

# 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)

<b>Submission date</b> 14/01/2023	<b>Recruitment status</b> Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 21/08/2023	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 05/11/2025	<b>Condition category</b> Eye Diseases	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> 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  $\geq 6$  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  $\geq 18$  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  $\geq 6$  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 March 2029

Who is funding the study?

Stoke Therapeutics Inc (USA)

Who is the main contact?

Dr Steven Gross, [clinicaltrials@stoketherapeutics.com](mailto:clinicaltrials@stoketherapeutics.com)

## Contact information

**Type(s)**

Scientific

**Contact name**

Dr Steven Gross

**Contact details**

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[clinicaltrials@stoketherapeutics.com](mailto:clinicaltrials@stoketherapeutics.com)

## Additional identifiers

Clinical Trials Information System (CTIS)

2023-506290-35

**Integrated Research Application System (IRAS)**  
1006380

**ClinicalTrials.gov (NCT)**  
Nil known

**Protocol serial number**  
STK-002-OA-101, IRAS 1006380, CPMS 54024

## 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

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

**Primary study design**  
Interventional

**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  $\geq 12$  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.

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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  $\geq 12$  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 (C<sub>max</sub>)

2.2. Time to maximum observed concentration (T<sub>max</sub>)

2.3. Fold change in C<sub>max</sub> compared with dose level

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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 (C<sub>max</sub>)

2.2. Time to maximum observed concentration (T<sub>max</sub>)

2.3. Fold change in C<sub>max</sub> 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 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

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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 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

### **Completion date**

31/03/2029

## **Eligibility**

### **Key inclusion criteria**

1. Patient must be  $\geq 18$  to  $< 55$  years to participate in Part A and  $\geq 6$  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  $\geq 35$  and  $\leq 70$  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  $\geq 5$  and  $\leq 35$  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

### **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**

31/03/2028

## **Locations**

**Countries of recruitment**

United Kingdom

England

Wales

Austria

Denmark

Germany

Italy

**Study participating centre**

**Addenbrookes**

Addenbrookes Hospital  
Hills Road  
Cambridge  
United Kingdom  
CB2 0QQ

**Study participating centre**

**University Hospital of Wales**

Heath Park  
Cardiff  
United Kingdom  
CF14 4XW

**Study participating centre**

**Moorfields Eye Hospital**

162 City Road  
London



United Kingdom  
EC1V 2PD

**Study participating centre**  
**Great Ormond Street Hospital**  
Great Ormond Street  
London  
United Kingdom  
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

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?
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes