ISRCTN98539585 https://doi.org/10.1186/ISRCTN98539585

A long-term study to evaluate if KVD900 is safe and effective in treating attacks in patients with hereditary angioedema

Submission date
13/07/2022

Recruitment status
No longer recruiting

Registration date
28/11/2022

Overall study status
Completed

Last Edited
06/06/2025

Condition category
Haematological Disorders

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

Plain English summary of protocol

Background and study aims
Hereditary Angioedema (HAE) is a genetic condition characterised by swelling of tissues. These swellings can occur on any part of the body.
Up to 150 patients (including a minimum of 12 adolescents) with HAE Type I or II are planned to be enrolled in this global trial for KVD900, an oral plasma kallikrein inhibitor which is designed to stop the beginning steps to make more plasma kallikrein, which lowers the amount of blood vessel swelling and helps treat HAE. Patients will treat each attack with a single dose of KVD900. Patients will be permitted to take additional doses of KVD900 if needed, based on the patient's symptoms. This trial is open-label, which means there is no placebo. Participation will last up to 2 years. The primary objective is to assess the safety of long-term administration of KVD900 in adolescent and adult patients with hereditary angioedema type I or II.

Who can participate?
Patients aged 12 years or older with HAE type I or II.

What does the study involve?
Eligible patients 12 years of age or older will undergo an in-clinic screening assessment for trial inclusion. For patients who roll over following participation in the KVD900-301 trial, this visit may be the same visit as the Final Visit in the KVD900-301 trial if the Final Visit in that trial is within 30 days of enrolment in KVD900-302. If the Final Visit of KVD900-301 was >30 days prior to rollover, the patient must complete a separate Enrolment Visit.
Participants will be asked to attend in-clinic and televisits. Trial procedures will include physical examinations, vital signs, an electrocardiogram, blood samples, completion of e-diary and questionnaires. Use of KVD900 as a short-term prophylactic will be allowed on a case-by-case basis.
There is an optional pharmacokinetic sub-trial in adolescents (ages 12-17), requiring the collection of three blood samples within the first six hours that follow the HAE attack that has been treated with the trial drug.

What are the possible benefits and risks of participating?
Benefits:
Taking part in this study may or may not help to treat HAE. Participants' health could improve, stay the same, or get worse. However, the data we get during this study may help doctors learn more about the study drug and the disease and this may help future patients with HAE.
Risks:
KalVista is still building its knowledge about the safety of KVD900. The study drug has so far only been used in small groups of healthy people and patients with HAE, therefore, some side effects are not yet known. The most common side effect experienced to date has been headache.

Where is the study run from?
Barts Health NHS Trust
Leeds Teaching Hospitals NHS Trust
Frimley Health NHS Trust
University Hospitals Birmingham NHS Foundation Trust
Cardiff and Vale University Health Board
Cambridge University Hospitals NHS Foundation Trust
Royal Free London NHS Foundation Trust

When is the study starting and how long is it expected to run for?
August 2022 to June 2026

Who is funding the study?
KalVista Pharmaceuticals (UK)

Who is the main contact?
Dr Sorena Kiani-Alikhan, skiani@nhs.net

Contact information

Type(s)
Scientific

Contact name
Mr Michael Smith

Contact details
KalVista Pharmaceutical Ltd
Porton Science Park
Bybrook Road
Porton Down
Salisbury
United Kingdom
SP4 0BF
+18018597818
mds@kalvista.com

Type(s)
Principal investigator

Contact name
Dr Sorena Kiani-Alikhan

Contact details
The Royal Free London NHS Foundation Trust
The Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG
+44 20 32460264
skiani@nhs.net

Additional identifiers

ClinicalTrials.gov (NCT)
NCT05505916

Clinical Trials Information System (CTIS)
EU-CT-2023-505904-41-00

Integrated Research Application System (IRAS)
1004964

Central Portfolio Management System (CPMS)
51714

Protocol serial number
KVD900-302

Study information

Scientific Title
An open-label extension trial to evaluate the long-term safety of KVD900, an oral plasma kallikrein inhibitor, for on-demand treatment of angioedema attacks in adolescent and adult patients with hereditary angioedema type I or II

Acronym
KONFIDENT-S

Study objectives
Primary objective:
To assess the safety of long-term administration of KVD900 in adolescent and adult patients with HAE type I or II.

Secondary objectives:
1. To assess the long-term efficacy of KVD900 in the treatment of attacks in adolescent and adult patients with HAE type I or II.
2. To assess the safety and efficacy of KVD900 when used as short-term prophylaxis in adolescent and adult patients with HAE types I or II.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 27/09/2022, Health and Social Care Research Ethics Committee B (HSC REC B, Office for Research Ethics Committee Northern Ireland (ORECNI), Business Services Organisation, Lissue Industrial Estate West, 5 Rathdown Walk, Moira Road, Lisburn, BT28 2RF, UK; +44 (0)28 9536 1400; info.orecni@hscni.net),ref: 22/NI/0124

Primary study design
Interventional

Study design
Interventional non randomized

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Hereditary Angioedema Type I or II

Interventions
Current interventions as of 06/06/2025:
This is an open-label extension and all patients will be receiving active drug for on-demand treatment of HAE attacks. For on-demand treatment of HAE attacks, patients will treat each attack with a single dose of KVD900. Patients will be permitted to take additional doses of KVD900 if needed, based on the patient's symptoms. Use of KVD900 as a short-term prophylactic will be allowed on a case-by-case basis.

Previous interventions:
This is an open-label extension and all patients will be receiving active drug for on-demand treatment of HAE attacks. For on-demand treatment of HAE attacks, patients will take a single dose of 600 mg KVD900 (i.e. 2 x 300 mg tablets) to treat each HAE attack. Patients will be permitted to take a second dose of 600 mg KVD900 separated by at least 3 hours following the first dose if attack symptoms persist without improvement. Use of KVD900 as a short-term prophylactic will be allowed on a case-by-case basis.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
KVD900 (sebetralstat)

Primary outcome(s)
Current primary outcome measure as of 02/04/2024:
1. Frequencies and percentages of patients with AEs, AEs within 2 days of IMP administration, serious AEs, and AEs causing premature discontinuation

2. Number and percentage of patients with normal or abnormal laboratory results at each scheduled visit
3. Number and percentage of patients with normal or abnormal vital sign results at each scheduled visit

Previous primary outcome measure:
The proportion of patients with at least one AE in adolescent and adult patients with HAE type I or II who have taken at least one dose of IMP, assessed throughout the trial.

Key secondary outcome(s)
1. PGI-C: HAE attacks with symptom relief defined as at least '' a little better'' (2 time points in a row) within 12 hours of initial dose of IMP administration.
2. PGI-S: HAE attacks with any decrease from baseline within 12 hours of initial dose of IMP administration.
3. PGI-S: HAE attacks that resolved, defined as ''none'' within 24 hours of initial dose of IMP administration.

Completion date
30/06/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 02/04/2024:
Rollover Patients:
1R. Randomized in the KVD900-301 trial.

Non-Rollover Patients:
1NR) Confirmed diagnosis of HAE type I or II at any time in the medical history:
a) Documented clinical history consistent with HAE (sc or mucosal, nonpruritic swelling episodes without accompanying urticaria) AND EITHER
i) Diagnostic testing results obtained prior to randomization that confirms HAE type I or II: C1-INH functional level <40% of the normal level. Patients with functional C1-INH level 40-50% of the normal level may be enrolled if they also have a C4 level below the normal range. Testing may be obtained from central or local laboratories or obtained from documented historical testing results. Patients may be retested at any time prior to randomization if results are incongruent with clinical history or believed by the Investigator to be confounded by recent prophylactic or therapeutic C1-INH use, OR
ii) Documented genetic results that confirm known mutations for HAE type I or II.
2NR) Patient has had at least 2 documented HAE attacks within 3 months prior to the Enrollment Visit.
3NR) If a patient is receiving long-term prophylactic treatment with one of the protocol-allowed therapies, they must have been on a stable dose and regimen for at least 3 months prior to the Enrollment Visit.

All Patients (AP):
1AP) Male or female patients 12 years of age and older.
2AP) Patients must meet one of the following contraception requirements as follows:
a) Female patients who are fertile and heterosexually active must agree to use contraception from the Enrollment Visit until the EOS or Early Termination (ET) Visit. Acceptable methods of contraception include one or more of the following:

i) Progestogen-only hormonal contraception associated with inhibition of ovulation: oral /injectable/implantable (hormonal contraception that contains estrogen including ethinylestradiol is excluded per Exclusion Criterion 5NR.
ii) Intrauterine device.
iii) Intrauterine hormone–releasing system. iv) Bilateral tubal occlusion.
v) Vasectomized partner (provided that the partner is the sole heterosexual partner of the female patient of childbearing potential and that the vasectomized partner has received a medical assessment of surgical success).
vi) Male or female condom.
vii) Cap, diaphragm, or sponge with spermicide.
b) Patients who are not fertile or not heterosexually active, as defined below, do not require contraception. If the patient's status changes during the course of the trial, they will be required to meet the requirements specified in Inclusion Criterion 2AP.
i) Female patients who refrain from heterosexual intercourse during the trial if the reliability of the heterosexual abstinence has been evaluated in relation to the duration of the clinical trial and is the preferred and usual lifestyle of the patient.
ii) Female patients who are surgically sterile (e.g. status post hysterectomy, bilateral oophorectomy, or bilateral tubal ligation) or post-menopausal for at least 12 months.
iii) Female patients who are premenarche.
c) Male patients (including female partners) do not require contraception.
3AP) Patients must be able to swallow trial tablets whole.
4AP) Patients, as assessed by the Investigator, must be able to appropriately receive and store IMP, and be able to read, understand, and complete the eDiary.
5AP) Investigator believes that the patient is willing and able to adhere to all protocol requirements.
6AP) Patient provides signed informed consent or assent (when applicable). A parent or LAR must also provide signed informed consent when required.

Previous inclusion criteria:
Patients may roll over from KVD900-301.
1. Confirmed diagnosis of HAE type I or II at any time in the medical history
2. Patient has had at least 2 documented HAE attacks within 3 months prior to the Enrollment Visit.
3. If a patient is receiving long-term prophylactic treatment with one of the protocol-allowed therapies, they must have been on a stable dose and regimen for at least 6 months prior to the Enrollment Visit.
4. Male or female patients 12 years of age and older.
5. Patients must meet the contraception requirements.
6. Patients must be able to swallow trial tablets whole.
7. Patients, as assessed by the Investigator, must be able to appropriately receive and store IMP, and be able to read, understand, and complete the eDiary.
8. Investigator believes that the patient is willing and able to adhere to all protocol requirements.
9. Patient provides signed informed consent or assent (when applicable). A parent or LAR must also provide signed informed consent when required.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
12 Years

Sex
All

Total final enrolment
145

Key exclusion criteria
Current exclusion criteria as of 02/04/2024:
Rollover Patients:
1R) Discontinued from the KVD900-301 trial for reasons of non-compliance, withdrawal of consent, or safety.
2R) Presence of any safety concerns that would preclude participation in the open-label trial as determined by the investigator.

Non-Rollover Patients:
1NR) Any concomitant diagnosis of another form of chronic angioedema, such as acquired C1-inhibitor deficiency, HAE with normal C1-INH (previously known as HAE type III), idiopathic angioedema, or angioedema associated with urticaria.
2NR) A clinically significant history of poor response to bradykinin receptor 2 (BR2) blocker, C1-INH therapy or plasma kallikrein inhibitor therapy for the management of HAE, in the opinion of the Investigator.
3NR) Use of attenuated androgens (e.g. stanozolol, danazol, oxandrolone, methyltestosterone, testosterone), or anti-fibrinolytics (e.g. tranexamic acid) within 28 days prior to the Enrollment Visit.
4NR) Use of angiotensin-converting enzyme (ACE) inhibitors within 7 days prior to the Enrollment Visit.
5NR) Any estrogen-containing medications with systemic absorption (such as oral contraceptives including ethinylestradiol or hormonal replacement therapy) within 7 days prior to the Enrollment Visit.
6NR) Inadequate organ function, including but not limited to:
a) Alanine aminotransferase (ALT) >2x ULN
b) Aspartate aminotransferase (AST) >2x ULN
c) Bilirubin direct >1.25x ULN
d) International normalized ratio (INR) >1.2
e) Clinically significant hepatic impairment defined as a Child-Pugh B or C
7NR) Any clinically significant comorbidity or systemic dysfunction, which in the opinion of the Investigator, would jeopardize the safety of the patient by participating in the trial.
8NR) History of substance abuse or dependence that would interfere with the completion of the trial, as determined by the Investigator.
9NR) Known hypersensitivity to KVD900 or to any of the excipients.
10NR) Participation in any gene therapy treatment or trial for HAE.
11NR) Participation in any interventional investigational clinical trial, including an investigational COVID-19 vaccine trial, within 4 weeks of the last dosing of the investigational drug prior to the Enrollment Visit.
12NR) Any pregnant or breastfeeding patient.

Previous exclusion criteria:
1. Discontinued from the KVD900-301 trial for reasons of non-compliance, withdrawal of consent, or safety.
2. Presence of any safety concerns that would preclude participation in the open-label trial as determined by the investigator.
3. Any concomitant diagnosis of another form of chronic angioedema, such as acquired C1 inhibitor deficiency, HAE with normal C1-INH (previously known as HAE type III), idiopathic angioedema, or angioedema associated with urticaria.
4. A clinically significant history of poor response to bradykinin receptor 2 (BR2) blocker, C1-INH therapy, or plasma kallikrein inhibitor therapy for the management of HAE, in the opinion of the Investigator.
5. Use of attenuated androgens (e.g., stanozolol, danazol, oxandrolone, methyltestosterone, testosterone), or anti-fibrinolytics (e.g., tranexamic acid) within 28 days prior to the Enrollment Visit.
6. Use of ACE inhibitors within 7 days prior to the Enrollment Visit.
7. Any estrogen-containing medications with systemic absorption (such as oral contraceptives including ethinylestradiol or hormonal replacement therapy) within 7 days prior to the Enrollment Visit.
8. Inadequate organ function, including but not limited to:
8.1. Alanine aminotransferase (ALT) >2x ULN
8.2. Aspartate aminotransferase (AST) >2x ULN
8.3. Bilirubin direct >1.25x ULN
8.4. INR >1.2
8.5. Clinically significant hepatic impairment defined as a Child-Pugh B or C
9. Any clinically significant comorbidity or systemic dysfunction, which in the opinion of the Investigator, would jeopardize the safety of the patient by participating in the trial.
10. History of substance abuse or dependence that would interfere with the completion of the trial, as determined by the Investigator.
11. Known hypersensitivity to KVD900 or to any of the excipients.
12. Participation in any gene therapy treatment or trial for HAE.
13. Participation in any interventional investigational clinical trial, including an investigational COVID-19 vaccine trial, within 4 weeks of the last dosing of investigational drug prior to the Enrollment Visit.
14. Any pregnant or breastfeeding patient.

Date of first enrolment
24/10/2022

Date of final enrolment
12/06/2024

Locations

Countries of recruitment
United Kingdom

England

Wales

Australia

Austria

Bulgaria

Canada

France

Germany

Greece

Hungary

Israel

Italy

Japan

Netherlands

New Zealand

Poland

Portugal

Romania

Saudi Arabia

Slovakia

South Africa

Spain

United States of America

Study participating centre

Barts Health NHS Trust
The Royal London Hospital
Whitechapel Road
Whitechapel
London
United Kingdom
E1 1BB

Study participating centre
Frimley Park Hospital
Frimley Health NHS Trust
Portsmouth Road
Frimley
Camberley
United Kingdom
GU16 7UJ

Study participating centre
Leeds Teaching Hospital NHS Trust
St James's University Hospital
Gledow Wing
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
Birmingham Heartlands Hospital
University Hospitals Birmingham NHS Foundation Trust
Bordesley Green East
Bordesley Green
Birmingham
United Kingdom
B9 5SS

Study participating centre
Cardiff and Vale University Health Board
University Hospital of Wales
Heath Park
Cardiff
United Kingdom
CF14 4XW

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Addenbrooke’s Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Royal Free London NHS Foundation Trust
The Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG

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
Current IPD sharing statement as of 01/03/2023:
The datasets generated during and/or analysed during the current study are not expected to be made available due to the stage of development (i.e., pre-marketing authorization) and to ensure the protection of IPD. Due to the rarity of the disease, it may be possible to link anonymized patient data back to individual patients. Therefore, only aggregate data will be shared through regular publicly available methods (e.g., clinicaltrial.gov, euclinicaltrials.eu, scientific publications).

Previous IPD sharing statement:
The current data sharing plans for this study are unknown and will be available at a later date

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