ISRCTN51111674 https://doi.org/10.1186/ISRCTN51111674

A phase I, open-label, single-centre study to evaluate the absorption, distribution, metabolism and excretion (ADME) of oral [14C]-ibrexafungerp in healthy male subjects after repeat dosing

Submission date
13/12/2022

Recruitment status
No longer recruiting

Registration date
14/12/2022

Overall study status
Completed

Last Edited
14/12/2022

Condition category
Infections and Infestations

[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, ibrexafungerp, for the potential treatment and prevention of fungal infections. Fungal infections are diseases caused by fungi, a type of living organism. These diseases most commonly affect the skin, hair, or nails. More serious fungal infections can develop inside the body's organs, and these may need to be treated in a hospital. This single-part, healthy volunteer study will try to identify how the test medicine is taken up, broken down and removed from the body. To help investigate this, the test medicine is radiolabelled, which means that it has a radioactive component (carbon-14) which helps us to track where the test medicine is in the body. The test medicine's safety and tolerability will also be studied.

Who can participate?
Healthy male volunteers aged 30-65 years old

What does the study involve?
This study will take place at one non-NHS site, and will consist of a single study period involving up to 6 volunteers. On Days 1, 2 and 3 volunteers will receive a single oral dose of the radiolabelled test medicine in the fasted state (on an empty stomach) on two occasions, once in the morning and once in the evening. On Day 4, volunteers will receive a final, single oral dose of the radiolabelled test medicine, in the morning, in the fasted state. Volunteers' blood, urine and faeces will be taken throughout the study for analysis of the test medicine and its breakdown products (metabolites) and for volunteer safety.

Volunteers will remain in the clinic until Day 15 but may be discharged as a group earlier, or have their stay extended until Day 17 (based on relevant radioactivity criteria being met). If criteria have not been met on Day 17, home collections of urine and/or faeces may be required.

Volunteers are expected to be involved in this study for approximately 8 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 fungal infections 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?
October 2022 to January 2023

Who is funding the study?
Scynexis Inc (USA)

Who is the main contact?
Mr Glen Park, glen.park@scynexis.com (USA)

Contact information

Type(s)
Public

Contact name
Mr Glen Park

Contact details
Scynexis Inc
1 Evertrust Plaza 13th Floor
Jersey City
United States of America
NJ 07302
+1 201 884-5485
glen.park@scynexis.com

Type(s)
Scientific

Contact name
Mr Glen Park

Contact details
Scynexis Inc
1 Evertrust Plaza 13th Floor
Jersey City
United States of America
NJ 07302
+1 201 884-5485
glen.park@scynexis.com

Type(s)
Principal Investigator

Contact name
Dr Nand Singh

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

Additional identifiers

EudraCT/CTIS number
2022-002824-10

IRAS number
1006333

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
SCY-078-122, IRAS 1006333

Study information

Scientific Title
A phase I, open-label, single-centre study to evaluate the absorption, distribution, metabolism and excretion (ADME) of oral [14C]-ibrexafungerp in healthy male subjects after repeat dosing

Study objectives
1. To assess the mass balance recovery of carbon-14 ([14C]) labelled ibrexafungerp ([14C]-ibrexafungerp) following repeat dosing of [14C]-ibrexafungerp
2. To provide plasma, urine and faecal samples for metabolite profiling and structural identification following repeat dosing of [14C]-ibrexafungerp
3. To assess the pharmacokinetics (PK) of ibrexafungerp following repeat dosing of [14C]-ibrexafungerp
4. To assess the PK of total radioactivity following repeat dosing of [14C]-ibrexafungerp
5. To determine the routes and rates of elimination of [14C]-ibrexafungerp
6. To identify the chemical structure of each metabolite accounting for more than 10% of circulating total radioactivity or accounting for 10% or more of the total cumulative dose in excreta
7. To evaluate the extent of distribution of total radioactivity into blood cells
8. To provide additional safety and tolerability information for ibrexafungerp

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved: 24/112022, London Brent - Research Ethics Committee (2nd Floor 2 Redman Place, Stratford, London, E20 1JQ, UK; +44 20 7104 8128, brent.rec@hra.nhs.uk), ref: 22/LO/0646
2. Approved 24/11/2022 MHRA (10 South Colonnade, Canary Wharf, London, E14 4PU, UK; +44 (0) 20 3080 6000; info@mhra.gov.uk), ref: none provided

Study design
Interventional non-randomized study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Other

Study type(s)
Other

Participant information sheet

Health condition(s) or problem(s) studied
Fungal disease

Interventions
This non-randomised study will consist of a single study period involving up to 6 male volunteers, aged 30-65 years old. There is no placebo. All subjects will receive the same treatment. Each volunteer will receive the test medicine twice daily (BID) on Days 1 to 3 and once on the morning of Day 4 of the study, in the fasted state. On Day 1 and Day 2, volunteers will receive a single 750 mg dose of the test medicine once in the morning and once in the evening. On Day 3, volunteers will receive a single 375 mg dose of the test medicine once in the morning and once in the evening. On Day 4, volunteers will receive a single 375 mg dose in the morning. Each dose will be given with approximately a 12-hour break in between. Volunteers are expected to be involved in this study for approximately 8 weeks from screening to discharge. Volunteers will visit the ward to be screened before they take part, to check they are healthy.

Intervention Type
Drug

Phase
Phase I

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

Primary outcome measure
1. Mass balance recovery of total radioactivity in urine, faeces and all excreta of the test medicine from the body measured using liquid scintillation counting from samples taken from Day 1 up to Day 26
2. Identify breakdown products of the test medicine in excreta measured using liquid chromatography with radio detection and high-resolution mass spectrometry from samples taken from Day 1 up to Day 26
3. Pharmacokinetics of the test medicine in plasma and whole blood measured in blood samples taken for LC-MS/MS assay of the test medicine from Day 1 up to Day 26

Secondary outcome measures
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 measured using liquid chromatography with radio detection and high-resolution mass spectrometry of samples taken between Day 1 up to Day 26
2. The pharmacokinetics of the test medicine and its metabolites in plasma measured in blood samples taken for LC-MS/MS assay of the test medicine, using samples taken between Day 1 to Day 26
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 26 for LC-MS/MS assay of the test medicine
4. 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. Other safety measures (including vital signs, ECGs and laboratory safety tests) will also be assessed by standard phase I unit monitoring, at screening, from Day 1 to discharge from the ward.

Overall study start date
14/10/2022

Completion date
27/01/2023

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 protocol
5. Healthy males
6. Body mass index (BMI) of 18.0 kg/m2 to 30.0 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

Age group
Adult

Lower age limit

18 Years

Sex
Male

Target number of participants
6

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, dermatological, chronic respiratory, haematological or GI disease, neurological or psychiatric disorder, irritable bowel syndrome, gastritis, intermittent vomitus or diarrhoea as judged by the investigator
4. Influenza or a viral infection within the 30 days prior to first IMP administration
5. Acute diarrhoea or constipation in the 7 days before the predicted first study day. If screening occurs >7 days before admission, this criterion will be determined admission/pre-first dose. Diarrhoea will be defined as the passage of liquid faeces and/or a stool frequency of greater than 3 times per day. Constipation will be defined as a failure to open the bowels more frequently than every other day
6. Subjects who do not have suitable veins for multiple venepunctures/cannulation as assessed by the investigator or delegate at screening
7. Evidence of current SARS-CoV-2 infection
8. Clinically significant abnormal clinical chemistry, haematology or urinalysis as judged by the investigator. Subjects with Gilbert's Syndrome are not allowed
9. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or HIV 1 and 2 antibody results
10. Subjects with ALT or AST or bilirubin values >ULN at screening
11. Haemoglobin or platelet count values <LLN at screening
12. Evidence of renal impairment at screening, as indicated by an estimated creatinine clearance (CLcr) of <80 mL/min using the Cockcroft-Gault equation
13. 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
14. Subjects who report to have previously received ibrexafungerp, including in SCY-078-116 (QSC202765)
15. 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
16. Subjects who have been administered IMP in an ADME study in the last 12 months
17. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood
18. 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 first IMP administration on Day 1 (see Section 11.4). Vaccines are not accepted concomitant medications. 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 19. Subjects who have received any vaccine 14 days prior to first IMP administration. Exceptions may apply on a case-by-case basis at the discretion of the investigator.
20. History of any drug or alcohol abuse in the past 2 years
21. 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)
22. A confirmed positive alcohol breath test at screening or admission
23. Current smokers and those who have smoked within the last 12 months.
24. A confirmed urine cotinine test at screening or admission
25. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months
26. Confirmed positive drugs of abuse test result
27. Subjects with pregnant or lactating partners
28. Subjects who are, or are immediate family members of, a study site or sponsor employee
29. Failure to satisfy the investigator of fitness to participate for any other reason

Date of first enrolment
15/12/2022

Date of final enrolment
27/01/2023

Locations

Countries of recruitment
England

United Kingdom

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

Sponsor information

Organisation
Scynexis (United States)

Sponsor details
1 Evertrust Plaza 13th Floor
Jersey City

United States of America
NJ 07302
+1 (201) 884-5485
glen.park@scynexis.com

Sponsor type
Industry

ROR
https://ror.org/03drnt809

Funder(s)

Funder type
Industry

Funder Name
Scynexis Inc

Results and Publications

Publication and dissemination plan
1. Internal Report
2. Submission to regulatory authorities
3. Other - it is unknown at this stage of the study if and/or how the sponsor may decide to share the results, and in the future they may publish an overview of the study via publications, posters or abstracts.
4. The findings of this Phase I study will be shared with the Sponsor 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.

Intention to publish date

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 the data being confidential.

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