Sponsor code: CPI-0610-07

Study information

Scientific Title
An Open-Label, Single-Dose, Single-Period Study to Assess the Mass Balance Recovery, Metabolite Profile and Metabolite Identification of [14C]-pelabresib in Healthy Male Subjects

Study objectives
The trial will meet the following primary and secondary objectives:
Primary objectives:
1. To determine the mass balance recovery after a single oral dose of carbon-14 ([14C])-pelabresib
2. To perform metabolite profiling and structural identification from plasma, urine and faecal samples
Secondary objectives:
1. To determine the routes and rates of elimination of [14C]-pelabresib
2. To further explore the oral pharmacokinetics (PK) of pelabresib, its metabolites M4, M5, M542 and M544 and total radioactivity in plasma
3. To evaluate the extent of distribution of total radioactivity into blood cells
4. To provide additional safety and tolerability information for pelabresib

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 14/11/2022, London Bridge REC (London HRA Centre, 2nd Floor, 2 Redman Place, Stratford, London, E20 1JQ, UK; +44 207 104 8019; londonbridge.rec@hra.nhs.uk), ref: 22/LO/0610

Study design
Absorption metabolism distribution and elimination (ADME)

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Myelofibrosis and other blood disorders

Interventions
Each participant will receive a single dose of [14C]-pelabresib Oral Suspension, 0.5 mg/mL, 20 mL (not more than [NMT] 37.0 kBq) on one occasion

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Pelabresib (CPI-0610)

Primary outcome(s)
1. Mass balance recovery of total radioactivity in all excreta (urine and faeces): CumAe and Cum% Ae at multiple timepoints up to 432 h post dose
2. Identification of the chemical structure of each metabolite accounting for more than 10% (in plasma) by AUC of circulating total radioactivity or accounting for 10% or more of the dose in excreta (urine and faeces) at multiple timepoints up to 432 h post dose

Key secondary outcome(s))
1. Determination of routes and rates of elimination of 14C by Ae, %Ae, CumAe and Cum%Ae by time interval
2. Assessment of the PK of an oral [14C]-pelabresib formulation by calculation of PK parameters, as appropriate, for pelabresib, its metabolites M4, M5, M542 and M544 and total radioactivity in plasma: Tmax, Cmax, AUC(0-last), AUC(0-inf) and T1/2 (additional parameters may be determined) at multiple timepoints up to 432 h post dose
3. Evaluation of whole blood:plasma concentration ratios for total radioactivity at multiple timepoints up to 432 h post dose
4. To provide additional safety and tolerability information for pelabresib by assessing: incidence of adverse events (AEs), serious AEs (SAEs) and changes in physical examinations, vital signs, electrocardiograms (ECGs), and laboratory results, from the time of signing the informed consent form up until discharge from the study

Completion date
23/12/2022

Eligibility

Key inclusion criteria
1. Must provide written informed consent
2. Must be willing and able to communicate and participate in the whole study
3. Aged 30 to 65 years inclusive at the time of signing informed consent
4. Must agree to adhere to the contraception requirements defined in the Clinical Protocol
5. Must not plan to father children or donate sperm in the 184 days (6 months + 5 half lives) after IMP administration
6. Healthy males
7. Body mass index (BMI) of 18.0 to 32.0 kg/m^2 as measured at screening

8. Weight of at least 60 kg as measured at screening
9. Must have regular bowel movements (i.e. average stool production of ≥1 and ≤3 stools per day)

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
30 years

Upper age limit
65 years

Sex
Male

Total final enrolment
8

Key exclusion criteria
1. Serious adverse reaction or serious hypersensitivity to any drug or formulation excipients
2. Presence or history of clinically significant allergy requiring treatment, as judged by the investigator. Hay fever is allowed unless it is active
3. History of clinically significant cardiovascular, renal, hepatic, testicular, dermatological, chronic respiratory or GI disease, neurological or psychiatric disorder, as judged by the investigator
4. Subjects who do not have suitable veins for multiple venepunctures/cannulation as assessed by the investigator or delegate at screening
5. Evidence of current SARS-CoV-2 infection within 4 weeks of first IMP administration
6. Clinically significant abnormal clinical chemistry, haematology or urinalysis as judged by the investigator. Subjects with Gilbert's Syndrome are not allowed
7. Any of the following: haemoglobin <130 g/L, platelets <150 × 109/L, neutrophils <2.0 × 109/L, or lymphocytes < 1.2 × 109/L as measured at screening
8. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) 1 and 2 antibody results
9. Evidence of renal impairment, as indicated by an estimated creatinine clearance (CLcr) of <80 mL/min using the Cockcroft-Gault equation as measured at screening
10. Subjects who have received any IMP in a clinical research study within the 90 days prior to Day 1
11. Radiation exposure, including that from the present study, excluding background radiation but including diagnostic x-rays and other 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
12. Administration of a 14C labelled product (e.g. in a 14C ADME or 14C microtracer study) in the 12 months (365 days) prior to IMP administration

13. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood
14. Subjects who are taking, or have taken, any prescribed or over the counter drug or herbal remedies (other than up to 4 g of paracetamol per day) in the 14 days before IMP administration. Exceptions may apply, as determined by the investigator, if each of the following criteria are met: medication with a short half life if the washout is such that no pharmacodynamic activity is expected by the time of dosing with IMP; and if the use of medication does not jeopardise the safety of the trial subject; and if the use of medication is not considered to interfere with the objectives of the study. Anti-COVID-19 vaccines are not accepted concomitant medications
15. Subjects who have had any anti-viral agents for COVID-19 infections within 14 days before IMP administration.
16. Use of any medications that are known to induce CYP3A4 within the 4 weeks prior to IMP administration
17. Subjects who have had an anti-COVID-19 vaccine within 7 days before IMP administration
18. History of any drug or alcohol abuse in the past 2 years
19. Regular alcohol consumption in males >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)
20. A confirmed positive alcohol breath test at screening or admission
21. Current smokers and those who have smoked within the last 6 months. A confirmed breath carbon monoxide reading of greater than ppm at screening or admission
22. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 6 months
23. Confirmed positive drugs of abuse test result
24. Subjects with pregnant or lactating partners
25. Subjects who are, or are immediate family members of, a study site or sponsor employee
26. Failure to satisfy the investigator of fitness to participate for any other reason

Date of first enrolment
22/11/2022

Date of final enrolment
23/12/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences Limited
Mere Way
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NG11 6JS

Sponsor information

Organisation
Constellation Pharmaceuticals (United States)

ROR
https://ror.org/04dxbz091

Funder(s)

Funder type
Industry

Funder Name
Constellation Pharmaceuticals

Alternative Name(s)
Constellation Pharmaceuticals Inc

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study are not expected to be made available because of their high commercial sensitivity and the negligible benefit to the public of publication of results of nontherapeutic clinical trials.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes