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First in human study with OKL-1111, a novel universal anticoagulant reversal agent: safety, pharmacokinetics and pharmacodynamics

Submission date
22/12/2022

Recruitment status
No longer recruiting

Registration date
03/01/2023

Overall study status
Completed

Last Edited
03/03/2025

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
OKL-1111 is a small molecule universal anticoagulant and platelet inhibitor reversal agent and is being developed to significantly shorten the time to treatment of intracranial haemorrhage associated with anticoagulant and platelet inhibitor use.

Who can participate?
Healthy adult volunteer men

What does the study involve?
The objective of this study was to evaluate the safety, tolerability and pharmacokinetics (PK; how a drug moves through the body) of OKL-1111 after single intravenous dosing in healthy male subjects. In addition, the pharmacodynamic (PD; how a drug affects the body) response of OKL-1111 in the presence and absence of dabigatran and apixaban was assessed ex vivo. Part B evaluated the safety, PK and PD of OKL-1111 after a single dose of 220mg dabigatran.

What are the possible benefits and risks of participating?
No benefits and risks given at update

Where is the study run from?
Alveron Pharma UK Ltd

When is the study starting and how long is it expected to run for?
November 2022 to December 2023

Who is funding the study?
Alveron Pharma UK Ltd

Who is the main contact?
Clinical director, edwin.spaans@Alveron.com

Contact information

Type(s)
Principal investigator

Contact name
Dr Denisa Wilkes

Contact details
HMR
Cumberland Avenue
London
United Kingdom
NW10 7EW
+44 (0)20 8961 4130
rec@hmrlondon.com

Type(s)
Scientific

Contact name
Mr Clinical Director

Contact details
Biocity
Pennyfoot Street
Nottingham
United Kingdom
NG1 1GF
+31 654997700
edwin.spaans@Alveron.com

Additional identifiers

Clinical Trials Information System (CTIS)
2022-003463-19

Integrated Research Application System (IRAS)
1005980

Protocol serial number
HMR code: 21-017; Sponsor code: OKL-1111-101

Study information

Scientific Title
A 2-part, randomised, double-blind, placebo controlled alternating group, partial crossover study to assess the safety and tolerability, pharmacokinetics, and pharmacodynamics of OKL-1111, a novel universal anticoagulant reversal agent, in healthy men

Study objectives
This randomised, placebo controlled, double-blind, single-ascending dose, first in human study evaluated the safety, tolerability, pharmacokinetics and pharmacodynamics of OKL-1111 after intravenous doses administered alone or following the anticoagulant dabigatran etexilate in healthy subjects.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 23/01/2023, London – Surrey Borders Research Ethics Committee (Skipton House, 80 London Road, SE1 6LH, London, UK; +44 (0)207 104 8104; surreyborders.rec@hra.nhs.uk), ref: 22/LO/0813
2. Approved 26/01/2023, MHRA (10 South Colonnade, Canary Wharf, London, E14 4PU, UK; +44 (0)20 3080 6000; info@mhra.gov.uk), ref: CTA 57307/0001/001-0001

Primary study design
Interventional

Study design
First-in-human safety tolerability pharmacokinetics and pharmacodynamics study

Study type(s)
Safety

Health condition(s) or problem(s) studied
Intracranial haemorrhagic bleed

Interventions
A 2-part, randomised, double-blind, single ascending dose, placebo controlled alternating group, partial crossover study to assess the safety and tolerability, pharmacokinetics, and pharmacodynamics of OKL-1111, a novel universal anticoagulant reversal agent, in healthy subjects.

Part A: OKL-1111 or Placebo
Part B: 220 mg dabigatran etexilate (in the fed state), followed an hour later by a single ascending IV bolus dose of OKL 1111 or placebo

Part A: Single ascending doses
Two groups of 6 subjects each were enrolled. Each subject had 3 study sessions, in which they received a single ascending IV bolus dose of OKL-1111 or placebo in the fasted state. Each subject received 1 dose of placebo and 2 of OKL 1111 during the trial. Subjects were randomized to 1 of 3 treatment sequences, such that in each session 4 received OKL-1111 and 2 received placebo. The groups were to be dosed alternately: Group A1 were to receive the first, third and fifth dose levels, and Group A2 were to receive the second, fourth, and sixth dose levels.

Part B: Single ascending doses in presence of dabigatran
Two groups of 6 subjects each were enrolled. Each subject had 2 study sessions in which they received a single oral dose of 220 mg dabigatran etexilate (in the fed state), followed an hour later by a single ascending IV bolus dose of OKL 1111 or placebo. In each study session, 4 subjects received OKL-1111 and 2 subjects received placebo.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
OKL-1111

Primary outcome(s)
Safety as assessed by Adverse event monitoring, physical examination, regular vital signs and 12-lead ECG recording, injection site assessment of local tolerability, adverse events (AEs) and clinical laboratory assessments (haematology, coagulation (including thrombin-antithrombin III complexes (TAT) and the fibrin split product D-dimer), clinical chemistry, and urinalysis) until 24 h postdose and 9 days (± 2 days) after the last dose. Continuous monitoring of QT intervals corrected with Fridericia's and Bazett's formula (QTcF and QTcB) was performed with a Mortara Surveyor Telemetry System (Mortara Instrument, Inc, Milwaukee, WI, USA) during the first 24 h postdose, and in case of QTcF or QTcB ≥ 500 ms, a 12-lead ECG was to be recorded. In addition, urinary markers of renal tissue injury were monitored: Vanin-1, neutrophil gelatinase associated lipocalin (NGAL) and N-acetyl-beta-D glucosaminidase (NAG)

Key secondary outcome(s)
PK plasma and urinary concentration time profiles were assessed and the following PK parameters were derived by non-compartmental analysis: Cmax, tmax, AUClast, AUCinf, AUC12, AUC24, %AUCextrap, λZ, t½, CL, VZ, MRTinf Ae24, and CLR. PD coagulation markers were thrombin generation in clotting plasma, using the Calibrated Automated Thrombogram® (CAT) assays: [lag time, peak height, time to peak, endogenous thrombin potential and derived velocity index]; thrombin generation in presence of an ex vivo challenge with DOACs (Part A only); Ecarin Chromogenic Assay (STA-ECA-II); Direct Thrombin Inhibitor (DTI); activated partial thromboplastin time (aPTT); prothrombin time (PT), expressed as international normalised ratio (INR) thrombotic and thrombolytic status (occlusion time, thrombus stability, lysis time.

Completion date
30/12/2023

Eligibility

Key inclusion criteria
1. Male
2. Aged 18–50 years, with a body mass index of 18.0–32.0 kg/m2
3. Deemed healthy on the basis of clinical history, physical examination, electrocardiogram (ECG), vital signs, and laboratory tests of blood, urine and faeces
4. Registered with a general practitioner
5. No contraindication for or sensitivity to dabigatran etexilate

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
50 Years

Sex
Male

Key exclusion criteria
1. Clinically relevant abnormal history, physical findings, ECG, or laboratory values at the pre-trial screening assessment that could interfere with the objectives of the trial or the safety of the volunteer.
2. Aspartate aminotransferase (AST), alanine aminotransferase (ALT) or total bilirubin values which are above the upper limit of normal (ULN).
3. Presence of acute or chronic illness or history of chronic illness sufficient to invalidate the volunteer's participation in the trial or make it unnecessarily hazardous.
4. Impaired endocrine, thyroid, hepatic, respiratory or renal function, diabetes mellitus, coronary heart disease, or history of any psychotic mental illness.
5. Surgery (eg stomach bypass) or medical condition that might affect absorption of medicines (Part B only).
6. Estimated glomerular filtration rate (eGFR) at screening < 80 mL/min/1.73 m2 (estimated using the method established by the Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI]).
7. Presence or history of severe adverse reaction to any drug (Parts A and B), or a history of sensitivity to dabigatran etexilate and/or major excipients (Part B only).
8. Presence or history of any contraindication for administration of dabigatran etexilate (Part B only).
9. Positive faecal occult blood sample at screening (Part B only).
10. Use of a prescription medicine during the 28 days before the first dose of trial medication or use of an over-the-counter medicine, with the exception of acetaminophen (paracetamol), during the 7 days before the first dose of trial medication.
11. Receipt of an investigational product (including prescription medicines) as part of another clinical trial within the 3 months before first admission to this study; in the follow-up period of another clinical trial at the time of screening for this study.
12. Presence or history of drug or alcohol abuse, or intake of more than 14 units of alcohol weekly.
13. Has not smoked or used nicotine-containing products for 6 months prior to screening for this study.
14. Mean blood pressure and mean pulse rate in supine position at the screening examination, or on Day –1 of Session 1 outside the ranges: blood pressure 90–140 mm Hg systolic, 40–90 mm Hg diastolic; pulse rate 40_100 beats/min. One set of repeats in triplicates is permitted if the mean 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 mean value is within range or still borderline, but deemed not clinically significant by the investigator.
15. QT value, measured at the screening visit or at baseline (predose on Day 1 of Session 1), outside the range 300–450 msec on 12-lead ECG, using Fridericia's formula (QTcF) for correction.

At screening and predose on Day 1 of Session 1, the mean of triplicate ECG recordings will be used for determining eligibility.
16. Possibility that the volunteer will not cooperate with the requirements of the protocol.
17. Evidence of drug abuse on urine testing.
18. Positive test for hepatitis B, hepatitis C or HIV.
19. Loss of more than 400 mL blood during the 3 months before the trial, eg as a blood donor.
20. Objection by GP to volunteer entering trial.

Date of first enrolment
30/01/2023

Date of final enrolment
30/09/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
HMR
Cumberland Avenue
Park Royal
London
United Kingdom
NW10 7EW

Sponsor information

Organisation
Alveron Pharma UK Ltd

Funder(s)

Funder type
Industry

Funder Name
Alveron Pharma UK Ltd

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?
HRA research summary			28/06/2023	No	No
Other unpublished results			03/03/2025	No	No