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ANAVEX3-71-002

Submission date 12/01/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 18/01/2023	**Overall study status** Completed	
Last Edited 02/02/2026	**Condition category** Nervous System Diseases	

Plain English summary of protocol

Background and study aims
The Sponsor is developing the test medicine, ANAVEX3-71, for the potential treatment of Alzheimer's disease and frontotemporal dementia. Dementia is the name for a group of symptoms associated with an ongoing decline in brain functioning. It can affect memory, thinking skills and other mental abilities. Alzheimer's disease is the most common cause of dementia in the UK. This study will look at and compare how different recipes of the test medicine are taken up by the body and how the body is affected by the different recipes of the test medicine. This study may also investigate the effect that food has on the body's ability to absorb the test medicine by administering the test medicine after a high-fat breakfast.

Who can participate?
This study will take place at one non-NHS site, enrolling up to 12 male and non-pregnant, non-lactating female volunteers aged 18-55 years.

What does the study involve?
Volunteers will receive a single oral dose of the test medicines on five occasions. In one of the periods, the reference IR oral capsule will be given, and in the other four periods, the MR tablet will be given. Period 5 may assess the effect of food on the MR tablet by administering the test medicine after a high-fat breakfast. Volunteers will be discharged from the study once they have completed the follow-up phone call in their final study period.

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. There will be an extended period of fasting for the volunteers taking part in this study. To ensure an adequate fluid intake, the volunteers will be allowed ad libitum fluids except for 1-

hour pre- and post-dosing and will be monitored for signs of dehydration and fatigue.
6. 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.
7. 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.
8. As the test medicine acts on the brain and nervous system it may have an effect on volunteers' mental health, and they will be required to complete a C-SSRS questionnaire at regular intervals during the study. The questionnaire assesses an individual's mood and mental wellbeing and will be performed by an appropriately trained physician.
9. Due to the unavailability of phototoxic data for ANAVEX3-71, volunteers will be advised to minimise exposure to sunlight until 6 days after each dose.

Where is the study run from?
Anavex Germany GmbH (Germany)

When is the study starting and how long is it expected to run for?
April 2023 to August 2023

Who is funding the study?
Anavex Germany GmbH (Germany)

Who is the main contact?
James Tran, Director Clinical Science
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Additional identifiers

Clinical Trials Information System (CTIS)
2022-003288-10

Integrated Research Application System (IRAS)
1006587

Sponsor code
ANAVEX3-71-002

Quotient code
QSC206403

Study information

Scientific Title
A Phase I, single-centre, open-label, one-part study designed to assess the pharmacokinetic profiles of ANAVEX3-71 and its metabolite M8 following administration of modified release formulation prototypes and an immediate release reference formulation in healthy male and female participants

Study objectives
The trial will meet the following primary and secondary objectives:

Primary objective:
1. To evaluate the plasma pharmacokinetic (PK) profiles of ANAVEX3-71 and its metabolite M8

following oral administration of ANAVEX3-71 Modified Release (MR) Prototype Tablets and ANAVEX3-71 Immediate Release (IR) Oral Capsules (reference formulation) in healthy participants.
2. To evaluate the relative bioavailability of the ANAVEX3-71 MR Prototype Tablets in comparison with ANAVEX3-71 IR Oral Capsules (reference formulation) in healthy participants in the fasted state.

Secondary objectives:
1. To provide additional information on the safety and tolerability of ANAVEX3-71 MR Prototype Tablets and the ANAVEX3-71 IR Oral Capsules (reference formulation) following oral administration in healthy participants.
2. To determine the plasma PK of a selected ANAVEX3-71 MR Prototype Tablet at the same dose in the fed versus the fasted state in healthy participants (optional).
3. To evaluate the urine samples for ANAVEX3-71 and its metabolite M8 following oral administration of ANAVEX3-71 IR Oral Capsules in healthy participants.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 13/03/2023, London Surrey Borders REC (London HRA Centre, 2nd Floor, 2 Redman Place, Stratford, London, E20 1JQ, UK; surreyborders.rec@hra.nhs.uk), ref: 23/LO/0006
2. Approved 13/03/2023, MHRA (10 South Colonnade, Canary Wharf, London, E14 4PU, UK; +44 (0)
20 3080 6000; info@mhra.gov.uk), ref: CTA 52215/0005/001-0001
The HRA has approved deferral of publication of trial details.

Primary study design
Interventional

Study design
Pharmacokinetics trial

Study type(s)
Other

Health condition(s) or problem(s) studied
Alzheimer’s disease (AD), frontotemporal dementia (FTD)

Interventions
This is a Phase I, single-centre, single-part, open-label study. This healthy volunteer study will try to assess what the body does to the test medicine (pharmacokinetics) and how the body takes up the test medicine when given in two forms, a modified release (delayed; MR) tablet versus an immediate release (IR) capsule (relative bioavailability). This study will take place at a single non-NHS site, enrolling up to 12 male and female volunteers of non-childbearing potential aged between 18 and 55 years. Volunteers will receive a single oral dose of the test medicines on five occasions. In one of the periods, the reference IR oral capsule will be given, and in the other four periods, the MR tablet will be given. Period five may assess the effect of food on the MR tablet. Volunteers will be discharged on Day 3 of each period and will return to the clinical unit on Day 4 and Day 5 for blood samples to measure the amount of the test medicine and its metabolite (breakdown product) in the blood. There will be a minimum washout period of 7 days between

each dosing. Volunteers will receive a follow-up phone call 7 to 9 days post-final dose. Volunteers' blood and urine will be taken throughout the study for analysis of the test medicine and its metabolite and for their safety. Volunteers are expected to be involved in this study for 13 weeks from screening to the follow-up call.

1. ANAVEX3-71 IR Oral Capsule (reference formulation), 5 mg
2. ANAVEX3-71 IR Oral Capsule (reference formulation), 20 mg
3. ANAVEX3-71 MR Prototype X Tablet, 150-300 mg

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
ANAVEX3-71

Primary outcome(s)
1. The appropriate ANAVEX3-71 and M8 plasma PK parameters of ANAVEX3-71 MR Prototype Tablets and IR oral capsules (reference formulation), measured using blood samples collected from Day 1 to 96 hours post-dose on Day 5 in Periods 1-5.
2. Calculation of the relative bioavailability (Frel) for ANAVEX3-71 Cmax, C8 (IR reference only), C24 (MR prototype tablets only), AUC(0-24) and AUC(0-inf) for the ANAVEX3-71 MR Prototype Tablets in comparison with an ANAVEX3-71 IR Oral Capsules (reference formulation), measured using blood samples collected from Day 1 to 96 hours post-dose on Day 5 in Periods 1-5.

Key secondary outcome(s)
1. Safety and tolerability measured using assessment of physical examinations, safety laboratory tests, vital signs, electrocardiograms (ECGs), adverse events (AEs) and C-SSRS from screening until discharge from the study.
2. The appropriate plasma PK parameters of ANAVEX3-71 following administration of a selected ANAVEX3-71 MR Prototype Tablet, measured using blood samples collected from Day 1 to 96 hours post-dose on Day 5 in Periods 1-5.
3. The appropriate urine PK parameters for the ANAVEX3-71 IR Oral Capsules for ANAVEX3-71 and its metabolite M8, measured using blood samples collected from Day 1 to 48 hours post-dose on Day 3 in Period 1.

Completion date
10/08/2023

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 18 to 55 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 be vaccinated for COVID-19 in accordance with current UK government guidance or have had a previous COVID-19 infection in the past 6 months. One of the following options must apply in order for a subject to be eligible:

5.1. An approved COVID-19 vaccine primary series (Moderna, Pfizer/BioNTech, Nuvaxovid vaccine (Novavax), Oxford/AstraZeneca vaccine, Janssen vaccine)
5.2. An approved COVID-19 vaccine primary series and a COVID-19 infection in the last 6 months prior to screening
5.3. A COVID-19 infection in the last 6 months prior to screening
6. Healthy males or non-pregnant, non-lactating healthy females of non-childbearing potential. Participants who are healthy as determined by medical evaluation including medical history, physical and neurological examination, vital signs, single 12-lead ECG, clinical laboratory profiles (haematology, clinical chemistry, coagulation and urinalysis), as deemed by the investigator or designee at screening
7. Body mass index (BMI) of 18.0 to 30.0 kg/m2 as measured at screening
8. Minimum weight ≥50.0 kg and maximum weight 120.0 kg at screening
9. Adequate peripheral venous access at screening

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
Yes

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
All

Total final enrolment
11

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 or GI disease, or neurological, as judged by the investigator
4. History of psychiatric disease needing treatment in the last 5 years
5. History of postural hypotension or unexplained syncope, or seizures
6. Participants with a history of cholecystectomy or gallstones
7. Evidence of current SARS-CoV-2 infection or reports to have had COVID-19 within 2 weeks of first IMP administration
8. Clinically significant abnormal clinical chemistry, haematology, coagulation or urinalysis as judged by the investigator.
- Participants with renal (urea or creatinine) and hepatic function test (total bilirubin, alanine aminotransferase [ALT], alkaline phosphatase, gamma glutamyl transferase [GGT]) results greater than the normal reference values at screening. Participants with Gilbert’s Syndrome are

not allowed
9. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) 1 and 2 antibody results
10. Females of childbearing potential including those who are pregnant or lactating (all female participants must have a negative highly sensitive serum pregnancy test). A woman is considered of childbearing potential unless she is permanently sterile (hysterectomy, bilateral salpingectomy, and bilateral oophorectomy) or is postmenopausal (had no menses for 12 months without an alternative medical cause and a serum follicle-stimulating hormone [FSH] concentration ≥40 IU/L)
11. Heart rate on ECG or vital signs <45 bpm or >100 bpm; PR >220 msec; Corrected QT interval by Fridericia's formula (QTcF) ≤350 msec or ≥450 msec for males or QTcF ≤360 msec or ≥460 msec for females; second degree or higher heart block at screening or pre-dose Period 1, Day 1
12. Participants who have received any IMP in a clinical research study within the 90 days prior to Period 1, Day 1, or less than 5 elimination half-lives prior to Period 1, Day 1, whichever is longer
13. Donation of blood or plasma within the previous 3 months or loss of greater than 400 ml of blood
14. Participants 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 and HRT) in the 14 days before IMP administration. COVID-19 vaccines are accepted concomitant medications. Exceptions may apply, as determined by the investigator and agreed to by the sponsor's medical monitor, 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 participant; and if the use of medication is not considered to interfere with the objectives of the study
15. History of any drug or alcohol abuse in the past 2 years
16. Regular alcohol consumption in males >21 units per week and females >14 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 6 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 6 months
20. Confirmed positive drugs of abuse test result
21. Male participants with pregnant or lactating partners
22. Participant answers "yes" to "Suicidal Ideation" items 1 or 2 on the Columbia Suicide Severity Rating Scale (C-SSRS) at screening or admission
23. Participants 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
26/04/2023

Date of final enrolment
10/08/2023

Locations

Countries of recruitment
United Kingdom

England

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Sponsor information

Organisation
Anavex Germany GmbH

Funder(s)

Funder type
Industry

Funder Name
Anavex Germany GmbH

Results and Publications

Individual participant data (IPD) sharing plan

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