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A three-part study in healthy male and female volunteers to explore how a new recipe of KVD824 is taken up in the body when taken by mouth in the fed or fasted state

Submission date
28/02/2022

Recruitment status
Stopped

Registration date
10/03/2022

Overall study status
Stopped

Last Edited
01/04/2025

Condition category
Genetic Diseases

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
The Sponsor is developing the test medicine, KVD824, for the potential prevention of hereditary angioedema (HAE) attacks. HAE is a disorder defined by recurring incidents of severe swelling. The most common areas of the body to develop swelling are the limbs, face, intestines and airways. This healthy volunteer study is trying to identify how new formulations of the test medicine are taken up by the body and the level of test medicine in the blood following oral dosing. To help investigate this, some of the test medicine is radiolabelled, which means that the test medicine has a radioactive component (indium-111) which helps us to track where the test medicine is in the body. The safety and tolerability of the test medicine are also being studied. The trial may also explore what the test medicine does to the body and the effect of food and the timing of dosing.

Who can participate?
Healthy males or non-pregnant, non-lactating healthy females aged 30 to 55 years inclusive for Part 1 and 18 to 55 years inclusive for Parts 2 and 3.

What does the study involve?
The study consists of 3 parts, two (Parts 1 and 2) consisting of six single-dose study periods with and one (Part 3) consisting of repeat dosing once daily (QD) or twice daily (BID) for 6 days, with a final morning dose on Day 7.
In Parts 1 and 2, volunteers enter the clinical unit on Day 1 (the day before their dose) and are discharged 48 hours after their dose for each period. In Part 1, when radiolabelled test medicine is administered, scintigraphic images will be taken at regular intervals over a 24-hour period after dosing. Volunteers' blood samples are taken throughout for analysis of the test medicine and for their safety. There is a minimum washout of 7 days between each dose. A follow-up phone call takes place 5 to 7 days post final dose. Volunteers are expected to be involved in this study for approximately up to 21 weeks from screening to the follow-up phone call.
In Part 3, volunteers enter the clinical unit on Day 1 (the day before their first dose) and are

discharged 48 hours after their final dose. Volunteers' blood samples are taken throughout the study for analysis of the test medicine, the effect of the test medicine on the body and for their safety. A follow-up phone call takes place 5 to 7 days post final dose. Volunteers are expected to be involved in this study for approximately 7 weeks from screening to the follow-up phone call.

What are the possible risks and benefits of participating?
Participants get no medical benefit from taking part in the study. However, the development of a treatment for hereditary angioedema 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 and Informed Consent Form. Volunteers are closely monitored during the study, and safety assessments are performed regularly.

Where is the study run from?
KalVista Pharmaceuticals Ltd (UK)

When is the study starting and how long is it expected to run for?
April 2022 to October 2022

Who is funding the study?
KalVista Pharmaceuticals Ltd (UK)

Who is the main contact?
clinicalstudies@kalvista.com

Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-006855-33

Integrated Research Application System (IRAS)
1004853

Protocol serial number
Study code: KVD824-104

Study information

Scientific Title
A Phase I, multiple-part, open-label trial to evaluate the pharmacokinetic profile of KVD824 following administration of KVD824 gastro-retentive formulation prototypes in healthy volunteers

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

Primary objectives:
1. To evaluate the pharmacokinetic (PK) profile and relative oral bioavailability of KVD824

following single oral dosing of KVD824 gastro-retentive (GR) prototype tablet formulations and a reference KVD824 modified release (MR) tablet formulation in the fed state (Part 1)
2. To evaluate the in vivo properties of KVD824 GR prototype tablet formulations using scintigraphic methods (Part 1)
3. To evaluate the PK profile and relative oral bioavailability of KVD824 following single oral dosing of selected KVD824 GR prototype tablet formulations in the fed state and/or at a different dosing time or with an alternative meal composition or in the fasted state (Part 2 – optional)
4. To evaluate the PK profile of KVD824 following multiple oral dosing of selected KVD824 GR prototype tablet formulations (Part 3)

Secondary objectives:
1. To provide information on the safety and tolerability of KVD824 GR prototype tablet formulations and a reference KVD824 MR tablet formulation (Part 1)
2. To provide additional information on the safety and tolerability of selected KVD824 GR prototype tablet formulations (Part 2 – optional)
3. To provide additional information on the safety and tolerability of multiple doses of selected KVD824 GR prototype tablet formulations (Part 3)

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 21/03/2022, Fast-Track Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ; fasttrackrec@hra.nhs.uk), ref: 22/FT/0040
2. Approved 21/03/2022 MHRA (10 South Colonnade, Canary Wharf, London E14 4PU; +44 (0) 20 3080 6000; info@mhra.gov.uk), ref: CTA 46326/0007/001-0001

The HRA has approved the deferral of publication of trial details.

Primary study design
Interventional

Study design
Pharmacokinetic and food effect study

Study type(s)
Other

Health condition(s) or problem(s) studied
Hereditary angioedema

Interventions
Each participant receives single oral doses of different KVD824 gastro-retentive (GR) prototype tablet formulations (which may be radiolabelled) in a fed or fasted state, and a reference KVD824 modified release (MR) tablet in the fed state across 6 treatment periods in a sequential manner with a minimum 7-day washout period between each dose (Part 1)

Each participant receives single oral doses of different KVD824 GR prototype tablet formulations in a fed or fasted state across up to 6 treatment periods (Periods 4 to 6 are optional) in a sequential manner with a minimum 7-day washout period between each dose (Part 2 – optional)

Each participant receives either once daily (QD) or twice daily (BID) oral doses of a KVD824 GR prototype tablet formulation in the fed state for 6 days, with a final morning dose on Day 7 (Part 3).

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
KVD824

Primary outcome(s)
1. Measurement of the following PK parameters in plasma: Tlag, Tmax, Cmax, C12, C24, AUC(0-12), AUC(0-24), AUC(0-last), AUC(0-inf), T1/2 and Frels (as appropriate) at multiple timepoints up to 48 hours post-dose (Part 1)
2. A comparison of the in vivo transit and radiolabel release from KVD824 GR prototype tablet formulations by measuring the following scintigraphic parameters: last time in stomach, gastric emptying (GE), small bowel transit, colon arrival (CA), time and location of initial radiolabel release (IRR) and complete radiolabel release (CRR) up to 24 hours post dose (Part 1)
3. Measurement of the following PK parameters in plasma: Tlag, Tmax, Cmax, C12, C24, AUC(0-12), AUC(0-24), AUC(0-last), AUC(0-inf), T1/2 and Frels (as appropriate) at multiple timepoints up to 48 hours post-dose (Part 2 – optional)
4. Measurement of the following PK parameters in plasma: Tmax, Cmax, C12, C24, AUC(0-tau) and T1/2 on Days 1 and 7, and Day 6 evening dose, as appropriate, at multiple timepoints up to 48 hours post-final dose and pre-dose concentrations on each dosing day following multiple dosing (Part 3)

Key secondary outcome(s)
Incidence of adverse events and assessment of safety laboratory tests, vital signs, electrocardiograms and physical examinations from the time of signing the informed consent form up until discharge from the study

Completion date
13/10/2022

Eligibility

Key inclusion criteria
1. Must provide written informed consent
2. Must be willing and able to communicate and participate in the whole trial part
3. Aged 30 to 55 years inclusive for Part 1 and 18 to 55 years inclusive for Parts 2 and 3 at the time of signing informed consent
4. Must agree to adhere to the contraception requirements defined in the Clinical Protocol
5. Healthy males or non-pregnant, non-lactating healthy females. In Part 1, females must be of

non-childbearing potential
6. Body mass index (BMI) of 18.0 to 32.0 kg/m2 as measured at screening
7. Willing to consume a high-fat meal, including pork (high-fat food-effect regimens only)

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
All

Total final enrolment
16

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 of clinically significant cardiovascular, renal, hepatic, dermatological, chronic respiratory or gastrointestinal disease (in Part 1, especially peptic ulceration, GI bleeding, ulcerative colitis, Crohn's Disease or irritable bowel syndrome), neurological or psychiatric disorder, as judged by the investigator
4. Volunteers with a history of cholecystectomy or gallstones (high-fat food-effect regimens only)
5. History of GI surgery (with the exception of appendectomy unless it was performed within the previous 12 months)
6. Part 1 only: Presence of non-removable metal objects such as metal plates, screws, etc, in the abdominal region of the body. Very small metal items (e.g. sterilisation clips, hernia repair staples) are permitted
7. Part 1 only: Acute diarrhoea or constipation in the 7 days before the predicted Day 1. If screening occurs >7 days before Day 1, this criterion will be determined on Day 1. Diarrhoea will be defined as the passage of liquid faeces and/or a stool frequency of greater than 3 times per day. Constipation will be defined as a failure to open the bowels more frequently than every other day
8. Volunteers who do not have suitable veins for multiple venepunctures/cannulation as assessed by the investigator or delegate at screening
9. Evidence of current SARS-CoV-2 infection
10. Clinically significant abnormal clinical chemistry, haematology, coagulation or urinalysis as judged by the investigator. Volunteers with Gilbert's Syndrome are allowed.
11. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human

immunodeficiency virus (HIV) 1 and 2 antibody results
12. Evidence of renal impairment at screening, as indicated by an estimated creatinine clearance (CLcr) of <70 mL/min using the Cockcroft-Gault equation
13. Females who are pregnant or lactating (all female volunteers must have a negative serum pregnancy test at screening and a negative highly sensitive urine pregnancy test at each admission)
14. Volunteers who have received any IMP in a clinical research trial within the 90 days prior to Day 1, or less than 5 elimination half-lives prior to Day 1, whichever is longer
15. Volunteers who have previously been administered IMP in this trial. Volunteers who have taken part in one part of the trial are not permitted to take part in another part of the trial
16. Volunteers who report to have previously received KVD824
17. Part 1 only: radiation exposure, including that from the present trial, 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 trial
18. Part 1 only: volunteers who have been administered IMP in an ADME trial in the last 6 months
19. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood
20. Volunteers 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, HRT or hormonal contraception) in the 14 days before IMP administration. COVID-19 vaccines are accepted concomitant medications. Exceptions may apply, as determined by the investigator, 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 volunteer; and if the use of medication is not considered to interfere with the objectives of the trial
21. History of any drug or alcohol abuse in the past 2 years
22. 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)
23. A confirmed positive alcohol breath test at screening or admission
24. Current smokers and those who have smoked within the last 12 months. A confirmed breath carbon monoxide reading of greater than 10 ppm at screening or admission
25. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months
26. Confirmed positive drugs of abuse test result
27. Male volunteers with pregnant or lactating partners
28. Volunteers who are, or are immediate family members of, a trial site or sponsor employee
29. History of difficulty in swallowing tablets
30. Failure to satisfy the investigator of fitness to participate for any other reason

Date of first enrolment
01/04/2022

Date of final enrolment
12/10/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences Limited
Mere Way, Ruddington Fields
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United Kingdom
NG11 6JS

Sponsor information

Organisation
KalVista Pharmaceuticals Ltd.

Funder(s)

Funder type
Industry

Funder Name
KalVista Pharmaceuticals 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