ISRCTN99651026 https://doi.org/10.1186/ISRCTN99651026

Admiral: a study of the safety of multiple increasing doses of STK-001 in children and adolescents with Dravet syndrome

Submission date
29/07/2021

Recruitment status
No longer recruiting

Registration date
02/09/2021

Overall study status
Completed

Last Edited
19/05/2025

Condition category
Nervous System Diseases

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

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 study will look at 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 between the ages of 2 years and less than 18 years with a diagnosis of Dravet syndrome.

What does the study involve?
The study will consist of a screening visit, which will be followed by an observation period of about 4 weeks (but can last up to 12 weeks). During this observation period, caregivers will be asked to track their child's seizure frequency and sleep. At the end of this month, the patients and caregivers will be required to visit the clinic for a series of baseline tests to confirm if the patient meets the enrolment criteria.
Patients who meet the enrolment criteria will be enrolled in the study and will be required to attend the study centre for three dosing visits to receive the study drug on Day 1, Day 57 and Day 85. The patient will also attend follow-up visits at the study centre (seven visits) and by telephone (six visits) which will take place between doses and in the follow-up period after all three doses have been given.

What are the possible benefits and risks of participating?
There is no guarantee that participants will receive a medical benefit from taking part in this study. However, the information from this study may help to better treat children with Dravet syndrome in the future. It is possible that the participant's condition 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 is currently unknown.

Where is the study run from?
IQVIA Limited, a contract research organisation in collaboration with Stoke Therapeutics (USA)

When is the study starting and how long is it expected to run for?
January 2021 to November 2023

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

Contact details
Stoke Therapeutics
139 Main St., 4th Floor
Cambridge
United States of America
02412
+1 (0)781 430 8200
clinicaltrials@stoketherapeutics.com

Type(s)
Scientific

Contact name
Dr Stoke Therapeutics General Mailbox

Contact details
Stoke Therapeutics
139 Main St., 4th Floor
Cambridge
United States of America
02412
+1 (0)781 430 8200
clinicaltrials@stoketherapeutics.com

Additional identifiers

Clinical Trials Information System (CTIS)

2020-006016-24

Integrated Research Application System (IRAS)
295734

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 295734, CPMS CHIL 48507

Study information

Scientific Title
An open-label study to investigate the safety and pharmacokinetics of multiple ascending doses of antisense oligonucleotide STK-001 in children and adolescents with Dravet syndrome

Acronym
STK-001-DS-102 (ADMIRAL)

Study objectives
Administration of multiple ascending doses of STK-001 is safe and well-tolerated in patients with Dravet syndrome between the ages of 2 and <18 years

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 03/06/2021, Wales REC 3 (Health and Care Research Wales Support Centre, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, UK; +44 (0)1874 615950, +44 (0) 2920 230457; Wales.REC3@wales.nhs.uk), REC ref: 21/WA/0107

Study design
Phase I/IIa multicentre interventional open-label study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Dravet syndrome

Interventions
This study is a Phase I/IIa open-label study consisting of three dose cohorts (cohorts 1, 2 and 3) with the option to include two additional cohorts. The proposed dosing levels for the cohorts are 30 mg, 45 mg and 70 mg per drug administration but are subject to change based on safety review, additional preclinical and/or clinical data or regulatory authorities' recommendation. The study will have the following main periods:

1. Screening and observation period (about 4 weeks, but can last up to 12 weeks)
2. Baseline visit
3. Treatment period (about 12 weeks or 3 months)
4. Follow-up period (about 24 weeks or 6 months)

During the observation period, patients will be sent home for one month with no change to their current antiepileptic drugs, ketogenic diet, or vagal nerve stimulator settings. Caregivers will be asked to track their child's seizure frequency and sleep during this month.

At the baseline visit, the patient and their caregivers will be required to visit the study clinic for a series of baseline tests including: blood and urine analyses, ECG, EEG and a series of questionnaires about the patient. The investigator will assess the data collected during the observation period to confirm that the patient meets the enrolment criteria.

Patients who meet the criteria will be enrolled and assigned a cohort. The assigned cohort dose level of the study drug will be administered via intrathecal injection (into the spinal canal) on 3 separate dosing days throughout the study with follow-up clinic and telephone visits between each dose to perform safety assessments and monitor adverse events.

A safety monitoring committee (SMC) will be established to review safety and PK data and to oversee the overall conduct of the study with the primary purpose of protecting the safety of the study participants. The SMC will meet several times throughout the course of the study to review the data and to recommend acceptability of continued dosing, and/or dose escalation to subsequent cohorts, and/or the need for optional cohorts or additional patients in the current cohort.

Up to 60 participants are anticipated to be enrolled in approximately 5-7 centres across the UK. Duration of participation is expected to last 40 weeks. If the observation period is extended, the duration could be up to 48 weeks

Intervention Type
Drug

Phase
Phase I/II

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

Primary outcome(s)
1. Safety and tolerability of multiple doses of STK-001 from screening (day -28) until 6 months after multiple drug dosing, measured using:
1.1. Incidence of adverse events
1.2. Incidence of abnormal vital signs
1.3. Abnormal physical examination findings
1.4. Abnormal 12-lead electrocardiogram (ECG)
1.5. Abnormal laboratory parameters
2. 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
3. Exposure of STK-001 in cerebrospinal fluid (CSF) by measurement of STK-001 concentrations using hybridization ELISA from day 1 (dosing) until 6 months after multiple drug dosing

Key secondary outcome(s))
1. Seizure frequency measured using a paper diary from screening (day -28) until 6 months after multiple drug dosing
2. Overall clinical status measured by the Caregiver Global Impression of Change Scale from baseline (day -1) until 6 months after multiple drug dosing
3. 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
4. Quality of life measured by EuroQoL-five dimensions, youth version (EQ-5D-Y) from baseline (day -1) until 6 months after multiple drug dosing

Completion date
07/11/2023

Eligibility

Key inclusion criteria
1. Patient must be between 2 and <18 years of age at Screening
2. Diagnosis of Dravet Syndrome (DS) with onset of recurrent focal motor or hemiconvulsive or generalized tonic-clonic seizures prior to 12 months of age, which are often prolonged and triggered by hyperthermia
2.1. No history of causal MRI lesion
2.2. No other known aetiology
2.3. Normal development at seizure onset
3. Documented pathogenic, likely pathogenic variant, or variant of uncertain significance in the SCN1A gene associated with DS
4. Use of at least two prior treatments for epilepsy that either had lack of adequate seizure control (requiring an additional antiepileptic drug [AED] or had to be discontinued due to an adverse event [AE])
5. Currently taking at least one AED at a dose which has been stable for at least 4 weeks prior to Screening
6. Stable epilepsy medications or interventions for epilepsy (including ketogenic diet or vagal nerve stimulator) for at least 4 weeks prior to Screening

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
2 years

Upper age limit
17 years

Sex
All

Total final enrolment
19

Key exclusion criteria
1. Known pathogenic mutation in another gene that causes epilepsy
2. Currently treated with an AED acting primarily as a sodium channel blocker, as maintenance treatment, 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 4 weeks prior to Screening or prior to dosing on Day 1, other than epilepsy
5. History of brain or spinal cord disease (other than epilepsy or DS), or history of bacterial meningitis or brain malformation
6. Spinal deformity or other condition that may alter the free flow of cerebrospinal fluid (CSF) or has an implanted CSF drainage shunt
7. Any other significant disease or disorder which, in the opinion of the Investigator, may either put the patient at risk because of participation in the study, may influence the results of the study, or may affect the patient's ability to participate in the study

Date of first enrolment
29/07/2021

Date of final enrolment
28/02/2023

Locations

Countries of recruitment
United Kingdom

England

Scotland

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

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

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

Study participating centre
Evelina Childrens Hospital
Westminster Bridge Rd
London
United Kingdom
SE1 7EH

Sponsor information

Organisation
Stoke Therapeutics, Inc

Funder(s)

Funder type
Industry

Funder Name
Stoke Therapeutics Inc.

Results and Publications

Individual participant data (IPD) sharing plan
Final data will be published as summary data at the end of the study; participant-level data will be held in a secure database until study close-out.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results	version 24	07/11/2024	11/11/2024	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes