A phase III, randomized, double-masked, placebo-controlled, parallel-group, multicenter study of the safety and efficacy of OT-101 (Atropine Sulfate 0.01%) in treating the progression of myopia in pediatric subjects

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To evaluate the efficacy of OT-101 Ophthalmic Solution in treating the progression of myopia in pediatric subjects following 3 years of treatment.To evaluate the safety and tolerability of OT-101 Ophthalmic Solution in pediatric subjects with myopia...

Ethical review	Not approved
Status	Will not start
Health condition type	Vision disorders
Study type	Interventional

Summary

ID

NL-OMON51907

Source
ToetsingOnline

Brief title
Dolphin Trial

Condition

- Vision disorders

Synonym
Eye Disease, Myopia

Research involving
Human

Sponsors and support

Primary sponsor: Ocumension (Hong Kong) Limited
Source(s) of monetary or material Support: Ocumension (Hong Kong) Limited

Intervention

Keyword: Atropine Eyedrops, Children, Myopia

Outcome measures

Primary outcome

Primary Efficacy Endpoint: Percentage of subjects with a -0.75D of progressive myopia at Month 36 defined as an increase in spherical equivalent of -0.75D or greater as assessed by cycloplegic autorefraction.

Secondary outcome

Key Secondary

* Change from baseline to Month 36 in study eye spherical equivalent (D) as assessed by cycloplegic autorefraction

* Change from baseline to Month 36 in study eye axial length as measured by cycloplegic biometry (will be selected and the same device to be used throughout the duration of this study)

Secondary

* Percentage of study eyes with annual myopia progression rate through Month 36

* -0.50 D

* Change from baseline to each visit through Month 36 in study eye spherical equivalent (D) as assessed by cycloplegic autorefraction

* Percentage of study eyes with a -0.75 D of progressive myopia from Month 36

to each post-Month 36 visit defined as an increase in spherical

equivalent of -0.75 D or greater as assessed by cycloplegic

autorefraction

* Change from Month 36 to each post-Month 36 visit in study eye spherical

equivalent (D) as assessed by cycloplegic autorefraction

* Change from baseline to each visit in study eye axial length as measured by

cycloplegic biometry (will be selected and the same device to be

used throughout the duration of this study)

* Change from baseline to Month 24 and 36 in study eye spherical equivalent (D)

as assessed by manual cycloplegic refraction

* Percentage of study eyes within each of the following change from baseline

spherical equivalent categories at each visit: *-0.50 D, -0.75 D, -1.0

D, -1.5 D or greater (in 0.5 D increments) as assessed by cycloplegic

autorefraction

Percentage of study eyes within each of the following change from Month 36

spherical equivalent categories to each post-Month 36visit: *-0.50 D, - 0.75 D,

-1.0 D, -1.5 D or greater (in 0.5 D increments) as assessed by cycloplegic

autorefraction

Study description

Background summary

Myopia (short-sightedness) is an ophthalmic condition in which light focuses in front of, instead of on, the retina (back of the eye). The condition occurs

when the eye grows too long (so slightly more of an oval shape) or due to a defect in the refractive power (bending of light) of the cornea (front part of the eye) and/or lens which makes distant objects look blurred. Myopia is a global problem, in the UK, the number of myopic children has more than doubled in the last 50 years.

The risks for becoming highly myopic (very short-sighted) include parents with myopia, East Asian ethnic origin, Myopia before the age of nine, limited time spent outdoors and increased time spent engaging in near vision activities (smartphone and computers). Early signs and symptoms of myopia include squinting, eyestrain and headaches. Myopia is a progressive disease (meaning the short-sightedness becomes worse as the eye grows). This progression of short-sightedness results in more frequent trips to the Ophthalmologist/Optometrist to update your glasses. The higher the glasses prescription becomes, the thicker and heavier the glasses are. Rather than treating short-sightedness, opticians and ophthalmologists currently treat the optical consequences of it by prescribing glasses and contact lenses or opting for laser refractive surgery, which is not available to patients under 18 years. However, potentially slowing, controlling and possibly treating myopia progression would reduce the burden of glasses/contact lens wear.

Study objective

To evaluate the efficacy of OT-101 Ophthalmic Solution in treating the progression of myopia in pediatric subjects following 3 years of treatment.
To evaluate the safety and tolerability of OT-101 Ophthalmic Solution in pediatric subjects with myopia.

Study design

Multi-center, randomized, double-masked, parallel-group, efficacy and safety study.
Control: vehicle (placebo).

This study will last approximately 4 years. Screening will last for approximately 2weeks. Stage 1, where subjects will be randomized in a 2:1 ratio to OT-101 Ophthalmic Solution or placebo, will last approximately 3 years. Stage 2, where subjects previously assigned to OT-101 Ophthalmic Solution will be re-randomized to either continue with OT-101 Ophthalmic Solution or switch to placebo and subjects previously assigned to placebo will continue with placebo, will last approximately 1 year.

Subjects will be stratified by age (baseline age:3-4, 5-8, 9-12, 13-15 years old) and refractive error (baseline refractive error: -1.00 D to -3.00 D, >-3.00 D to -6.00 D.

Intervention

All subjects will receive one drop of study drug in each eye at bedtime:
* OT-101 Ophthalmic Solution (QD)
* Placebo (vehicle) ophthalmic solution (QD)

Study burden and risks

Patients, parents -and/or guardians will have to come to the study site for 11 visits in 4 years. It could be that the child miss out on school / kindergarden / creche. They will have to complete a diary at home to keep eye drop intake. Patients will be followed for safety during the trial.

For patients who wish to end study medication treatment for any reason, they will be offered the option to remain in the study for safety visits.

Safety Assessments that will be done:
* Best-corrected distance VA
* Slit lamp biomicroscopy
* Dilated indirect ophthalmoscopy
* IOP
* Endothelial cell assessments
* Adverse events (AEs) (reported, elicited, and observed)
* Dosing and AE diary
* Accommodative amplitude from autorefractor
* Pupil diameter

Allergic reactions can occur with any drug. Risks related to the eye drops can be in the form of itching, difficulty breathing, and a skin rash and/or drop in blood pressure. In very rare cases, a child could suffer a life threatening allergic reaction. Observed side effects of atropine sulphate 0.01% ophthalmic solution is photophobia (1.0% - 9.6% occurrence in other studies), poor/ blurred near visual acuity/ reading problems (0%-5.0% occurrence), allergic conjunctivitis, recurrent allergic blepharitis (2.7% - 4% occurrence in other studies), pupil dilatation (1.0-5.0% occurrence).

A child may or may not receive any direct benefit from taking part in the research study. We hope that if a child receives atropine then this may treat the progression of their myopia so it does not worsen. However this cannot be guaranteed. The information we get from this research study may help us tp reduce myopia progression in future patients and may help us to better understand myopia.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Children (2-11 years)

Inclusion criteria

Subjects must:
1. A parent or legal guardian of each subject must provide written informed consent and sign the HIPAA form (or equivalent, if applicable), approved by the appropriate Institutional Review Board (IRB)/Ethical Committee (EC). Whenever practical and appropriate per local requirements, a child*s assent should also be sought before inclusion into the study;
2. Be able to comply with study requirements, attend all study visits, have ability to read and understand native language of subject and be accompanied by a parent/legal guardian;
3. Be between 3-15 years of age of either sex and any race or ethnicity at Visit 1 (Day -14 to -1);
4. Have refractive error by cycloplegic autorefraction at baseline (Visit 1) of:

a) myopia between -1.00D and -6.00 D, inclusive of spherical equivalent
b) astigmatism less than or equal to 1.50 DC
5. Have anisometropia * 1.0D of spherical equivalent at Visit 1;
6. Have a best-corrected distance visual acuity of (BCVA) of logarithm of the minimum angle of resolution (logMAR) *0.4 (approximately Snellen 20/50) for 3 year olds; logMAR *0.3 (approximately Snellen 20/40) for 4 year olds; logMAR *0.18 (approximately Snellen 20/30) for *5 year olds) in each eye as measured using an Early Treatment for Diabetic Retinopathy Study (ETDRS) chart [R,1 or 2], or Lea Chart for subjects who do not know the alphabet, at Visit 1 and Visit 2;
7. Be able and willing to avoid all prohibited medications during the washout period between screening and randomization and during the study without significant risk to the subject.

Exclusion criteria

Subjects must not:
1. Have known contraindications or sensitivity to atropine, the study medications, or their components;
2. Have clinically significant abnormal findings on slit lamp biomicroscopy exam (e.g. cataract) which may impact best corrected visual acuity measures in either eye at screening or a known history of a clinically significant slit lamps findings in either eye;
3. Have clinically significant abnormal findings on indirect dilated fundoscopy exam in either eye at screening or a known history of a clinically significant retinal findings in either eye;
4. Have any evidence of an eye movement disorder or restriction of extraocular movement (e.g. nystagmus);
5. Have an active ocular infection (i.e. bacterial, viral, or fungal);
6. Have active or a history of chronic or recurrent episodes of ocular inflammation (e.g. moderate to severe blepharitis, allergic conjunctivitis, peripheral ulcerative keratitis, scleritis) in either eye;
7. Have a history of ocular herpetic infection, iritis, scleritis, or uveitis, whether active or inactive at screening;
8. Have undergone any myopia control treatment including atropine, orthokeratology, rigid gas-permeable contact lenses, bifocal contact lenses, progressive addition spectacle lenses, or other lenses to reduce myopia progression in the previous 6 months. Myopic correction in the form of single-vision eyeglasses and/or single-vision soft contact lenses are allowed;
9. Have undergone any form of refractive eye surgery including incisional keratotomy, photorefractive keratectomy [PRK], laser in situ keratomileusis [LASIK], laser-assisted sub- epithelial keratectomy [LASEK]), corneal inlay procedures, conductive keratoplasty, small incision lenticule extraction (SMILE), cataract extraction, or any form of intraocular lens implantation;
10. Have intraocular pressure (IOP) that is < 9 millimeters of mercury (mmHg)

or > 21 mmHg in either eye, or have a prior diagnosis of ocular hypertension or glaucoma or currently being treated with any type of topical IOP lowering (glaucoma) medication;
11. Have had surgical intervention (ocular or systemic) within 6 months prior to Visit 1, or planned surgical intervention during the study;
12. Use any of the following disallowed medications or therapies by any route of administration during the 2 weeks (14 days) prior to Visit 2 (Day 1):
a. any prescription or over the counter ophthalmic products (Use of preservative-free artificial tears is allowed but may not be used within 2 hours of administration of study medication. Use of lubricating ointment form of artificial tears before bedtime is allowed but must be used at least 15 minutes after administration of study medication.)
b. monoamine oxidase inhibitors
c. atropine, pirenzepine, or other anti-muscarinic agent
d. any medication affecting the pupil or accommodation
e. orthoK, rigid gas-permeable, bifocal, progressive-addition, multi-focal, or other lenses to reduce myopia progression
In addition, Groups b * e above are not allowed for the duration of the study.
13. The anticipated need to use chronic ophthalmic or systemic oral corticosteroids during the study. Intranasal, inhaled, topical dermatologic, intra-articular, perianal steroids, and short-term oral steroids (< 2 weeks) are permitted;
14. Participation in any other study of investigational therapy during the study period or within 30 days before Visit 1;
15. Female subjects who are pregnant, nursing, or plan to become pregnant at any time during the study;
16. History or current evidence of a medical condition predisposing the patient to degenerative myopia (e.g., Marfan syndrome, Stickler syndrome) or a condition that may affect visual function or development (e.g., diabetes mellitus, chromosome anomaly)
17. Have a central nervous system disorder (e.g., epilepsy, cerebral disorders, Down syndrome)
18. Have a condition or a situation, which in the Investigator*s opinion, may put the subject at increased risk, confound study data, or interfere significantly with the subject*s study participation, including but not limited to unstable: cardiovascular, hepatic, renal, respiratory, gastrointestinal, endocrine,immunologic, dermatologic, hematologic, neurologic, or psychiatric disease.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	15
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Atropine 0.01% (OT-101)
Generic name:	Atropine Sulfaat 0.01%

Ethics review

Approved WMO

Date:	07-10-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Not approved

Date:	24-03-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2020-003976-42-NL
ClinicalTrials.gov	NCT04770610
CCMO	NL76536.078.21