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A study to investigate the pharmacokinetic profile of ALXN2050 modified release prototype formulations and immediate release reference tablet in healthy adult participants

Submission date 07/02/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 14/03/2023	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 20/12/2023	**Condition category** Other	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
The sponsor is developing a new test medicine to treat complement alternative pathway (AP)-medicated diseases. This healthy volunteer study aims to assess how different recipes of the test medicine are taken up by the body, and how the body affects the test medicine (pharmacokinetics) when compared to a reference product. It also aims to assess the safety and tolerability of the test medicine and the impact of food.

Who can participate?
Healthy male and non-pregnant, non-lactating female volunteers aged 18 to 55 years.

What does the study involve?
The study consists of 2 parts. Part 1 consists of 6 study periods and involves up to 30 volunteers split across 2 cohorts, and Part 2 consists of one study period and involves up to 15 volunteers in a single cohort. In Part 1 each cohort will receive up to 6 oral doses of the test medicine as different recipes on 6 separate occasions. The recipes will be at different dose levels and given in the fasted or fed state. There will be a minimum 7-day break between each dose. Volunteers will be discharged on Day 5 at the end of each study period. In Part 2 volunteers will receive single oral doses of a selected test medicine recipe for six consecutive days in the fasted or fed state. Volunteers will be discharged on Day 10. In both parts volunteers will return for a followup visit 7-9 days post final dose. Volunteer's blood and urine will eb taken throughout the study for analysis of the test medicine and for their safety. Volunteers are expected to be involved in this study for approximately 15 weeks from screening to the follow-up visit in Part 1, and approximately 6 weeks in Part 2.

What are the potential benefits and risks of participating?
Participants get no medical benefit from taking part in this study. However, development of a treatment for AP-mediated diseases may benefit the population as a whole. It is considered that the risk/benefit evaluation in this study supports the use of healthy volunteers. Full information

on possible side effects is provided to volunteers in the Participant Information Sheet/Informed Consent Form. Volunteers are closely monitored during the study and safety assessments are performed regularly.

Where is the study run from?
Quotient Sciences Limited (UK)

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

Who is funding the study?
Alexion Pharmaceuticals Inc. (USA)

Who is the main contact?
Raja.veerasingham@alexion.com

Contact information

Type(s)
Principal investigator

Contact name
Dr Sharan Sidhu

Contact details
Quotient Sciences Limited
Mere Way
Ruddington Fields
Ruddington
Nottingham
United Kingdom
NG11 6JS
+44 (0)330 303 1000
recruitment@weneedyou.co.uk

Type(s)
Scientific

Contact name
Dr Raja Veerasingham

Contact details
121 Seaport Boulevard
Boston, Massachusetts
United States of America
MA 02210
+1 (0)585 7343931
Raja.Veerasingham@alexion.com

Type(s)
Public

Contact name
Dr Sharan Sidhu

Contact details
Quotient Sciences Limited
Mere Way
Ruddington Fields
Ruddington
Nottingham
United Kingdom
NG11 6JS
+44 (0)330 303 1000
recruitment@weneedyou.co.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2022-003874-22

Integrated Research Application System (IRAS)
1006989

ClinicalTrials.gov (NCT)
NCT05780645

Protocol serial number
ALXN2050-HV-114, IRAS 1006989, QSC205131

Study information

Scientific Title
A two-part phase 1 study to evaluate the pharmacokinetic profile of ALXN2050 modified release prototype formulations and immediate release reference tablet in healthy adult participants

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

Primary objectives:
Part 1
1.1. To evaluate the PK profile of ALXN2050 following a single dose of ALXN2050 MR prototype formulations in healthy participants.
1.2. To determine the relative BA of ALXN2050 MR prototypes compared with the IR tablet formulation.
Part 2
2.1. To evaluate the PK profile of ALXN2050 following multiple oral dosing of a selected ALXN2050 MR prototype formulation in healthy participants, as data allow.

Secondary objectives:
Part 1

1.1. To determine the safety and tolerability of ALXN2050 following administration of ALXN2050 MR prototypes and the IR tablet formulation.
Part 2
2.1. To assess the safety and tolerability of ALXN2050 following multiple oral dosing of a selected ALXN2050 MR prototype.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 15/03/2023, London Surrey Borders REC (2nd Floor, 2 Redman Place, Stratford, London, E20 1JQ; UK; +44 207 104 8057; surreyborders.rec@hra.nhs.uk), ref 23/LO/0016
2. Submitted 15/03/2023, MHRA (10 South Colonnade, Canary Wharf, London E14 4PU, UK; +44 20 3080 6000; info@mhra.gov.uk), ref - CTA 19553/0277/001-0001

Study design
Interventional single center multi-period open label study to assess PK, safety and tolerability in 45 healthy volunteers

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Complement alternative pathway-mediated diseases

Interventions
Different volunteers will be enrolled in Part 1 and Part 2. In Part 1, up to 30 volunteers will be split into 2 cohorts. Each cohort will receive up to 6 oral doses of the test medicine as different recipes on 6 separate occasions. The recipes will be at different dose levels and given in the fasted or fed state.
Part 2 is optional. Up to 15 volunteers will receive single oral doses of a test medicine recipe (selected based on Part 1 results) for six consecutive days, in the fasted or fed state.

Randomisation will be used in Part 1 to minimise bias in the assignment of participants to cohorts.

The following IMPs to be administered in this study and corresponding starting doses are:
ALXN2050 Film Coated Tablet, 180 mg
ALXN2050 MR Prototype Tablet, starting dose of 250 mg
ALXN2050 MR Prototype Mini-Tablet, starting dose of 250 mg

Future cohort doses are selected based on safety and PK data from previous cohorts.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
ALXN2050 Film Coated Tablet, 60 mg; ALXN2050 MR Prototype Tablet, 50 mg; ALXN2050 MR Prototype Mini-Tablet, 3.33 mg

Primary outcome(s)
Part 1
1.1. PK parameters for ALXN2050 including but not limited to: Cmax, Tmax, C24, Clast, AUC(0-24), AUC(0-last), AUC(0-inf) and T1/2.
1.2. Calculation of the relative bioavailability for Cmax, AUC(0-last) and AUC(0-inf) of the ALXN2050 MR prototype formulations compared with the IR tablet formulation.
Part 2
2.1. PK parameters for ALXN2050 including but not limited to: Cmax, Tmax, Ctrough and AUC(0-tau).

Key secondary outcome(s))
Part 1
1.1. To provide additional safety and tolerability information for ALXN2050 by assessing: incidence of adverse events (AEs), physical examinations and change from baseline for vital signs, electrocardiograms (ECGs), and laboratory safety tests.
Part 2
2.1. To provide additional safety and tolerability information for ALXN2050 by assessing: incidence of AEs, physical examinations and change from baseline for vital signs, ECGs, and laboratory safety tests.

Completion date
04/12/2023

Eligibility

Key inclusion criteria
1. Participant must be 18 to 55 years inclusive at the time of signing the informed consent.
2. Healthy males or non-pregnant, non-lactating healthy females.
3. Participants who are overtly healthy as determined by medical evaluation including medical history, physical or neurological examination, vital signs, 12-lead ECG, screening clinical laboratory profiles (hematology, biochemistry, coagulation, and urinalysis), as deemed by the Investigator or designee.
4. BMI within the range of 18.0 to 30.0 kg/m² (inclusive), with a minimum body weight of 50.0 kg at screening.
5. Female participants of childbearing potential and male participants must follow protocol specified contraception guidance.
6. Capable of giving signed informed consent as described in the clinical protocol which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in the protocol.

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. History of clinically significant respiratory, cardiovascular, dermatological, hepatic, renal, GI, endocrinological, haematological, psychological, psychiatric, or neurological disorders capable of significantly altering the absorption, metabolism, or elimination of drugs;
constituting a risk when taking the study intervention; or interfering with the interpretation of data.
2. History of meningococcal infection.
3. History of clinically significant hypersensitivity reactions to commonly used antibacterial agents, including beta lactams, penicillin, aminopenicillins, fluoroquinolones (specifically including ciprofloxacin), cephalosporins, and carbapenems, which in the opinion of the Investigator would make it difficult to properly provide either empiric antibiotic therapy or treat an active infection.
4. History of clinically significant hypersensitivity or idiosyncratic reaction to the study drugs or related compounds.
5. History of significant multiple and/or severe allergies (eg, drug, latex allergy, band aids, adhesive dressing, or medical tape). Hay fever is allowed unless it is active.
6. History of seizures including childhood seizures.
7. History of significant head injury, or head trauma requiring medical evaluation.
8. History of malignancy within 5 years of screening, with the exception of non-melanoma skin cancer or carcinoma in situ of the cervix that has been treated with no evidence of recurrence.
9. Any previous procedure, including history of stomach or intestinal surgery or resection, cholecystectomy, gallstones, TIPS, or surgical shunt, that could alter absorption or excretion of orally administered drugs.
10. Significant current or chronic history of liver disease.
11. Known hepatic or biliary abnormalities (with the exception of Gilbert's syndrome).
12. Participants who do not have suitable veins for multiple venipunctures/cannulation as assessed by the Investigator or delegate at screening
13. Participants who are taking, or have taken, any prescribed or over-the-counter drug or vitamins/herbal remedies (other than up to 4 g paracetamol per day, hormonal contraception and HRT) in the 14 days before first study intervention administration. COVID-19 vaccines are accepted concomitant medication. Exceptions may apply, as determined by the Investigator.
14. Participants who have taken any CYP or P-gp inhibitors or inducers within 14 days prior to first administration of study intervention.
15. Donation of whole blood or loss of greater than 400 mL of blood from 3 months prior to first dosing, or donation of plasma from 30 days before first dosing.
16. Receipt of blood products within 6 months prior to first dosing.
17. Participants who have received any study intervention (IMP) in a clinical research study within the 90 days, or less than 5 elimination half-lives, whichever is longer, prior to first planned dose.

18. Participants who have taken part in Part 1 are not permitted to take part in Part 2.
19. The following laboratory evaluations at screening, including:
19.1. Serum creatinine > upper limit of normal (ULN)
19.2. Alanine aminotransaminase (ALT) > ULN; Aspartate transaminase (AST) > ULN; Alkaline phosphatase (ALP) > ULN; or Total bilirubin > ULN
19.3. Hemoglobin (Hb) < LLN, white blood cell count < LLN
19.4. Abnormal coagulation profile including, platelet count < LLN, activated partial thromboplastin time > ULN, international normalized ratio > ULN reference range, or prothrombin time > ULN.
20. Evidence of current severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection within 2 weeks of first study intervention administration.
21. Clinically significant abnormal biochemistry, hematology, coagulation or urinalysis as judged by the Investigator
22. Evidence of hepatitis B (positive HBsAg or hepatitis C viral infection (HCV antibody positive) at screening.
23. Evidence of human immunodeficiency virus (HIV 1 and 2 antibody positive) infection at screening.
24. Participants who have a positive highly sensitive pregnancy test at Screening or Day -1.
25. History of any drug or alcohol abuse in the past 2 years.
26. Regular alcohol consumption in males 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).
27. A confirmed positive alcohol breath test at screening or admission.
28. Current smokers and those who have smoked within the last 6 months.
29. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 6 months.
30. A confirmed breath carbon monoxide reading of greater than 10 ppm at screening or admission.
31. Confirmed positive drugs of abuse test result.
32. Any major surgery within 8 weeks of screening.
33. Pregnant, lactating, or intending to conceive during the course of the study.
34. Participants who are, or are immediate family members of, a study site or Alexion employee.
35. Failure to satisfy the Investigator of fitness to participate for any other reason.

Date of first enrolment
15/03/2023

Date of final enrolment
04/12/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences Limited
Mere Way

Ruddington Fields
Ruddington
Nottingham
United Kingdom
NG11 6JS

Sponsor information

Organisation
Alexion Pharmaceuticals (United States)

ROR
https://ror.org/031ywxc85

Funder(s)

Funder type
Industry

Funder Name
Alexion Pharmaceuticals

Alternative Name(s)
Alexion

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

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 nontherapeutic 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
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes