ISRCTN41725621 https://doi.org/10.1186/ISRCTN41725621

A study to investigate the safety, tolerability, and exposure of single doses of the study medicine STK-002, in patients with autosomal dominant optic atrophy (ADOA)

Submission date
14/01/2023

Recruitment status
Recruiting

Registration date
21/08/2023

Overall study status
Ongoing

Last Edited
10/07/2026

Condition category
Eye Diseases

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

Plain English summary of protocol

Background and study aims
Autosomal dominant optic atrophy (ADOA) is a genetic disease characterised by progressive loss of vision as a result of the breakdown of cells within the retina of the eye. Signs of this degeneration typically begins within the first decade of life, with symptoms generally emerging between the ages of 4 and 6. Between 65 to 90% of ADOA cases are caused by a mutation to the gene OPA1 leading to a reduction in the levels of functional OPA1 protein. This protein is critically involved in the maintenance of retinal mitochondria (small structures found within the retinal cells). Patients may experience a decrease in sharp vision, blurred vision, reduced contrast and abnormal color vision, that cannot be corrected with glasses. From early childhood, patients experience a worsening of the central part of the vision that allows for proper seeing of small letters and reading. So far there is no treatment available that stops or cures the disease. Study STK-002-OA-101 is an early phase study to investigate the safety, tolerability and exposure of single ascending doses of STK-002 (the study drug) in patients with ADOA. STK-002 is an antisense oligonucleotide, a short chain of nucleotides (the basic building block of nucleic acids, like RNA) designed to increase the levels of functioning OPA1 protein in the eye, thereby halting or slowing the progression of the disease leading to an improved quality of life.

Who can participate?
Patients aged ≥6 to <55 years old with ADOA

What does the study involve?
The study will be split into two parts. Part A will assess how safe STK-002 is for participants aged ≥18 to <55 years. Once data from Part A are reviewed, they will be used to determine the dosage of STK-002 in Part B of the study, which will enrol participants ages ≥6 to <18. Participants will receive one dose of the study drug in an affected eye. The study will last approximately 48 weeks with multiple study site visits to monitor participants.

What are the possible benefits and risks of participating?
As with all medications, the study drug could cause some side effects. Each person reacts differently to a new medication and the participants may experience some or none of the side effects that have been observed in animals tested with the study drug. Furthermore, participants could experience side effects that are severe that are not known at this time. There is always a risk involved in taking an experimental drug. The participant will be closely monitored by the study team and will be instructed to contact the study team immediately in the event of side effects. The side effects that have been observed in animals tested with the study drug are detailed in the Participant Information Sheets to ensure the participant is fully informed.
There are also risks from study procedures such as discomfort when blood samples are taken, and pain and discomfort from the eye injection. All known risks are detailed in the Participant Information Sheet to ensure the participant is fully informed.
The risk of causing harm to an unborn child is unknown. Therefore, women who are pregnant, or who intend to become pregnant during the study, are not permitted to take part in this study. Also, it is not known whether the study drug causes harm to a breastfeeding infant. Therefore, women who are breastfeeding should not take part in the study. The known risks and requirements regarding pregnancy and contraception are detailed in the Participant Information Sheet to ensure the participant is fully informed.

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

When is the study starting and how long is it expected to run for?
January 2023 to June 2029

Who is funding the study?
Stoke Therapeutics Inc (USA)

Who is the main contact?
Dr Steven Gross, clinicaltrials@stoketherapeutics.com

Contact information

Type(s)
Scientific

Contact name
Dr Steven Gross

Contact details
45 Wiggins Avenue
Bedford
United States of America
MA 01730
+1 (0)813 695 9151
clinicaltrials@stoketherapeutics.com

Additional identifiers

Clinical Trials Information System (CTIS)

2023-506290-35

Integrated Research Application System (IRAS)
1006380

Central Portfolio Management System (CPMS)
54024

Protocol serial number
STK-002-OA-101

Study information

Scientific Title
Osprey: An open-label study to investigate the safety, tolerability, and exposure of single ascending doses of the antisense oligonucleotide STK-002 in patients with autosomal dominant optic atrophy

Study objectives
1. To evaluate the safety and tolerability of single ascending doses of STK-002 in patients with autosomal dominant optic atrophy (ADOA)
2. To determine the exposure in serum following single intravitreal (IVT) doses of STK-002
3. To evaluate changes in visual function and ocular structure following single doses of STK-002
4. To evaluate the effect of single doses of STK-002 on quality of life in patients with ADOA

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 16/03/2023, North East - Newcastle and North Tyneside 1 Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8384; newcastlenorthtyneside1.rec@hra.nhs.uk), ref: 23/NE/0031

Primary study design
Interventional

Study design
Open-label phase I multi-centre single-ascending-dose study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Autosomal dominant optic atrophy

Interventions
Current interventions as of 08/03/2024:

STK-002-OA-101 is an open-label study in which a participant will receive a single dose of the study drug STK-002, via an injection to the affected eye, at visit 3 (Day 1) of their participation in the study.

Participants in part A of the study will be assigned to one of four groups. Each group will receive a different dose of the study drug starting at a safe, low dose in group 1, which was calculated by data collected through pre-clinical studies, and escalating to higher doses in groups 2, 3 and 4.

Group 1 will be the first to receive the study drug and data collected from participants will be reviewed by a Safety Monitoring Committee (SMC). The SMC will use this data to determine whether the dose can be escalated and given to the next group. This process will be repeated for all groups. An optional two additional groups may be added to Part A, with the dose in these groups escalated further. Administration of the study drug will take approximately 5-10 minutes. However, the total time for administration procedure may take up to 2 hours if patients require sedation.

Data from Part A of the study will be reviewed by the SMC to determine a safe dose of the study drug to be given to participants in Part B of the study. In Part B, the first paediatric participant (sentinel) to receive the study drug will be ≥12 and <18 years of age. The SMC will meet again after dosage to determine whether to continue to dose, and for dose escalation/de-escalation for additional groups in Part B.

There are currently 10 planned visits to the research site and via one planned telephone call to follow up with participants. Follow-up will last approximately up to 50 weeks after study drug administration, to evaluate the safety and tolerability of the study drug.

———

Previous interventions:

STK-002-OA-101 is an open-label study in which a participant will receive a single dose of the study drug STK-002, via an injection to the affected eye, at visit 3 (Day 1) of their participation in the study.

Participants in part A of the study will be assigned to one of four groups. Each group will receive a different dose of the study drug starting at a safe, low dose in group 1, which was calculated by data collected through pre-clinical studies, and escalating to higher doses in groups 2, 3 and 4.

Group 1 will be the first to receive the study drug and data collected from participants will be reviewed by a Safety Monitoring Committee (SMC). The SMC will use this data to determine whether the dose can be escalated and given to the next group. This process will be repeated for all groups. An optional two additional groups may be added to Part A, with the dose in these groups escalated further. Administration of the study drug will take approximately 5-10 minutes. However, the total time for administration procedure may take up to 2 hours if patients require sedation.

Data from Part A of the study will be reviewed by the SMC to determine a safe dose of the study drug to be given to participants in part B of the study. The first group of paediatric participants to receive the study drug will be ≥12 and <18 years of age. The SMC will meet again after dosage to determine dose escalation/de-escalation for other groups in Part B.

There are currently 7 planned visits to the research site and via one planned telephone call to follow up with participants. Follow-up will last approximately up to 52 weeks after study drug administration, to evaluate the safety and tolerability of the study drug.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
STK-002

Primary outcome(s)
Current primary outcome measure as of 08/03/2024:

Evaluation of these endpoints will occur at up to 48 weeks (+/- 2 weeks) after Study Drug Administration:
1. Safety variables for analysis include:
1.1. The incidence, type, and severity of adverse events (AEs) in the treated eye throughout the study
1.2. Changes in vital signs at day 1, 2, 8, 29 and 337
1.3. Laboratory parameters in up to 7 of the 10 visits
1.4. Age-Related Eye Disease Study (AREDS) Clinical Lens Grading System scores at day 2, 8, 29, 85, 169, 253 and 337
1.5. Assessment of inflammation (Standardization of Uveitis Nomenclature [SUN] Anterior Chamber Cell score and NEI Vitreous Haze scores) at baseline, day 8, 29, 85, 169, 253 and 337
1.6. Corneal epithelial grading using Efron corneal grading scale at baseline, day 2, 8, 29, 85, 169, 253, and 337
1.7. Physical examination at day 2, 8, 29 and 337
1.8. Immunogenicity parameters at baseline, day 29, 85, 169 and 337
1.9. Retinal Toxicity assessed by full-field electroretinogram (ERG), retinal thinning by optical coherence tomography (OCT) at baseline, day 29, 85, 169, 253, and 337
2. The exposure of STK-002 in serum will be determined measured pre-dose, at 1, 2, 4, 6, 24 hours post dose and on days 8, 29, 85, 169 and 337. Pharmacokinetic (PK) parameters may include:
2.1. Maximum observed concentration (Cmax)
2.2. Time to maximum observed concentration (Tmax)
2.3. Fold change in Cmax compared with dose level

———

Previous primary outcome measure:

Evaluation of these endpoints will occur at up to 48 weeks (+/- 2 weeks) after Study Drug Administration:
1. Safety variables for analysis include:
1.1. The incidence, type, and severity of adverse events (AEs) throughout the study
1.2. Changes in vital signs at day 1, 2, 8, 29 and 337
1.3. Laboratory parameters in up to 7 of the 10 visits
1.4. Age-Related Eye Disease Study (AREDS) Clinical Lens Grading System scores at day 2, 8, 29,

85, 169, 253 and 337
1.5. Assessment of inflammation (Standardization of Uveitis Nomenclature [SUN] Anterior Chamber Cell score and NEI Vitreous Haze scores) at baseline, day 8, 29, 85, 169, 253 and 337
1.6. Corneal epithelial grading using Efron corneal grading scale at baseline, day 4, 8, 29, 85, 69, 253, and 337
1.7. Physical examination at day 2, 8, 29 and 337
1.8. Immunogenicity parameters at baseline, day 29, 85, 169 and 337
2. The exposure of STK-002 in serum will be determined measured pre-dose, at 1, 2, 4, 6, 24 hours post dose and on days 2, 8, 29, 85, 169 and 337. Pharmacokinetic (PK) parameters may include:
2.1. Maximum observed concentration (Cmax)
2.2. Time to maximum observed concentration (Tmax)
2.3. Fold change in Cmax compared with dose level
2.4. Retinal toxicity assessed by full-field electroretinogram (ERG), retinal thinning by optical coherence tomography (OCT)

Key secondary outcome(s)

Current key secondary outcome(s) as of 29/04/2026:

Secondary endpoints for STK-002 evaluated by dose level and change from baseline at each visit are assessed at up to 48 weeks (+/- 2 weeks) after Study Drug Administration:
1. Peripapillary retinal nerve fiber layer (RNFL) and macular ganglion cell layer (GCL, or ganglion cell complex) thicknesses as assessed by optical coherence tomography (OCT) at baseline, day 29, 85, 169, 253 and 337
2. Best-corrected visual acuity (BCVA) measured using Early Treatment Diabetic Retinopathy Study (ETDRS) optotypes at screening, and days 8, 29, 85, 169, 253 and 337
3. Contrast sensitivity assessed by low contrast BCVA (at 25% and 5% contrast levels) at baseline, and days 29, 85, 169, 253 and 337
4. Visual field as assessed by automated, static perimetry [10-2 Swedish Interactive Threshold Algorithm (SITA) FAST] and 24-2 Short Wavelength Automated Perimetry [SWAP] at baseline, and days 29, 85, 169, 253 and 337
5. Electrical activity of the retina as assessed by photopic negative response (PhNR) ERG, at baseline, and days 29, 85, 169, 253 and 337
6. Continuous text reading acuity as assessed by MNREAD Acuity Charts at baseline, and days 29, 85, 169, 253 and 337
7. Quality of life measured by scores on the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25), Impact of Vision Impairment for Children (IVI-C), and the European Quality of Life-5 Dimensions (EQ-5D)/EQ-5D-Y questionnaire at baseline, and days 29, 85 and 337

———

Previous secondary outcome measures as of 08/03/2024:

Secondary endpoints for STK-002 evaluated by dose level and change from baseline at each visit are assessed at up to 48 weeks (+/- 2 weeks) after Study Drug Administration:
1. Peripapillary retinal nerve fiber layer (RNFL) and macular ganglion cell layer (GCL, or ganglion cell complex) thicknesses as assessed by optical coherence tomography (OCT) at baseline, day 29, 85, 169, 253 and 337
2. Best-corrected visual acuity (BCVA) measured using Early Treatment Diabetic Retinopathy Study (ETDRS) optotypes at screening, and days 8, 29, 85, 169, 253 and 337
3. Contrast sensitivity assessed by low contrast BCVA (at 25%, 5% and 2.5% contrast levels) at baseline, and days 29, 85, 169, 253 and 337

4. Visual field as assessed by automated, static perimetry [10-2 and 24-2 Swedish Interactive Threshold Algorithm (SITA) FAST] at baseline, and days 29, 85, 169, 253 and 337
5. Electrical activity of the retina as assessed by photopic negative response (PhNR) ERG, if available, at baseline, and days 29, 85, 169, 253 and 337
6. Continuous text reading acuity as assessed by MNREAD Acuity Charts at baseline, and days 29, 85, 169, 253 and 337
7. Quality of life measured by scores on the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25), Impact of Vision Impairment for Children (IVI-C), and the European Quality of Life-5 Dimensions (EQ-5D)/EQ-5D-Y questionnaire at baseline, and days 29, 85 and 337

———

Previous secondary outcome measures:

Secondary endpoints for STK-002 evaluated by dose level and change from baseline at each visit are assessed at up to 48 weeks (+/- 2 weeks) after Study Drug Administration:
1. Peripapillary retinal nerve fiber layer (RNFL) and macular ganglion cell layer (GCL, or ganglion cell complex) thicknesses as assessed by optical coherence tomography (OCT) at baseline, day 29, 85, 169, 253 and 337
2. Best-corrected visual acuity (BCVA) measured using Early Treatment Diabetic Retinopathy Study (ETDRS) optotypes at screening, and days 8, 29, 85, 169, 253 and 337
3. Contrast sensitivity assessed by the Pelli-Robson chart and low contrast BCVA (at 25%, 10%, and 5% contrast levels) at baseline, and days 29, 85, 169, 253 and 337
4. Visual field as assessed by automated, static perimetry [24-2 Swedish Interactive Threshold Algorithm (SITA) FAST] at baseline, and days 29, 85, 169, 253 and 337
5. Electrical activity of the retina as assessed by pattern electroretinogram (p-ERG) and/or phototopic negative response (PhNR) ERG, if available, at baseline, and days 29, 85, 169, 253 and 337
6. Continuous text reading acuity as assessed by MNREAD Acuity Charts at baseline, and days 29, 85, 169, 253 and 337
7. Quality of life measured by scores on the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25), Impact of Vision Impairment for Children (IVI-C), and the European Quality of Life-5 Dimensions (EQ-5D)/EQ-5D-Y questionnaire at baseline, and days 29, 85 and 337

Completion date
18/06/2029

Eligibility

Key inclusion criteria
Current key inclusion criteria as of 10/07/2026:

1. Patient must be ≥18 to <55 years to participate in Part A and ≥6 to <18 years to participate in Part B
2. Patient must have a clinical diagnosis of ADOA and have a heterozygous OPA1 gene variant confirmed at Screening by central lab genotyping
3. Patient must have a BCVA EDTRS letter score of ≥35 and ≤70 in the intended treated eye, with the exception of the first two patients in Cohort 1 of Part A who must have a BCVA ETDRS letter score ≥5 and ≤35 in the intended treated eye
4. Patient’s screening/baseline full field electroretinogram (ffERG) and optical coherence tomography (OCT) images are acceptable prior to dosing

———

Previous key inclusion criteria as of 29/04/2026:

1. Patient must be ≥18 to <55 years to participate in Part A and ≥6 to <18 years to participate in Part B
2. Patient must have a clinical diagnosis of ADOA and have a heterozygous OPA1 gene variant confirmed at Screening by central lab genotyping
3. Patient must have a BCVA EDTRS letter score of ≥35 and ≤70 with each eye individually, with the exception of the first two patients in Cohort 1 of Part A who must have a BCVA ETDRS letter score ≥5 and ≤35 in each eye
4. Patient's screening/baseline full field electroretinogram (ffERG) and optical coherence tomography (OCT) images are acceptable prior to dosing

———

Previous key inclusion criteria:

1. Patient must be ≥18 to <55 years to participate in Part A and ≥6 to <18 years to participate in Part B
2. Patient must have a clinical diagnosis of ADOA and have a heterozygous OPA1 gene variant confirmed at Screening by central lab genotyping
3. Patient must have a BCVA EDTRS letter score of ≥35 and ≤70 with each eye individually, with the exception of the first two patients in Cohort 1 of Part A who must have a BCVA ETDRS letter score ≥5 and ≤35 in each eye

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
6 Years

Upper age limit
60 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Patient has a gain-of-function variant, or compound heterozygous or homozygous pathogenic or likely pathogenic variant in the OPA1 gene
2. Patient has extraocular phenotypic manifestations of (syndromic) ADOA (ADOA-plus) or has

Behr syndrome
3. Patient has or has a history of, any ocular condition in either eye that, in the opinion of the Investigator, could affect study parameters
4. Patient is considered to be at risk for uveitis or ocular infection during the study period
5. Patient is taking or has taken at any time, any medication or treatment that can or might cause an optic neuropathy

Date of first enrolment
26/09/2025

Date of final enrolment
19/06/2028

Locations

Countries of recruitment
United Kingdom

England

Wales

Austria

Denmark

Germany

Italy

Study participating centre
Addenbrookes
Addenbrookes Hospital
Hills Road
Cambridge
England
CB2 0QQ

Study participating centre
University Hospital of Wales
Heath Park
Cardiff
Wales
CF14 4XW

Study participating centre
Moorfields Eye Hospital
162 City Road
London
England
EC1V 2PD

Study participating centre
Great Ormond Street Hospital
Great Ormond Street
London
England
WC1N 3JH

Study participating centre
AKH/Medical University of Vienna
Department of Ophthalmology and Optometry
Waehringer Guertel 18-20
Vienna
Austria
1090

Study participating centre
Copenhagen University Hospital (Rigshospitalet-Glostrup)
Department of Ophthalmology
Valdemar Hansens Vej 1-23
Glostrup
Denmark
2600

Study participating centre
Universitaets-Augenklinik Tuebingen
Elfriede-Aulhorn-Str. 7
Tuebingen
Germany
72076

Study participating centre
Justus-Liebig Universitaet
Klinik und Poliklinik für Augenheilkunde
Friedrichstr. 18

Giessen
Germany
35392

Study participating centre
IRCCS Ospedale San Raffaele
Via Olgettina, 60
Milan
Italy
20132

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

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