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Efficacy, safety and mechanisms of atropine eyedrops in slowing the progression of shortsightedness (myopia) in children

Submission date 20/09/2017	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 04/10/2017	**Overall study status** Completed	
Last Edited 20/01/2025	**Condition category** Eye Diseases	

Plain English summary of protocol

Current plain English summary as of 25/07/2018:
Background and study aims
Short-sightedness (or myopia) is the most common eye problem in Ireland and is growing all over the world. It now affects up to 90% of young adults in Asia and up to 50% in Western countries. As well as the costs and frustrations of not being able to see well without glasses, myopia is also bad for the health of the eyes. As people get older their eyes are at risk of a range of diseases that can damage eyesight in a way that can no longer be corrected with glasses or contact lenses. These diseases include glaucoma and cataract. Even people with mild levels of myopia face double the risk of getting these conditions. Myopia increases the risk of other conditions, such as a retinal detachments and myopic maculopathy, by up to 10-fold. To put this into perspective, being short-sighted is as bad for eye health as smoking or high blood pressure is for the heart. Currently there are no established treatments to stop people becoming short-sighted, and no treatments to stop them getting worse if they do. This project is designed to test a promising new treatment that might stop myopia getting worse. Over two years a painless eye drop will be tested (containing a drug called atropine) that is given once a day at night. Atropine has been used safely for decades by ophthalmologists to treat other eye disorders in children. A very small dose is used, 100 times lower than the normal clinical dose. This has been proven in Asia to be the most effective dose for long-term myopia control. The aim of this study is to see whether the eye drops work and to make sure they are safe and acceptable to young people with myopia. As well as testing the drop, the study looks at how the eye grows in myopia, what role genes play in myopia, what people think about myopia and how a successful treatment might benefit society. This project is the first of its kind in Ireland, or indeed Europe.

Who can participate?
Children aged 6-16 with myopia

What does the study involve?
Each participant visits the Centre for Eye Research Ireland (CERI) on a minimum of 8 occasions. This includes a pre study visit to check for eligibility 6 months before the baseline visit, the baseline visit followed by a visit at 6, 12, 18, 24, 30 and 36 months. Each visit takes about 90

minutes. At the pre study visit vision and health checks are carried out to determine if the child is suitable to take part in the study. Parents and children also have the chance to ask any questions about the study. No drops are dispensed at the pre study visit. If the child appears to be suitable at the pre study eye test, they are asked to return to CERI at least 6 months after this visit. At this visit it will be checked whether the child's shortsightedness has progressed over the past 6 months as they only need to participate if their glasses prescription is getting worse. If their shortsightedness is progressing and they are suitable to participate in the study they are then registered into the study and start treatment. The parent/guardian is randomly allocated to be given either atropine or placebo (dummy) eye drops to take home and instill one drop every night into both eyes for a given duration. A parent/guardian also fills out a questionnaire about their thoughts/attitudes to glasses, eye drops and sight tests as well as their daily routine activities and their time spent outdoors. The participants who do not receive atropine at first start on atropine treatment later, so that all participants ultimately receive atropine treatment.

What are the possible benefits and risks of participating?
The participant may or may not receive any direct benefit from taking part in the study. However, information obtained during the course of the study may help improve the understanding of myopia. It is hoped that the treatment the child receives may prevent the progression of their myopia. However, this cannot be guaranteed. The information we get from this research study may help to reduce myopia progression in future patients. There are no disadvantages in taking part in this study. There are no risks associated with the tests administered for the purpose of this study over those of a normal eye examination. They are all completely non-invasive. Regarding atropine eye drops, there are associated possible risks including an increase in pupil size (which may cause glare) and a lesser ability to accommodate (which may lead to difficulty reading up close). However, with the diluted low dose of atropine used in this study the risk of glare is minimised. Uncommon side effects of atropine include local skin allergy, eye irritation, conjunctivitis, increased intraocular pressure, swelling of the eyelids and flushing.

Where is the study run from?
The Centre for Eye Research Ireland (CERI) at the Technological University of Dublin

When is the study starting and how long is it expected to run for?
October 2017 to September 2023

Who is funding the study?
1. Health Research Board (Ireland)
2. RP Fighting Blindness (UK)

Who is the main contact?
Prof. Ian Flitcroft (scientific)
ian.flitcroft@tudublin.ie

Previous plain English summary:
Background and study aims
Short-sightedness (or myopia) is the most common eye problem in Ireland and is growing all over the world. It now affects up to 90% of young adults in Asia and up to 50% in Western countries. As well as the costs and frustrations of not being able to see well without glasses, myopia is also bad for the health of the eyes. As people get older their eyes are at risk of a range of diseases that can damage eyesight in a way that can no longer be corrected with glasses or contact lenses. These diseases include glaucoma and cataract. Even people with mild levels of myopia face double the risk of getting these conditions. Myopia increases the risk of other

conditions, such as a retinal detachments and myopic maculopathy, by up to 10-fold. To put this into perspective, being short-sighted is as bad for eye health as smoking or high blood pressure is for the heart. Currently there are no established treatments to stop people becoming short-sighted, and no treatments to stop them getting worse if they do. This project is designed to test a promising new treatment that might stop myopia getting worse. Over two years a painless eye drop will be tested (containing a drug called atropine) that is given once a day at night. Atropine has been used safely for decades by ophthalmologists to treat other eye disorders in children. A very small dose is used, 100 times lower than the normal clinical dose. This has been proven in Asia to be the most effective dose for long-term myopia control. The aim of this study is to see whether the eye drops work and to make sure they are safe and acceptable to young people with myopia. As well as testing the drop, the study looks at how the eye grows in myopia, what role genes play in myopia, what people think about myopia and how a successful treatment might benefit society. This project is the first of its kind in Ireland, or indeed Europe.

Who can participate?
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What does the study involve?
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What are the possible benefits and risks of participating?
The participant may or may not receive any direct benefit from taking part in the study. However, information obtained during the course of the study may help improve the understanding of myopia. It is hoped that the treatment the child receives may prevent the progression of their myopia. However, this cannot be guaranteed. The information we get from this research study may help to reduce myopia progression in future patients. There are no disadvantages in taking part in this study. There are no risks associated with the tests administered for the purpose of this study over those of a normal eye examination. They are all completely non-invasive. Regarding atropine eye drops, there are associated possible risks including an increase in pupil size (which may cause glare) and a lesser ability to accommodate (which may lead to difficulty reading up close). However, with the diluted low dose of atropine used in this study the risk of glare is minimised. Uncommon side effects of atropine include local skin allergy, eye irritation, conjunctivitis, increased intraocular pressure, swelling of the eyelids and flushing.

Where is the study run from?
The Centre for Eye Research Ireland (CERI) at the Environmental Sustainability and Health Institute (ESHI) (Ireland)

When is the study starting and how long is it expected to run for?
October 2017 to October 2021

Who is funding the study?
1. Health Research Board (Ireland)
2. RP Fighting Blindness (UK)

Who is the main contact?
Prof. James Loughman (scientific)
james.loughman@dit.ie

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2016-003340-37

Protocol serial number
1.7_26-4-2017

Study information

Scientific Title
Myopia Outcome Study of Atropine in Children (MOSAIC): a randomised controlled trial

Acronym
MOSAIC

Study objectives
Current study hypothesis as of 24/11/2022:
The aim of this study is to examine the efficacy, safety and mechanisms of action of 0.01% and 0.05% atropine on myopia development for the first time in a predominantly Caucasian population.

Previous study hypothesis:
The aim of this study is to examine the efficacy, safety and mechanisms of action of 0.01% atropine on myopia development for the first time in a predominantly Caucasian population.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/11/2017, amendment approved 09/04/2021, Mater Misericordiae University Hospital Institutional Review Board (Eccles Street, Dublin 7, Northern Ireland, UK; +353 1 8032000; mmh@mater.ie), ref: 1/478/81

Primary study design
Interventional

Study design
Two-phase double-masked placebo-controlled randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Myopia

Interventions
Current interventions as of 24/11/2022:
Assignments to treatment will be allocated with concealment according to an objective computer-generated randomisation software program.

Phase I
Children will be allocated to the treatment or control group according to a 2:1 treatment to control ratio to maximise recruitment success. Subjects will be randomised to a study number unrelated to treatment assignment. Randomisation will be completed at the baseline visit. The intervention for the trial is 0.01% atropine eye drops inserted into both eyes nightly for 2 years. Atropine is an anti-cholinergic agent that is relatively selective for muscarinic receptors. It is licensed for ophthalmic and systemic use in humans in oral form, through topical ophthalmic drops or by injection. It is licenced for use in Ireland and the UK as an eye drop at the 1% dose as a mydriatic and cycloplegic agent, for pre-operative use in ophthalmic surgery and for treatment of uveitis and refraction. The active ingredient in topical ophthalmic atropine is atropine sulphate, and is available as an eye drop. A 1% atropine eye drop solution contains 10 mg of atropine sulphate for each mL, this is equivalent to 8.3 mg of atropine. A total of 250 children will be recruited (167 in the intervention group; 83 in the placebo group). Trial subjects will

include male and female children aged between 6-16 years, with myopia of -1.0 D or worse (spherical equivalent) in each eye and an astigmatic refractive error less than -1.50D. Subjects must have progressive myopia of at least -0.50D over the last year and have no ocular or systemic diseases affecting vision or refractive error. This study will reflect the multi-racial nature of modern Irish society, but a large proportion to the children must be of Caucasian ethnic background to achieve its scientific goals. To ensure the study population is representative of the Irish population, recruitment will be capped by ethnic background in accordance with 2011 Irish Census, or the 2016 Irish Census if available by the start of the recruitment process. Subjects apply once nightly eye drops in both eyes from randomisation at baseline visit to month 24. Subjects will be reviewed at month 6, 12, 18 and 24.

Phase II
Subjects initially randomised to the placebo arm in Phase I will crossover to receive 0.05% atropine for a 12 month treatment period. These subjects will be reviewed at month 30 and 36. All subjects initially assigned to the 0.01% atropine intervention group will be re-randomised in a 2:1:1 ratio to one of three new study intervention arms. These include: 50% will continue to receive 0.01% atropine on a tapered dosing regimen. Instead of nightly dosing, these subjects will initially use atropine on alternate days only from month 25 to 27, then reduce to twice weekly dosing from month 28 to 30, once weekly from month 31 to 33, followed by no drops for the final three month period from month 34 to 36. 25% will be randomised to receive placebo eyedrops on the same tapered dosing regimen. 25% will be randomised to receive placebo eyedrops on a nightly dosing regimen. These subjects will also be reviewed at month 30 and 36. The crossover design will facilitate an additional analysis of the effect of a 0.05% atropine intervention relative to placebo and relative to 0.01% atropine in the same subject cohort. Further, it will allow an investigation of the effect of a gradual cessation of treatment (0.01% tapered dosing regimen) compared to sudden cessation (crossover to placebo).

The primary and secondary outcome measures will be assessed using the following endpoint assessments:
1. Visual acuity
Participants' aided and unaided visual acuity will be measured using the SLOAN letterset of a computerised logMAR chart. It is anticipated the unaided visual acuity of subjects treated with atropine will not deteriorate as much on average as participants receiving the placebo eye drop, while aided visual acuity will be expected to remain virtually static in both study arms.
2. Objective refraction
Refractive error will be measured by cycloplegic auto-refraction using the Grand Seiko WAM5500 open field autorefractor at the 6 month pre trial and baseline visit. Any increase in myopic refractive error measured by cycloplegic auto-refraction should be lower on average in subjects treated with atropine. Cycloplegic auto-refraction will also be completed during the washout period to examine if there is any rebound acceleration in refractive error as seen in other studies that have utilised higher concentrations of atropine relative to our study.
3. Ocular biometry
The Topcon Alladin optical biometer will be used to determine anatomical measurements of the eye by partial-coherence interferometry. Axial length, anterior chamber depth and lens thickness will be measured. Increases in ocular axial length are expected to be less on average in subjects treated with atropine compared to the control group. These measurements will also be completed during the washout period to examine if there is any rebound acceleration in axial length as seen in other studies that have utilised higher concentrations of atropine compared with this study.
4. Off-axis refraction
Off-axis refraction at 15o and 30o nasally and temporally will be measured using the Grand Seiko WAM5500 open field autorefractor at baseline and at each study visit to assess if subjects who

become more myopic had more peripheral hyperopic refractive error initially, and whether this changes with myopic progression.
Effect on ocular function, physiology and visual performance:
5. Amplitude of accommodation, near point of convergence, near VA and reading speed will be measured at the endpoint to assess visual function in subjects who have been using atropine eye drops. The results will be compared to the subjects' baseline assessment and also compared to the control group measurements. These tests will also be completed during the washout period to ensure visual function returns to baseline normal if any changes are detected.
Retinal vasculature:
6. The Heidelberg Spectralis OCT will be used to photograph the interior surface of the eye, including the retina, retinal vasculature, optic disc, macula, and posterior pole at the endpoint visit and compared to previous visits to the control group to assess changes in peripheral retinal structure as a means to understand the mechanism of action of atropine.
7. Corneal topography
The Topcon Alladin biometer will be used to map a three-dimensional image of the cornea. This will ensure any eye drops prescribed to the participants (atropine or vehicle eye drops) have not interfered with the surface curvature of the cornea.
8. Slit lamp assessment
The slit lamp will be used to perform a complete examination of the external eye. This will include examination of the cornea, conjunctiva, iris, pupil lids and adnexa to determine any adverse reaction to the drops and assess ocular health as part of our safety evaluation.
9. IR pupillometry
The Alladdin and Neuroptics IR Pupillometer will measure pupillary reactivity and size in each participant at each visit including the end point visit. Atropine causes pupillary dilation, particularly at higher doses used in previous trials. However as stated, the lower dose atropine concentration used in this clinical trial, should minimally affect pupil size and reactivity. Participants' pupil size and reactivity will be measured at the endpoint visit and compared to their baseline measurement to assess the effect of 0.01% atropine on the pupil.
10. Tonometry
As higher concentrations of atropine cause pupillary dilation this could potentially result in an increase in intraocular pressure in participants with narrow angles. However the lower dose atropine concentration used in this clinical trial, should not cause such side effects. IOPs will be measured at each study visit including the end point visit.
12. Quality of life
The quality of life impact of atropine use will be assessed at six monthly intervals using the Amblyopia Treatment Index, an atropine-related quality of life questionnaire, as used and validated in the PEDIG trials for amblyopia treatment. The questionnaire will be completed by parents and by children where appropriate. Additional information in this regard will be ascertained through analysis of attrition rates in the intervention and placebo control groups.

Previous interventions:
Assignments to treatment will be allocated with concealment according to an objective computer-generated randomisation software program. Children will be allocated to the treatment or control group according to a 2:1 treatment to control ratio to maximise recruitment success. Subjects will be randomised to a study number unrelated to treatment assignment. Randomisation will be completed at the baseline visit.

The intervention for the trial is 0.01% atropine eye drops inserted into both eyes nightly for 2 years. Atropine is an anti-cholinergic agent that is relatively selective for muscarinic receptors. It is licensed for ophthalmic and systemic use in humans in oral form, through topical ophthalmic drops or by injection. It is licenced for use in Ireland and the UK as an eye drop at the 1% dose as a mydriatic and cycloplegic agent, for pre-operative use in ophthalmic surgery and for treatment

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A total of 250 children will be recruited (167 in the intervention group; 83 in the placebo group). Trial subjects will include male and female children aged between 6-16 years, with myopia of -1.0 D or worse (spherical equivalent) in each eye and an astigmatic refractive error less than -1.50D. Subjects must have progressive myopia of at least -0.50D over the last year and have no ocular or systemic diseases affecting vision or refractive error. This study will reflect the multi-racial nature of modern Irish society, but a large proportion to the children must be of Caucasian ethnic background to achieve its scientific goals. To ensure the study population is representative of the Irish population, recruitment will be capped by ethnic background in accordance with 2011 Irish Census, or the 2016 Irish Census if available by the start of the recruitment process.

Six months before their proposed trial start date, subjects will undergo a series of ocular examinations. This will ensure subjects are progressive myopes before they are registered for the trial at the baseline visit. Subjects apply once nightly eye drops in both eyes from randomisation at baseline visit to month 24. Subjects will be reviewed at month 6, 12, 18 and 24. No treatment will be given from month 24 to 36 (washout period) for those subjects initially randomised to the intervention arm. These subjects will be monitored for a minimum period of 12 months, where the subject will be reviewed at month 30 and 36. All subjects initially assigned to the placebo group will crossover to the intervention arm of the study, and for the period from month 24 to 36, will instill 0.01% atropine eye drops once nightly. These subjects will also be reviewed at month 30 and 36. The crossover design will facilitate an additional analysis of the effect of atropine intervention relative to placebo in the same subject cohort, and will also facilitate recruitment objectives given that all participants will receive the active intervention at some stage during the trial.

The primary and secondary outcome measures will be assessed using the following endpoint assessments:
1. Visual acuity
Participants' aided and unaided visual acuity will be measured using the SLOAN letterset of a computerised logMAR chart. It is anticipated the unaided visual acuity of subjects treated with atropine will not deteriorate as much on average as participants receiving the placebo eye drop, while aided visual acuity will be expected to remain virtually static in both study arms.
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Refractive error will be measured by cycloplegic auto-refraction using the Grand Seiko WAM5500 open field autorefractor at the 6 month pre trial and baseline visit. Any increase in myopic refractive error measured by cycloplegic auto-refraction should be lower on average in subjects treated with atropine. Cycloplegic auto-refraction will also be completed during the washout period to examine if there is any rebound acceleration in refractive error as seen in other studies that have utilised higher concentrations of atropine relative to our study.
3. Ocular biometry
The Topcon Alladin optical biometer will be used to determine anatomical measurements of the eye by partial-coherence interferometry. Axial length, anterior chamber depth and lens thickness will be measured. Increases in ocular axial length are expected to be less on average in subjects treated with atropine compared to the control group. These measurements will also be completed during the washout period to examine if there is any rebound acceleration in axial length as seen in other studies that have utilised higher concentrations of atropine compared with this study.
4. Off-axis refraction

Off-axis refraction at 15o and 30o nasally and temporally will be measured using the Grand Seiko WAM5500 open field autorefractor at baseline and at each study visit to assess if subjects who become more myopic had more peripheral hyperopic refractive error initially, and whether this changes with myopic progression.

Effect on ocular function, physiology and visual performance:
5. Amplitude of accommodation, near point of convergence, near VA and reading speed will be measured at the endpoint to assess visual function in subjects who have been using atropine eye drops. The results will be compared to the subjects' baseline assessment and also compared to the control group measurements. These tests will also be completed during the washout period to ensure visual function returns to baseline normal if any changes are detected.

Retinal vasculature:
6. The Heidelberg Spectralis OCT will be used to photograph the interior surface of the eye, including the retina, retinal vasculature, optic disc, macula, and posterior pole at the endpoint visit and compared to previous visits to the control group to assess changes in peripheral retinal structure as a means to understand the mechanism of action of atropine.
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The quality of life impact of atropine use will be assessed at six monthly intervals using the Amblyopia Treatment Index, an atropine-related quality of life questionnaire, as used and validated in the PEDIG trials for amblyopia treatment. The questionnaire will be completed by parents and by children where appropriate. Additional information in this regard will be ascertained through analysis of attrition rates in the intervention and placebo control groups.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)

Atropine

Primary outcome(s)
Change in spherical equivalent refraction from baseline to 24 months, measured by cycloplegic autorefraction using the Grand Seiko WAM5500 open field autorefractor

Key secondary outcome(s)
Current secondary outcome measures as of 09/04/2021:
1. Efficacy, assessed by:
1.1.Change in ocular axial length at 12, 24 and 36 months, measured using a Topcon ALADDIN optical biometer
1.2. Change in spherical equivalent refraction at 12 months and 36 months, assessed by cycloplegic auto-refraction using the Grand Seiko WAM 5500 open field autorefractor
1.3. Percentage of participants who progress 0.75D in 24 months, assessed by cycloplegic auto-refraction using the Grand Seiko WAM 5500 open field autorefractor
1.4. Difference in rate of change in spherical equivalent refraction from 24 to 36 months between tapered and sudden treatment cessation, assessed by cycloplegic auto-refraction using the Grand Seiko WAM 5500 open field autorefractor
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1.4. Difference in rate of change in spherical equivalent refraction from 24 to 36 months between tapered and sudden treatment cessation, assessed by cycloplegic auto-refraction using the Grand Seiko WAM 5500 open field autorefractor
1.5. Difference in rate of change in axial from 24 to 36 months between tapered and sudden treatment cessation, assessed by Aladdin optical biometry.
2. Mechanisms of action, assessed by:
2.1. Effects on off-axis refraction at 24 months. Off-axis refraction at 30° nasally and temporally will be measured using the open field Shin Nippon autorefractor
2.2. Effects on ocular growth at 24 months, assessed using:
2.2.1. The following, measured using the Topcon ALADDIN optical biometer:
2.2.1.1. Ocular biometry
2.2.1.2. Corneal curvature
2.2.1.3. Anterior chamber depth
2.2.2. The following, measured using the Heidelberg Spectralis (a non-invasive Optical Coherence Tomographer):
2.2.2.1. Appearance of retinal vascular morphology
2.2.2.2. Retinal nerve fibre layer
2.2.2.3. Choroidal thickness
3. Safety and acceptability. assessed by:
3.1. Changes in visual performance at 24 months and 36 months, assessed by:
3.1.1. Reading speed, measured with the Wilkins Rate of Reading Test
3.1.2. Distance and near visual acuity measured using the ETDRS chart
3.2. Effects on ocular function (amplitude of accommodation, near point of convergence, pupil size and pupil reactivity) at 24 months and 36 months
3.3. Quality of life impact associated with atropine at 24 months and 36 months, assessed using a validated and atropine-specific quality of life questionnaire
3.4. Frequency of occurrence of adverse events recorded on study-specific adverse report forms

Previous secondary outcome measures from 25/07/2018 to 09/04/2021:
1. Efficacy, assessed by:

1.1.Change in ocular axial length at 24 months, measured using a Topcon ALADDIN optical biometer
1.2. Change in spherical equivalent refraction at 12 months, assessed by cycloplegic auto-refraction using the Grand Seiko WAM 5500 open field autorefractor
1.3. Change in ocular axial length at 12 months, measured using a Topcon ALADDIN optical biometer
1.4. Percentage of participants who progress 0.75D in 24 months, assessed by cycloplegic auto-refraction using the Grand Seiko WAM 5500 open field autorefractor
1.5. Any rebound acceleration in myopic refractive error after cessation of atropine treatment at 36 months, assessed by cycloplegic auto-refraction using the Grand Seiko WAM 5500 open field autorefractor
2. Mechanisms of action, assessed by:
2.1. Effects on off-axis refraction at 24 months. Off-axis refraction at 30° nasally and temporally will be measured using the open field Shin Nippon autorefractor
2.2. Effects on ocular growth at 24 months, assessed using:
2.2.1. The following, measured using the Topcon ALADDIN optical biometer:
2.2.1.1. Ocular biometry
2.2.1.2. Corneal curvature
2.2.1.3. Anterior chamber depth
2.2.2. The following, measured using the Heidelberg Spectralis (a non-invasive Optical Coherence Tomographer):
2.2.2.1. Appearance of retinal vascular morphology
2.2.2.2. Retinal nerve fibre layer
2.2.2.3. Choroidal thickness
3. Safety and acceptability. assessed by:
3.1. Changes in visual performance at 24 months, assessed by:
3.1.1. Reading speed, measured with the Wilkins Rate of Reading Test
3.1.2. Distance and near visual acuity measured using the ETDRS chart
3.2. Effects on ocular function (amplitude of accommodation, near point of convergence, pupil size and pupil reactivity) at 24 months
3.3. Quality of life impact associated with atropine at 24 months, assessed using a validated and atropine-specific quality of life questionnaire
3.4. Frequency of occurrence of adverse events recorded on study-specific adverse report forms

Previous secondary outcome measures (16/07/2018):
1. Efficacy, assessed by:
1.1.Change in ocular axial length at 24 months
1.2. Change in spherical equivalent refraction at 12 months
1.3. Change in ocular axial length at 12 months
1.4. Percentage of participants who progress 0.75D in 24 months
1.5. Any rebound acceleration in myopic refractive error after cessation of atropine treatment at 36 months
2. Mechanisms of action, assessed by:
2.1. Effects on off-axis refraction at 24 months
2.2. Effects on ocular growth (including retinal vascular morphology, ocular biometry, corneal curvature, anterior chamber, retinal nerve fibre layer and choroidal thickness) at 24 months
3. Safety and acceptability. assessed by:
3.1. Changes in visual performance (reading speed, distance and near visual acuity) at 24 months
3.2. Effects on ocular function (amplitude of accommodation, near point of convergence, pupil size and pupil reactivity) at 24 months
3.3. Quality of life impact associated with atropine at 24 months
3.4. Frequency of occurrence of adverse events recorded on study-specific adverse report forms

Previous secondary outcome measures:
1. Change in ocular axial length at 2 years (from baseline to 24 months), measured by partial-coherence interferometry using the Topcon Alladin optical biometer
2. Change in rate of progression of spherical equivalent refraction and axial growth after cessation of atropine (average annual progression during treatment versus average annual progression during washout)
3. Change in off-axis refraction at 2 years (from baseline to 24 months), measured using the Grand Seiko WAM5500 open field autorefractor
4. Change in reading speed, distance and near visual acuity at 2 years (from baseline to 24 months)
5. Change in amplitude of accommodation, near point of convergence, pupil size and pupil response dynamics at 2 years (from baseline to 24 months)
6. Change in ocular growth metrics including corneal curvature, lens thickness, anterior chamber depth, retinal nerve fibre layer and choroidal thickness and vascular morphology at 2 years (from baseline to 24 months)
7. Change in quality of life at 2 years (from baseline to 24 months), assessed using a modified Amblyopia Treatment Index
8. Occurrence of adverse events recorded on study-specific adverse report forms
9. Drop-out rate over the 2 year trial duration (baseline to 24 months)

Completion date
30/09/2023

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 16/07/2018:
1. Between 6-16 years old of either gender
2. A spherical equivalent refractive error of -1.0D or worse
3. Myopic progression of at least -0.50DS over the last year
4. Astigmatism less than or equal to -2.50D
5. An intraocular difference in spherical equivalent <= 1D
6. Corrected visual acuity better or equal to logMAR 0.2 in both eyes
7. A difference between non-cycloplegic and cycloplegic spherical refraction of less than 1.00 D
8. Normal IOP (<= 21mmHg)
9. Normal ocular health
10. Good general health with no history of cardiac/respiratory diseases
11. Be willing to commit to the 2 year clinical trial as well as randomisation to the placebo

Previous participant inclusion criteria:
1. Between 6-16 years old of either gender
2. A spherical equivalent refractive error of -1.0D or worse
3. Myopic progression of at least -0.50DS over the last year
4. Astigmatism less than or equal to -1.50D
5. An intraocular difference in spherical equivalent <= 1D
6. Corrected visual acuity better or equal to logMAR 0.2 in both eyes
7. A difference between non-cycloplegic and cycloplegic spherical refraction of less than 1.00 D
8. Normal IOP (<= 21mmHg)

9. Normal ocular health
10. Good general health with no history of cardiac/respiratory diseases
11. Be willing to commit to the 2 year clinical trial as well as randomisation to the placebo

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Child

Lower age limit
6 Years

Upper age limit
16 Years

Sex
All

Total final enrolment
250

Key exclusion criteria
1. Any ocular or systemic condition affecting vision or refractive error or where atropine is contraindicated
2. Any known allergy to atropine, cyclopentolate hydrochloride and/or proxymetacaine hydrochloride
3. Defective binocular vision, amblyopia or strabismus
4. Experienced previous pharmaceutical or optical myopia control interventions
5. If subjects (or parent/guardian) are unable to provide written informed consent

Date of first enrolment
11/07/2019

Date of final enrolment
30/09/2020

Locations

Countries of recruitment
Ireland

Study participating centre
Centre for Eye Research Ireland
Technological University of Dublin
Dublin

Ireland
Dublin 7

Sponsor information

Organisation
Technological University of Dublin

ROR
https://ror.org/04t0qbt32

Funder(s)

Funder type
Government

Funder Name
Health Research Board

Alternative Name(s)
Health Research Board, Ireland, An Bord Taighde Sláinte, HRB

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Ireland

Funder Name
RP Fighting Blindness

Alternative Name(s)
British Retinitis Pigmentosa Society, RP Fighting Blindness

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. James Loughman (james.loughman@dit.ie). In order to access the data, a data request form will be available on the project website. The form should be completed, signed and sent by email to james.loughman@dit.ie. Data will be disseminated through a dedicated access controlled website, on receipt of a fully completed, signed form. Incomplete or unsigned forms will be returned to the data requester for completion. The data request form will include:
1. Name and contact details
2. Dataset requested
3. Intended use of data
4. A list all users who will have access to and use of the data
5. Terms of use that the End User must undertake and agree
6. Indemnity
7. Disclaimer
8. Signatures

Consent: In compliance with the National Consent Policy of Ireland (2013 -16 Document reference QPSD-D-026- 1), parental consent and child consent/assent (dependent on child age and maturity) will be required before any study-related procedures being undertaken. Information leaflets will be provided to community practitioners through whom participants will be recruited. Study investigators will ensure that parents and children understand the trial completely including all information on the information leaflet. All participants will be afforded a minimum 1 week period to consent to participation, and may withdraw consent at any time. Subjects (or parent/guardian) unable to provide written informed consent will be excluded from the trial.

Data anonymisation: In Ireland, the Data Protection Acts 1988 and 2003 regulate research activities including the collection, storing, accessing and disclosing of personal data held in either electronic or manual filing systems by individuals or in general organisational records. In terms of this legislation, which does not expressly specify a particular age threshold for consent, the agreement to allow disclosure of identifiable information on a child research participant must be sought from the child's parent or guardian. However, good practice principles require that the child, depending on age and competence, be fully informed of these issues and provides assent where applicable.

Protection Measures:
Dublin Institute of Technology and its employees, under the Data Protection Act 1988 and the Data Protection (Amendment) Act 2003 is required to safeguard the privacy rights of individuals in relation to the processing of personal data. The Data Protection Acts confer rights on individuals as well as responsibilities on those persons processing personal data.

The study will maintain strict measures to protect patient and subject confidentiality:
1. Information will be distinguished using a personal identification number generated for each

participant
2. The document containing participant's personal information will be stored/accessed separately from the anonymised data
3. Samples collected will be anonymised
4. Access to data will be restricted to the investigators, password protected and encrypted
5. The office where the data and atropine drops are to be stored is locked when not occupied
6. All study laptops will be locked when not in use. Desktop computers and laptops will be password secured and encrypted. Only the trial investigators and research assistant will know the password
7. Data that is highly sensitive or that is potentially identifiable is not included in the public release dataset
8. No sensitive data will be released
9. Any potentially identifiable data, that is data based on which an individual could be identified, on its own or in combination with other publically available data sources will to be either top-coded, grouped or dropped completely

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	2-year changes in macular choroidal thickness	29/12/2024	02/01/2025	Yes	No
Results article	Efficacy and Safety of Different Atropine Regimens for the Treatment of Myopia in Children: Three-Year Results of the MOSAIC Randomized Clinical Trial	09/01/2025	20/01/2025	Yes	No
Protocol article	protocol	23/07/2019	03/02/2020	Yes	No
Interim results article	2-year results	11/09/2023	27/09/2024	Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes