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A study in healthy male volunteers to look at how the test medicine ([14C]-ATH434) is taken up, broken down and removed from the body when taken as a capsule

Submission date
05/08/2022

Recruitment status
No longer recruiting

Registration date
01/09/2022

Overall study status
Deferred

Last Edited
16/05/2025

Condition category
Nervous System Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] 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, ATH434, for the potential treatment of atypical parkinsonisms such as Multiple System Atrophy. The symptoms of parkinsonism are tremors, slowness of movement, rigidity and problems with balance causing instability when standing.

This single period healthy volunteer study will try to look at how the test medicine is taken up, broken down and removed by the body when given orally as a capsule or tablet. To help investigate how this happens, one dose of the test medicine will be radiolabelled (the test medicine has a radioactive component, in this case Carbon-14 which is a type of naturally occurring radioactivity). The pharmacokinetics (what the body does to the drug), safety and tolerability of this test medicine will also be studied.

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

What does the study involve?
Volunteers will take a 75 mg oral dose of ATH434 tablet in the fed state, twice daily on Day 1 to Day 7. On Day 8, volunteers will take a single 75 mg oral dose of radiolabelled [14C]-ATH434 oral capsule, in the fed state.

Volunteers will be admitted to the clinic the evening before the day of dosing (Day 1). Volunteers will be discharged on Day 15, however their stay may be extended to Day 17 depending on the results of blood, urine and faeces tests. Volunteers will receive a follow up phone call 3-7 days post-discharge.

Volunteer’s blood and urine and faeces will be taken throughout the study for analysis of the test medicine and its breakdown products, and for their safety.

Volunteers are expected to be involved in this study for approximately 8 weeks from screening to the follow up call.

What are the possible risks and benefits of participating?
1. As this is a Phase I study, the most relevant population is healthy volunteers. It is considered that the risk/benefit evaluation in this study supports the use of healthy volunteers.
2. There is always a risk that the stipend in healthy volunteer studies could represent coercion. The time spent in the clinic, travel, inconvenience and other expenses factor in calculating the stipend. Perception of risk is not considered in this calculation.
3. When investigating new medicines there is always a risk of unexpected side effects and occasionally allergic reactions. Volunteers will be closely monitored during the study.
4. Volunteers may experience side effects from the test medicine in this study. Full information on possible side effects is provided to volunteers in the Participant Information Sheet and Informed Consent Form.
5. Blood samples will be collected during the study. Collection of these samples can cause soreness and bruising of the arms but these problems usually clear up within a few days to a few weeks.
6. ECG stickers on volunteers' chests and limbs may cause some local irritation and may be uncomfortable to remove but volunteers will be closely monitored to ensure any local irritation does not persist.
7. The test medicine has the potential to increase the skins sensitivity to sunlight. Volunteers will be advised to restrict sun exposure until at least 14 days after the final dose.
8. Volunteers will be exposed to 1.0 milliSieverts (mSv) of radioactivity during the study, which is equivalent to approximately 4.5 months’ exposure to the average yearly background radiation in the UK (2.7 mSv). That amount of radiation poses negligible risk to the volunteers’ health.

Participants will get no medical benefit from taking part in this study, however, development of a treatment for atypical parkinsonism may benefit the population as a whole.

Where is the study run from?
Alterity Therapeutics Limited (Australia)

When is the study starting and how long is it expected to run for?
Oct 2022 – Nov 2022

Who is funding the study?
Alterity Therapeutics Limited (Australia)

Who is the main contact?
Cynthia Wong
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Principal Investigator

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Additional identifiers

EudraCT/CTIS number
202200051666

IRAS number
1005308

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Sponsor code: ATH434-103

Study information

Scientific Title
An Open-Label, Single-Period Study Designed to Assess the Mass Balance Recovery, Metabolite Profile and Metabolite Identification of [14C]-ATH434 in Healthy Male Subjects

Study objectives
The trial will meet the following primary objectives:
- To assess mass balance recovery after multiple oral doses of ATH434 followed by a single oral dose of carbon-14 [14C]-ATH434
- To quantify the total radioactivity in whole blood, plasma, urine and faeces
- To evaluate the pharmacokinetics (PK) of ATH434 and metabolites in plasma and total radioactivity in plasma and whole blood after multiple oral doses of ATH434 followed by a single oral dose of [14C]-ATH434
- To provide plasma, urine and faecal samples for metabolite profiling and structural confirmation and identification

The trial will meet the following secondary objectives:
- To determine the rate and routes of elimination after multiple oral doses of ATH434 followed by a single oral dose of [14C]-ATH434
- 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 dose in excreta
- To evaluate the extent of distribution of total radioactivity into blood cells
- To provide additional safety and tolerability information for ATH434

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 30/08/2022, Fast-Track Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; N/A; fasttrack.rec@hra.nhs.uk), ref: 22/FT/0096

Study design
Single-centre open-label non-randomized single-period study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Pharmaceutical testing facility

Study type(s)
Other

Participant information sheet
Not available in web format

Health condition(s) or problem(s) studied
Atypical Parkinsonism

Interventions
Volunteers receive the following oral regimens across Days 1 to 8 of the study:
- Regimen A: ATH434 Tablet, 75 mg twice daily (BID) on Day 1 to Day 7, in the fed state
- Regimen B: [14C]-ATH434 Oral Capsule, 75 mg (not more than [NMT] 4.3 MBq), single dose on Day 8, in the fed state

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic, Mass balance recovery, metabolite profiling and metabolite identification

Phase
Phase I

Drug/device/biological/vaccine name(s)
ATH434 Tablet, 75 mg; [14C]-ATH434 Oral Capsule, 75 mg (NMT 4.3 MBq)

Primary outcome measure
1. Mass balance recovery of total radioactivity in all excreta (urine and faeces): CumAe and Cum% Ae collected from Day 7 of the study until discharge.
2. Collection of whole blood, plasma, urine and faeces samples for analysis of total radioactivity collected from Day 7 of the study until up to discharge.
3. PK parameters for ATH434, metabolites and total radioactivity: Tlag, Tmax, Cmax, AUC(0-last), AUC(0-inf), AUC(0-tau), T1/2 and metabolite ratios, where applicable, in plasma samples collected throughout the study until Day 15.
4. Collection of plasma, urine and faeces samples for metabolite profiling, structural identification, and quantification analysis, collected throughout the study until up to discharge.

Secondary outcome measures
1. Determination of rate and routes of elimination of total radioactivity by Ae, %Ae, CumAe and %CumAe, by collection interval using urine and faeces samples collected throughout the study until up to discharge.
2. Identification of the chemical structure of each metabolite accounting for more than 10% by AUC of circulating total radioactivity or accounting for 10% or more of the dose in excreta in plasma, urine and faeces samples collected throughout the study until up to discharge.
3. Evaluation of whole blood:plasma concentration ratios for total radioactivity in plasma samples collected from Day 8 until Day 15.
4. To provide additional safety and tolerability information for ATH434 by assessing: incidence of adverse events (AEs), physical examinations and change from baseline for vital signs, electrocardiograms (ECGs), and laboratory safety tests from admission until discharge.

Overall study start date
14/07/2022

Completion date
26/11/2022

Eligibility

Key inclusion criteria
1. Must provide written informed consent
2. Must be willing and able to eat the standard breakfasts and evening meals provided on Days 1 to 8
3. Must be willing and able to communicate and participate in the whole study
4. Age 30 to 65 years inclusive at the time of signing informed consent
5. Must agree to adhere to the contraception requirements
6. Healthy males
7. Body mass index (BMI) of 18.0 to 32.0 kg/m2 as measured at screening
8. 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
30 Years

Upper age limit
65 Years

Sex
Male

Target number of participants
6

Total final enrolment
6

Key exclusion criteria
1. Serious adverse reaction or serious hypersensitivity to any drug or the 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 or evidence of clinically significant cardiovascular, renal, hepatic, dermatological, chronic respiratory or gastrointestinal disease, neurological or psychiatric disorder, as judged by the investigator
4. History of seizures, including history of febrile seizures during childhood
5. Subjects who do not have suitable veins for multiple venepunctures/cannulation as assessed by the investigator or delegate at screening
6. Evidence of current SARS-CoV-2 infection within 4 weeks of first IMP administration or not fully recovered from COVID-19 symptoms by the screening visit

7. Clinically significant abnormal clinical chemistry, haematology or urinalysis as judged by the investigator. Subjects with Gilbert's Syndrome are not allowed
8. Haemoglobin below the lower limit of the laboratory reference range at screening
9. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) 1 and 2 antibody results
10. Evidence of renal impairment at screening, as indicated by an estimated glomerular filtration rate (eGFR) of <75mL/min/1.73 m2 using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation 2009.
11. 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
12. 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
13. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood
14. Use of any of the following within 28 days prior to dosing
– CYP1A2 inhibitors or inducers
– UGT inhibitors or inducers
– Herbal supplements
– Inducers of CYP enzymes
15. Use of any prescription medication not referenced in Exclusion 14 within 14 days prior to dosing.
16. Use of any non-prescription medication (including non-steroidal anti-inflammatory drugs), herbal remedy (including St. John's Wort) not referenced in Exclusion 14 or vitamin supplement, within 7 days prior to dosing and throughout the study
17. History of any drug or alcohol abuse in the past 2 years
18. 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)
19. A confirmed positive alcohol breath test at screening or admission
20. Current smokers and those who have smoked within the last 12 months. A confirmed positive urine cotinine test at screening or admission
21. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months
22. Confirmed positive drugs of abuse test result at screening or admission
23. Subject answers "yes" to "Suicidal Ideation" Items 1 or 2 on the Columbia-Suicide Severity Rating Scale (C-SSRS) at screening
24. Subjects who are, or are immediate family members of, a study site or sponsor employee
25. Failure to satisfy the investigator of fitness to participate for any other reason

Date of first enrolment
12/10/2022

Date of final enrolment
26/11/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Quotient Sciences Limited
Mere Way, Ruddington Fields
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Sponsor information

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Sponsor type
Industry

ROR
https://ror.org/01yxtmr67

Funder(s)

Funder type
Industry

Funder Name
Alterity Therapeutics Limited

Results and Publications

Publication and dissemination plan
In accordance with the approved HRA deferral, full trial details have now been published in the registry

Intention to publish date
22/05/2025

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 non-therapeutic clinical trials.

IPD sharing plan summary
Not expected to be made available