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Longwing: An extension study for patients with Dravet syndrome, a severe form of epilepsy, who previously participated in studies of STK-001 in the United Kingdom

Submission date
16/06/2022

Recruitment status
No longer recruiting

Registration date
28/06/2022

Overall study status
Ongoing

Last Edited
01/08/2023

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and Study aims
Dravet syndrome (DS) is a rare form of epilepsy that begins in the first year of a child's life and has a poor long-term prognosis. DS is among the most drug-resistant forms of epilepsy, with more than 90% of patients continuing to have uncontrolled seizures despite treatment with multiple antiepileptic drugs, as well as many other significant symptoms such as cognitive, mood, sleep, and movement problems. DS is most commonly caused by a mutation in a gene, called SCN1A, which usually leads to the SCN1A protein not functioning as well as normal.

This extension study will continue research into a new investigational drug, called STK-001, which is intended to increase the levels of SCN1A from the normal gene, to find out how safe it is and how it is tolerated when given at different increasing doses in children and adolescents with DS.

Who can participate?
Patients aged 2.5 years old and over with a diagnosis of Dravet syndrome who have previously participated in a Stoke Therapeutics' study of STK-001.

What does the study involve?
It is expected that patients enrolled in the main study, STK-001-DS-102 (ADMIRAL) will roll over without interruption to this extension study. In the event that a patient does not roll over immediately, the patient still has the option to enroll in this study within 4 weeks of their End of Study Visit from Study STK-001-DS-102.

The duration of the study for each patient is up to 15 months or, for patients tolerating treatment, the study duration will continue with treatment every 4 months (16 weeks), until the end of the study, or unacceptable toxicity, withdrawal of consent, or Investigator/Sponsor

decision, whichever comes first. Dosing beyond the initial dose on Day 1 will not occur until after MHRA provides approval for this study to proceed with the 2nd and consecutive doses of STK-001.

Patients will receive intrathecal administration (injection into the spinal canal) of study drug STK-001 at the dose level they received while participating in Study STK-001-DS-102, or at a dose level recommended by the Safety Monitoring Committee.

After completion of treatment, patients will enter a 24-week Follow-up Period for safety monitoring that consists of a non-clinic telephone visit by either the Principal Investigator (PI) or a Sub-Investigator (Sub-I).

What are the possible benefits and risks of participating?
There is no guarantee that participants will receive medical benefits from taking part in this study. However, the information from this study may help better treat children with Dravet syndrome in the future. It is possible that the participants will not improve during the study or may even worsen. Treatment with this study drug may also involve risks to the participant's future health that are currently unknown.

Where is the study run from?
Stoke Therapeutics (USA)

When is the study starting and how long is it expected to run for?
October 2021 to November 2027

Who is funding the study?
Stoke Therapeutics (USA)

Who is the main contact?
Stoke Therapeutics General Mailbox, clinicaltrials@stoketherapeutics.com

Contact information

Type(s)
Public

Contact name
Dr Stoke Therapeutics General Mailbox

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45 Wiggins Ave
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Type(s)
Scientific

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Principal Investigator

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Additional identifiers

EudraCT/CTIS number
2021-005626-14

IRAS number
1004380

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
STK-001-DS-502, IRAS 1004380, CPMS CHIL 51531

Study information

Scientific Title
Longwing: An open-label extension study for patients with Dravet syndrome who previously participated in studies of STK-001

Acronym
Longwing

Study objectives
Administration of multiple doses of STK-001 is safe and well tolerated in patients with DS ages 2.5 years and older

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved: 26/04/2022, Scotland A Research Ethics Committee (Research Ethics Service, 2nd Floor, Waverley Gate, 2-4 Waterloo Place, Edinburgh, EH1 3EG, Scotland; +44 (0)131 465 5680; ruth.fraser4@nhslothian.scot.nhs.uk), Ref: 22/SS/0005

Study design
Multicentre interventional open-label extension long-term safety tolerability study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Dravet syndrome (participants ≥2.5 years of age)

Interventions
Current intervention as of 01/08/2023:
Participants who have completed the ADMIRAL (STK-001-DS-102) study will have the possibility of rolling over on to the Longwing (STK-001-DS-502) extension study. This rollover can be completed on the same day as the End of Study visit for the ADMIRAL study or up to 4 weeks after.

1. Treatment Period
Patients who meet the eligibility criteria will undergo pre-dose evaluations and will receive doses of STK-001 every 4 months as follows:
1.1. An initial dose on Day 1 after their transition from the ADMIRAL Study (STK-001-DS-102)
1.2. Doses 2 and 3 on Weeks 16 and 32, respectively, which may occur only after MHRA provides approval for patients in this study to proceed with their 2nd and 3rd doses of STK-001. Note: MHRA provided approval for patients in this study to proceed with their 2nd, 3rd and additional doses of STK-001.
1.3. Patients who are tolerating treatment may then continue with doses every 4 months with an End of Study/Follow-up Visit 24 weeks after the last dose of study drug. Patients who do not

continue treatment after Dose 3 will have a follow-up Visit (V5) at Week 48 and an End of Study Visit at Week 56.

Patients will receive intrathecal (IT) administration of study drug STK-001 at the dose level they received while participating in Study STK-001-DS-102, or at a dose level recommended by the Safety Monitoring Committee. The highest dose administered may not exceed that evaluated previously in the ADMIRAL (STK-001-DS-102) study or approved for Longwing (STK-002-DS-502).

In addition to study visits, the study centre will monitor the patient's condition through telephone contacts after each study drug administration. During this time, information on seizures will be collected by paper diary.

2. Follow-up Period
After completion of treatment, patients will enter a 24-week Follow-up Period for safety monitoring that consists of a non-clinic telephone visit and an Onsite End of Study Visit.

3. Duration of Participation
The duration of the study for each patient is up to 15 months or, for patients tolerating treatment, study duration will continue with treatment every 4 months (16 weeks), until the end of the study, or unacceptable toxicity, withdrawal of consent, or Investigator/Sponsor decision, whichever comes first. Dosing beyond the initial dose on Day 1 will not occur until after MHRA provides approval for this study to proceed with the 2nd and consecutive doses of STK-001.
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Previous intervention:
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Patients will receive intrathecal (IT) administration of study drug STK-001 at the dose level they received while participating in Study STK-001-DS-102, or at a dose level recommended by the Safety Monitoring Committee. The highest dose administered may not exceed that evaluated previously in the ADMIRAL (STK-001-DS-102) study.

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Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
STK-001

Primary outcome measure
Current primary outcome measures as of 01/08/2023:
1. Safety and tolerability of multiple doses of STK-001 from screening (day-1) until 6 months after multiple drug dosing, based on:
1.1. Incidence, type, severity, and seriousness of adverse events (AEs) measured by review of all reported events for all participants
1.2. Incidence of abnormal vital signs (including body temperature, heart rate, systolic and diastolic blood pressure, and respiratory rate) measured using standard methods such as thermometer and blood pressure cuff
1.3. Incidence of abnormal 12-lead electrocardiogram (ECG) findings (including PR, QRS, and QT intervals) measured using 12-lead electrocardiograms
1.4. Incidence of abnormal laboratory parameters (including haematology, coagulation, clinical chemistry and urine tests) measured using validated assays of blood and urine samples
1.5. Incidence of immunogenicity (anti-drug antibodies) measured using a validated assay in serum
1.6. Percent change from baseline in locomotor skill ability assessed using the Gillette Functional Assessment Questionnaire (FAQ) total score

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1. Safety and tolerability of multiple doses of STK-001 from screening (day-1) until 6 months after multiple drug dosing, based on:
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1.2. Incidence of abnormal vital signs (including body temperature, heart rate, systolic and diastolic blood pressure, and respiratory rate) measured using standard methods such as thermometer and blood pressure cuff
1.3. Incidence of abnormal 12-lead electrocardiogram (ECG) findings (including PR, QRS, and QT intervals) measured using 12-lead electrocardiograms
1.4. Incidence of abnormal laboratory parameters (including haematology, coagulation, clinical chemistry and urine tests) measured using validated assays of blood and urine samples

1.5. Incidence of immunogenicity (anti-drug antibodies) measured using a validated assay in serum

Secondary outcome measures
1. Pharmacokinetic (PK) parameters measured by analysis of plasma concentrations of STK-001 using hybridization ELISA from day 1 (dosing) until 6 months after multiple drug dosing
2. Exposure of STK-001 in cerebrospinal fluid (CSF) by measurement of STK-001 concentrations using hybridization ELISA from day 1 (dosing) until the last study drug dosing day
3. Seizure frequency measured using a paper diary from screening (day -1) until 6 months after multiple drug dosing
4. Overall clinical status as measured by the Clinician-assessed Global Impression of Change Scale from baseline (day -1) until 6 months after multiple drug dosing
5. Quality-of-life measured by EuroQoL-five dimensions, youth version (EQ-5D-Y) from baseline (day -1) until 6 months after multiple drug dosing

Overall study start date
15/10/2021

Completion date
22/11/2027

Eligibility

Key inclusion criteria
1. Completed dosing with STK-001 and the End of Study Visit in Study STK 001-DS-102, with an acceptable safety profile per the Investigator's judgment
2. Satisfactory compliance with study visits and procedures in Study STK 001-DS-102 per Investigator and Sponsor judgment
3. Completed Study STK-001-DS-102 within 4 weeks of the start of their participation in Study STK-001-DS-502, unless approved by the Sponsor

Participant type(s)
Patient

Age group
Child

Sex
Both

Target number of participants
Up to ~60

Key exclusion criteria
1. Met any withdrawal criteria from Study STK-001-DS-102
2. Current treatment as maintenance therapy with an antiepileptic drug acting primarily as a sodium channel blocker including phenytoin, carbamazepine, oxcarbazepine, lamotrigine, lacosamide, or rufinamide
3. Clinically significant unstable medical conditions other than epilepsy
4. Clinically relevant symptoms or a clinically significant illness (in the judgment of the

Investigator) in the 4 weeks prior to Screening/Baseline of Study STK-001-DS-502, other than epilepsy
5. Spinal deformity or other condition that may alter the free flow of CSF or has an implanted CSF drainage shunt
6. Prior treatment (or is being treated) with an investigational product (other than STK-001) since participating in Study STK 001 DS-102
7. Participating in an observational study

Date of first enrolment
09/05/2022

Date of final enrolment
08/11/2023

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
Great Ormond Street Hospital for Children
Great Ormond Street
London
United Kingdom
WC1N 3JH

Study participating centre
Sheffield Children's Hospital
Western Bank
Sheffield
United Kingdom
S10 2TH

Study participating centre
Royal Hospital For Children
1345 Govan Road
Glasgow
United Kingdom
G51 4TF

Sponsor information

Organisation
Stoke Therapeutics, Inc

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clinicaltrials@stoketherapeutics.com

Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Stoke Therapeutics, Inc

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
22/11/2028

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			26/07/2023	No	No