ISRCTN16794199 https://doi.org/10.1186/ISRCTN16794199

A study in healthy male volunteers to look at how the test medicine ([Cyclohexane-U-14C]-MBS2320) is taken up, broken down and removed from the body when given by mouth

Submission date
29/08/2022

Recruitment status
No longer recruiting

Registration date
07/09/2022

Overall study status
Completed

Last Edited
07/11/2023

Condition category
Skin and Connective Tissue Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
The Sponsor is developing the test medicine, MBS2320, for the potential treatment of rheumatoid arthritis (RA) and idiopathic pulmonary fibrosis (IPF). Rheumatoid arthritis is a long-term condition that causes pain, swelling and stiffness in the joints. Idiopathic pulmonary fibrosis is a condition in which the lungs become scarred and breathing becomes increasingly difficult.

This single period healthy volunteer study will try to identify how the test medicine is taken up, broken down and removed by the body when given in liquid form (oral solution). To help us investigate how this happens, the test medicine will be radiolabelled. 'Radiolabelled' means that the test medicine has a radioactive component (carbon-14) which helps us to track where the test medicine is in the body and how it is removed.

Who can participate?
This study will take place at one non-NHS site, enrolling up to 6 healthy male volunteers aged between 30 to 65.

What does the study involve?
On Day 1, volunteers will receive a a single administration of [Cyclohexane-U-14C]-MBS2320, 15 mg (NMT 4.5 MBq) as an oral solution, in the fasted state.
Volunteers will remain in the clinical unit Day 8, however if the relevant radioactivity criteria have not been met, volunteers may be required to remain at the clinic until Day 10. If relevant criteria have not been met at this point, home collections of urine and/or faeces may be required.
Volunteer's blood, urine and faeces will be taken throughout the study for analysis of the test medicine and for their safety.
Volunteers are expected to be involved in this study for 6 weeks from screening to discharge.

What are the possible benefits and risks of participating?
Participants will get no medical benefit from taking part in this study. We hope that the development of a product for the potential treatment of rheumatoid arthritis (RA) and idiopathic pulmonary fibrosis (IPF) will be of benefit to patients with this condition.

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

When is the study starting and how long is it expected to run for?
April 2022 to October 2022

Who is funding the study?
Modern Biosciences Ltd (UK)

Who is the main contact?
Dr Somasekhara Menakuru, recruitment@weneedyou.co.uk
Kerry Hylands, IST04@istesso.co.uk

Contact information

Type(s)
Principal investigator

Contact name
Dr Somasekhara Menakuru

Contact details
Mere Way
Ruddington Fields
Nottingham
United Kingdom
NG11 6JS
+44 330 303 1000
recruitment@weneedyou.co.uk

Type(s)
Public

Contact name
Ms Kerry Hylands

Contact details
2nd Floor, 3 Pancras Square
London
United Kingdom
N1C 4AG
-
IST04@istesso.co.uk

Type(s)
Scientific

Contact name
Dr Somasekhara Menakuru

Contact details
Mere Way
Ruddington Fields
Nottingham
United Kingdom
NG11 6JS
+44 330 303 1000
recruitment@weneedyou.co.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2022-001537-36

Integrated Research Application System (IRAS)
1005686

Protocol serial number
IST-04

Study information

Scientific Title
An open label, single-dose, single-period study designed to assess the pharmacokinetics and mass balance recovery, metabolite profile and metabolite identification of ([Cyclohexane-U-14C]-MBS2320) in healthy male subjects

Acronym
IST-04

Study objectives
1. To assess the mass balance recovery and routes and rates of elimination after a single oral dose of [Cyclohexane-U-14C]-MBS2320
2. To perform metabolite profiling and structural identification from plasma, urine and faecal samples
3. To evaluate the blood and plasma total radioactivity PK
4. To identify the chemical structure of each metabolite accounting for more than 10% of plasma total radioactivity or accounting for 10% or more of the dose in excreta
5. To further explore the oral PK of MBS2320
6. To evaluate the extent of distribution of total radioactivity into blood cells
7. To provide additional safety and tolerability information for MBS2320

Ethics approval required
Ethics approval required

Ethics approval(s)

Approved 18/08/2022, Fast Track REC (Health Research Authority) (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; None provided; fasttrack.rec@hra.nhs.uk), ref: 22/FT/0085

Approved 18/08/2022, Fast Track REC (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; no telephone number provided; fasttrack.rec@hra.nhs.uk), ref: 22/FT/0085

Primary study design
Interventional

Study design
Interventional non-randomized

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Potential treatment of rheumatoid arthritis (RA) and idiopathic pulmonary fibrosis (IPF).

Interventions
There is a single treatment arm, and all 6 healthy male participants will receive the same treatment. There is no placebo. Participants will take the test medicine once. Participants will swallow a single dose of a solution of radiolabelled test medicine containing [14C]. Participants will be involved in the study for about 6 weeks (from screening to final follow-up). They will visit the ward to be screened before they take part, to check that they are healthy. They will stay on the ward for 8-10 days after taking the test medicine.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
[14C]-MBS2320

Primary outcome(s)
1. Mass balance recovery of total radioactivity of excreta and the rates and routes of elimination of the test medicine from the body will be assessed by liquid scintillation counting from samples taken between Day 1 up to Day 10.
2. Identify breakdown products of the test medicine in excreta by liquid chromatography with radio detection and high resolution mass spectrometry, from samples taken from Day 1 up to Day 10.
3. Pharmacokinetics of the radiolabeled test medicine in plasma and whole blood will be assessed by taking blood samples for LC-MS/MS assay of the test medicine from Day 1 up to Day 10.

Key secondary outcome(s)
1. Identification of the chemical structure of each metabolite (breakdown product) accounting for more than 10% by AUC of plasma total radioactivity or accounting for 10% or more of the dose in excreta, by liquid chromatography with radio detection and high resolution mass

spectrometry using samples taken between Day 1 up to Day 10
2. The pharmacokinetics of the test medicine and its main breakdown product (MBS2473) in plasma will be assessed by taking blood samples for LC-MS/MS assay of the test medicine, using samples taken between Day 1 up to Day 8.
3. Evaluation of whole blood:plasma concentration ratios for total radioactivity (to evaluate the extent of distribution of total radioactivity into blood cells), using samples taken between Day 1 up to Day 10 for LC-MS/MS assay of the test medicine.
4. Adverse events (to assess tolerability of the test medicine) will be collected by often asking volunteers how they are feeling, from the start of the trial until follow up. Other safety measures (including vital signs, ECGs and laboratory safety tests) will also be assessed by standard phase 1 unit monitoring, at screening, from Day –1 to discharge from the ward.

Completion date
26/10/2022

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
5. Healthy males
6. Body mass index (BMI) of 18.0 to 35.0 kg/m² as measured at screening
7. 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
18 Years

Sex
Male

Total final enrolment
6

Key exclusion criteria
1. Serious adverse reaction or serious hypersensitivity to any drug or formulation excipients
2. History of any allergy to sulphonamides. 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, dermatological, chronic

respiratory or GI, 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 or history of contact with an individual known to have COVID-19 infection in the 14 days prior to IMP administration.
6. Clinically significant abnormal clinical chemistry, haematology or urinalysis as judged by the investigator. Subjects with Gilbert's Syndrome are allowed. Subjects with white cell count, lymphocyte count or neutrophil count less than the lower limit of normal
7. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) 1 and 2 antibody results
8. Evidence of renal impairment at screening, as indicated by an estimated CLcr of <80 mL/min using the Cockcroft-Gault equation)
9. Subjects who have received any IMP in a clinical research study within the 90 days prior to Day 1, or less than 5 elimination half-lives prior to Day 1, whichever is longer
10. Subjects who report to have previously received MBS2320
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. Donation of blood or plasma or loss of greater than 400 mL of blood within the previous 3 months
13. 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 PD 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
14. Subjects who have had any COVID-19 vaccines within 72 h before admission
15. History of any drug or alcohol abuse in the past 2 years
16. 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)
17. A confirmed positive alcohol breath test at screening or admission
18. Current smokers and those who have smoked within the last 12 months. A confirmed breath carbon monoxide reading of greater than 10 ppm at screening or admission
19. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months
20. Confirmed positive drugs of abuse test result
21. Male subjects with pregnant or lactating partners
22. Subjects who have consumed liquids or eaten food containing grapefruit, cranberry, caffeine or other xanthines from 24 h prior to admission
23. Subjects who are, or are immediate family members of, a study site or sponsor employee
24. Failure to satisfy the investigator of fitness to participate for any other reason

Date of first enrolment
08/09/2022

Date of final enrolment
16/10/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences Limited
Mere Way
Ruddington
Ruddington Fields
Nottingham
United Kingdom
NG11 6JS

Sponsor information

Organisation
Modern Biosciences Ltd

Funder(s)

Funder type
Industry

Funder Name
Modern Biosciences Ltd

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 due to this being a Phase 1 healthy volunteer study to assess the pharmacokinetics and mass balance recovery, metabolite profile and metabolite identification of an investigational drug.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

HRA research summary	28/06/2023	No	No