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A Phase 1, Open-Label, Drug-Drug Interaction (DDI) Study to Assess the Effect of ASN51 on the Pharmacokinetics of a CYP3A4 Probe Substrate in Healthy Subjects

Submission date
26/03/2024

Recruitment status
No longer recruiting

Registration date
02/04/2024

Overall study status
Completed

Last Edited
16/05/2025

Condition category
Other

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Background and study aims
Neurodegenerative diseases are conditions that affect the nerve cells in the brain and spinal cord, causing them to slowly stop working or die over time. Alzheimer's disease (AD) is the most common neurodegenerative disease. Though certain medicines can slow down the progression of AD, these medicines may not work for all patients at all times. Some medicines may also cause some serious side effects in patients. Therefore, there is always a need to find new treatments. ASN51, the study drug, is being developed for the possible treatment of tauopathy, which are neurodegenerative diseases that cause abnormal buildup of a protein called the tau protein in the brain. This can damage the brain cells, causing memory loss, movement problems, and so on. The purpose of this study was to evaluate how ASN51 affects the body when taken along with another medicine called midazolam. It also investigated how ASN51 influences the distribution of midazolam throughout different parts of the body (this is called pharmacokinetics or PK). Additionally, the study assessed the safety of ASN51 both with and without the co-administration of midazolam in healthy participants.

Who can participate?
Healthy males and females aged 18-55 years took part in the study.

What does the study involve?
Participants were part of this study for approximately 26 days from the start of the treatment. The study had three parts:
1. Screening period of 28 days, wherein participants underwent some tests and/or procedures to ensure that they were eligible to take part in the study.
2. Treatment period during which participants received ASN51, by mouth, once daily (QD), on Days 2-15 along with midazolam, also given by mouth, on Days 1, 3 and 16.
Participants stayed at the clinic from the day before their first dose (Day –1) until six days after their final ASN51 dose (Day 21). During this time, they were regularly monitored by the study doctor to assess how their bodies processed the medicines and to check for any side effects.

Participants had the right to stop the treatment and leave the study at any time if they chose to do so. This is an open-label study. This means everyone involved, including the participant and the study doctor, will know the study treatment the participant has been given.
3. Safety follow-up during which participants had to come back for a check-up about 24-26 days after receiving the last dose of the study drug. This was to check on the participants' health after treatment was completed.

What are the possible benefits and risks of participating?
ASN51 is an experimental drug and was given purely for research purposes. There were no direct health benefits for study participants from the receipt of study medication. But the information learned from this study may be useful to treat future patients with such conditions. An indirect health benefit to the healthy participants enrolled in this trial was the free medical examination received at screening and during the study. The participants may have side effects from the study drug or procedures used in this study. Side effects can vary from mild to very serious and may be different from person to person.
ASN51
Potential side effects of ASN51 were feeling less hungry than usual, loss of body weight, high blood pressure, increased heart rate, changes in coagulation parameters (body's ability to form blood clots), altered taste (dysgeusia), increase in liver enzymes etc.
Midazolam
Common side effects of midazolam include tiredness, drowsiness, reduced alertness, confusion, not being able to remember new things after a certain point in time (anterograde amnesia), headache, dizziness, muscle weakness, loss of coordination of movements (ataxia), etc.
Participants who took part were informed about the risks and benefits, as well as any additional procedures or tests they had to undergo. All details of the study were described in an informed consent document.

Where is the study run from?
Asceneuron (Switzerland)

When is the study starting and how long is it expected to run for?
February 2024 to September 2024

Who is funding the study?
Asceneuron (Switzerland)

Who is the main contact?
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Contact information

Type(s)
Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
1009554

Protocol serial number
HMR code: 23-011, Sponsor code: ASN51-105

Study information

Scientific Title
A Phase 1, Open-Label, Drug-Drug Interaction (DDI) Study to Assess the Effect of ASN51 on the Pharmacokinetics of a CYP3A4 Probe Substrate in Healthy Subjects

Study objectives
To assess the potential CYP induction and inhibition effect of ASN51 on the PK of midazolam in healthy subjects

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 04/04/2024, South Central – Oxford A Research Ethics Committee (Ground Floor, Temple Quay House, 2 The Square, Bristol, BS1 6PN, United Kingdom; +44 (0)207 104 8171; oxforda.rec@hra.nhs.uk), ref: 24/SC/0041

2. Approved 05/04/2024, Medicines and Healthcare products Regulatory Agency (MHRA) (10 South Colonnade, Canary Wharf, London, E14 4PU, United Kingdom; +44 (0)20 3080 6000; info@mhra.gov.uk), ref: CTA 50212/0004/001-0001

Primary study design
Interventional

Study design
Drug-drug interaction trial in up to 16 healthy volunteers

Study type(s)
Other

Health condition(s) or problem(s) studied
Healthy volunteers

Interventions
In this study, all healthy participants are enrolled to receive same treatment.
Treatment details: Day 1: single dose midazolam 2.5 mg
Days 2 – 15: ASN51 QD
Day 3: midazolam 2.5 mg (in addition to ASN51)
Day 16: single dose of midazolam 2.5 mg

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
ASN51 and midazolam

Primary outcome(s)
1. Maximum Plasma Concentration (Cmax) of Midazolam and 1-hydroxymidazolam with and without the co-administration of ASN51
2. Dose-normalised Cmax (Cmax/Dose) of Midazolam with and without the co-administration of ASN51
3. Time to Reach Maximum Plasma Concentration (Tmax) of Midazolam and 1-hydroxymidazolam with and without the co-administration of ASN51
4. Terminal Half-life (T1/2) of Midazolam and 1-hydroxymidazolam with and without the co-administration of ASN51
5. Terminal Rate Constant (Lambda z) of Midazolam and 1-hydroxymidazolam with and without the co-administration of ASN51
6. Area Under the Plasma Concentration-time Curve From Time Zero to Time of Last (AUClast) measurable concentration of Midazolam and 1-hydroxymidazolam with and without the co-administration of ASN51
7. Area Under the Plasma Concentration-Time Curve From Time Zero to Infinity (AUCinf) measurable concentration of Midazolam and 1-hydroxymidazolam with and without the co-administration of ASN51
8. Dose-normalised AUC to Infinity (AUCinf/Dose) of Midazolam with and without the co-administration of ASN51
9. Apparent Total Clearance (CL/F) from plasma after non-intravenous administration of Midazolam with and without the co-administration of ASN51
10. Apparent Volume of Distribution (Vz/F) after non-intravenous administration of Midazolam with and without the co-administration of ASN51

Key secondary outcome(s)

1. Number of Participants With Clinically Significant Abnormalities in Clinical Laboratory Parameters
2. Number of Participants With Clinically Significant Abnormalities in Vital Signs
3. Number of Participants With Clinically Significant Abnormalities in 12-lead Electrocardiogram (ECG) Parameters
4. Number of Participants With Clinically Significant Abnormalities in Physical and Neurological Examination
5. Number of Participants With Positive Columbia-Suicide Severity Rating Scale (C-SSRS) Results
6. Number of Participants With at Least One Treatment Emergent Adverse Events (TEAEs)

Completion date
22/09/2024

Eligibility

Key inclusion criteria
1. Male healthy volunteers or healthy female volunteers of non-childbearing potential. A woman is considered to be of non-childbearing potential if she meets one of the following criteria:
2. Post-menopausal (amenorrhea for at least 12 months, and follicle-stimulating hormone (FSH) at screening confirms post-menopausal status)
3. Has no uterus, ovaries or fallopian tubes
4. Aged 18–55 years.
5. Deemed healthy based on medical history, physical examination, ECG, vital signs, neurological examination, and laboratory tests of blood and urine.
6. Body weight ≥ 50.0 kg (men) or ≥ 45.0 kg (women).
7. Body mass index (BMI; Quetelet index) in the range 18.0–30.9 kg/m2 (inclusive).
8. Sufficient intelligence to understand the nature of the trial and any hazards of participating in it. Ability to communicate satisfactorily with the investigator and to participate in, and comply with the requirements of, the entire trial (ie be fluent in the local language).
9. Willingness to give written consent to participate after reading the ICF, and after having the opportunity to discuss the trial with the investigator or their delegate.
10. Agree not to donate blood or blood products during the study and for up to 3 months after the final visit.
11. Willingness to give written consent to have data entered into The Overvolunteering Prevention System (TOPS).

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
All

Key exclusion criteria
1. Clinically relevant abnormal medical history, physical or neurological findings, ECG, or laboratory values at screening, or before the first dose of trial medication, that could interfere with the objectives of the trial or the safety of the volunteer.
2. History or presence of acute or chronic illness, or clinically-significant medical abnormality, sufficient to invalidate the volunteer's participation in the trial or make it unnecessarily hazardous.
3. History or presence of any disease, medical condition, or surgery (eg stomach bypass), likely to affect the absorption, distribution, metabolism, or excretion of medicines. Subjects with a history of cholecystectomy should be excluded.
4. Impaired endocrine, thyroid, hepatic, respiratory or renal function, diabetes mellitus, coronary heart disease, or history of any psychotic mental illness.
5. Presence or history of severe or clinically significant adverse reaction to any drug; or a history of sensitivity to ASN51 or midazolam, or any components of those medications.
6. History of psychiatric disorders, including substance use disorders, according to the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) criteria.
7. Any diagnosis of intellectual disability (intellectual developmental disorder) or mental retardation.
8. History of epilepsy or seizures, other than a single instance of benign febrile convulsion in childhood.
9. History of clinically significant head trauma, including closed head injury with loss of consciousness.
10. History of clinically significant orthostatic hypotension (ie postural syncope).
11. History of neuroleptic malignant syndrome.
12. History of chronic urinary tract infections.
13. Suicidal ideation, as determined by the C-SSRS, during the previous 6 months.
14. Blood pressure and pulse rate in supine position at the screening examination or Day -1 outside the following ranges: blood pressure 90–140 mm Hg systolic, 40–90 mm Hg diastolic; pulse rate 40_100 beats/min. The median of triplicate measurements (each 5 min apart) will be used to assess eligibility. Repeat measurements are permitted if values are borderline (ie values that are within 5 mm Hg for blood pressure or 5 beats/min for pulse rate) or if requested by the investigator. Subjects can be included if the repeat value is within range.
15. Significant (> 10%) weight loss or gain within 30 days before the (first) screening visit or before the first dose of trial medication.
16. Unsatisfactory venous access.
17. Subjects with a COVID-19 vaccination within 2 weeks of screening, or who are due to receive a dose of a COVID-19 vaccine while participating in the study.
18. Positive test for hepatitis B, hepatitis C or human immunodeficiency virus (HIV).

Date of first enrolment
23/04/2024

Date of final enrolment
22/06/2024

Locations

Countries of recruitment

United Kingdom

England

Study participating centre
Hammersmith Medicines Research (HMR)
Cumberland Avenue, Park Royal
London
United Kingdom
NW10 7EW

Sponsor information

Organisation
Asceneuron (Switzerland)

ROR
https://ror.org/02sbchm13

Funder(s)

Funder type
Industry

Funder Name
Asceneuron S.A.

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 non-therapeutic 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?
Basic results			29/04/2025	No	No