Childhood Atropine for Myopia Progression (CHAMP): A 3-Arm Randomized, Double-Masked, Placebo-Controlled, Phase 3 Study of Atropine Sulfate Ophthalmic Solution 0.01% and 0.02%

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Primary Objective: To evaluate the safety and efficacy of 2 concentrations of Atropine Sulfate OphthalmicSolution (0.01% and 0.02%) compared to Vehicle (placebo) for slowing the progression of myopia inchildren over a 3-year treatment period....

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Vision disorders
Study type	Interventional

Summary

ID

NL-OMON55813

Source
ToetsingOnline

Brief title
Childhood Atropine for Myopia Progression

Condition

- Vision disorders

Synonym
Myopia Progression, worsening shortsightedness

Research involving
Human

Sponsors and support

Primary sponsor: Vyluma Inc.
Source(s) of monetary or material Support: Vyluma Inc.

Intervention

Keyword: Atropine, Childhood, Myopia Progression

Outcome measures

Primary outcome

The between-treatment group difference in proportion of subjects who show <

-0.50 D myopia progression (SER) at the Month 36 visit.

Secondary outcome

1. Between- treatment group difference in mean change from baseline in SER at

the Month 36 visit.

2. Between-treatment group difference in the proportion of subjects who show

<-0.5 D myopia progression (SER) from baseline at the month 36 visit.

Study description

Background summary

Ametropia in children is common, and if left uncorrected causes decreased vision, visual
discomfort (eye strain), strabismus, and/or amblyopia (AAPOS 2013). The most common form
of refractive error is myopia (nearsightedness), which has its onset in children 6 to 12 years of
age (Zadnik 2015). The American Association for Pediatric Ophthalmology and Strabismus
(AAPOS) and American Academy of Ophthalmology (AAO) Joint Policy Statement in 2013

reports that it is important that myopia be addressed early in life because, in addition to correcting imperfect vision, good vision is essential for proper physical development and educational progress in growing children. If a growing child's eye does not provide a clear, focused image to the developing brain, irreversible loss of vision in one or both eyes may result (AAPOS 2013).

There are currently no Food and Drug Administration (FDA)-approved drug products to treat the progression of myopia in children. Topical ophthalmic drugs such as 1% atropine and 2% pirenzepine (both antimuscarinic agents) have been shown to slow myopia progression (Brodstein 1984; Yen 1989; Chua 2006; Fan 2007; Yi 2015); however, pirenzepine is not FDA approved for ophthalmic use, and although 1% atropine is approved by the FDA for topical ocular use (cycloplegia, mydriasis, and penalization of the healthy eye in the treatment of amblyopia), it is not approved to slow the progression of myopia. Further, treatments such as orthokeratology and the use of multifocal lenses have been used as therapy to slow the progression of myopia in children, however, neither has shown efficacy equivalent to that of antimuscarinic agents (Walline 2011).

Recent reviews (Walline 2011; Huang 2016; Gong 2017) have concluded that antimuscarinic topical medication is an effective treatment to slow myopia progression.

Study objective

Primary Objective: To evaluate the safety and efficacy of 2 concentrations of Atropine Sulfate Ophthalmic Solution (0.01% and 0.02%) compared to Vehicle (placebo) for slowing the progression of myopia in children over a 3-year treatment period.
Exploratory Objective: To observe safety and efficacy in subjects re-randomized to 1 year of treatment with Atropine Sulfate Ophthalmic Solution, 0.01% or 0.02%, or Vehicle following 3 years of treatment in children with progressive myopia.

Study design

This will be a 3-arm randomized, multicenter, double-masked, placebo-controlled study
conducted in 2 stages. Stage 1 is a safety and efficacy phase of 3 years (36 months) in duration,
during which subjects will be allocated 1 of 3 study medications. Stage 2 is a randomized
cross-over phase of 1 year (12 months) in duration, during which subjects will be re-randomized
to receive 1 of the 3 study medications with subjects initially randomized to Vehicle only eligible
for randomization to 0.01% or 0.02% Atropine Sulfate Ophthalmic Solution. Subjects (aged 3 to
<= 17.0 years) will enter the study with myopia SER of at least -0.50 D and no greater than -6.00
D myopia in each eye as measured by cycloplegic autorefraction, and following successful
eligibility screening at the Screening/Baseline visit will be randomized to one of the following 3
treatment groups in a 2:2:3 ratio:
* Vehicle (placebo) (N = 138)
* Atropine Sulfate Ophthalmic Solution, 0.01% (N = 138)
* Atropine Sulfate Ophthalmic Solution, 0.02% (N = 207)

Intervention

The allocated study medication will be administered, one drop in each eye once daily (QD), at bedtime, for 3 years.
Treatment arms are:
* Atropine Sulfate Ophthalmic Solution, 0.01%
* Atropine Sulfate Ophthalmic Solution, 0.02%
* Vehicle (placebo)

Study burden and risks

The subject's myopia may or may not get worse while taking part in this study. The results of this study may help children with myopia in the future. If Atropine eye drops are effective in treating the progression of myopia, participants receiving placebo may not receive the same benefit as those who receive the active drug.

SIDE EFFECTS THAT MAY OCCUR WHILE USING ATROPINE SULFATE:
• Eye discomfort
• Glare
• Blurred near vision

• Light sensitivity
• Pain and stinging at time of drop
• Inflammation of the cornea (clear layer on the front of the eye)
• Dry eye
• Redness and swelling of the eye or eyelid
• Irritability
• Fast heart beat
• Restlessness
• Dryness of skin, mouth or throat
• Flushed skin on face and neck

There may be other risks or side effects of Atropine eye drops that are unknown at this time. Allergic reactions can occur with any drug.

POSSIBLE RISKS OR SIDE EFFECTS OF THE STUDY PROCEDURES
Possible risks of numbing drops
The numbing drops that are used for checking the eye pressure may sting for a few seconds when they are first placed in the eyes. It is important that the subjects don*t rub their eyes while they are numb to avoid scratching the surface of the eyes.

Possible risks of dilating drops
The drops used to dilate the eyes may sting when they are first placed in the eyes. They may cause blurry vision for a few hours, especially thereading vision, and cause sensitivity to light. To protect the eyes and minimize discomfort, the subject should wear sunglasses while outside, until the effects of the drops wear-off.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

1. Children (male or female) aged 3 to <= 17.0 years.
2. Myopia SER of at least -0.50 D and no greater than -6.00 D myopia in each eye as measured
by cycloplegic autorefraction.
3. If present, astigmatism of no more than -1.50 D in each eye as measured by cycloplegic
autorefraction.
4. Anisometropia SER of < 1.50 D as measured by cycloplegic autorefraction.
5. Normal intraocular pressure of < 21 mm Hg in each eye.
6. Distance vision correctable to at least 0.1 logMAR or 20/25 Snellen equivalent in each eye.
7. Female subjects of childbearing potential (post menarche) must have a negative urine
pregnancy test at screening.
8. Subject*s parent or legal guardian must provide informed consent on behalf of the subject, and
the subject should provide assent when applicable, per Institutional Review Board (IRB)/Ethic
Committee (EC) guidelines. If a subject becomes an adult (depending on country regulations)
during the study, they will need to sign an informed consent form to continue in the study

Exclusion criteria

1. Allergy to atropine or any of the excipients of the eye drops.
2. Current or history of amblyopia or manifest strabismus including intermittent tropia.

3. Heart rate is persistently (for more than 10 minutes) > 120 beats per minute at
screening/baseline.
4. History of any disease or syndrome that predisposes the subject to severe myopia (e.g., Marfan
syndrome, Stickler syndrome, retinopathy of prematurity).
5. History in either eye of abnormal ocular refractive anatomy (e.g., keratoconus, lenticonus,
spherophakia).
6. History in either eye of previous intraocular or ocular laser/non-laser surgery.
7. Current or history of glaucoma; anatomic narrow anterior chamber angles.
8. Serious systemic illness that, in the Investigator*s opinion, would render the subject ineligible
9. Chronic use of any topical or systemic antimuscarinic/anticholinergic medications (e.g.,
atropine, scopolamine, tropicamide) within 21 days prior to screening, and/or anticipated need
for chronic use during the study period (i.e., more than 7 consecutive days in 1 month or more
than 30 total days in 1 year). (Use of cycloplegic drops for dilated ocular exam are allowable.)
10. Chronic use (more than 3 days per week) of any topical ophthalmic medications (prescribed or
over-the-counter) other than the assigned study medication. Use of artificial tears is allowed
but may not be used within 2 hours of administration of study medication.
11. 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 (i.e., < 2 weeks) are permitted.
12. Prior myopia control treatment including orthokeratology, bifocal contact lenses, or
progressive addition spectacle lenses. The only allowable prior treatments are myopic
correction in the form of single-vision eyeglasses and/or single-vision or toric soft contact
lenses.
13. Preplanned hospitalization during the study period.
14. Unwilling or unable to complete study procedures or to be followed up for the 48-month
duration of the study.
15. Participation in any other study of investigational therapy during the study period or within the
last 30 days.
16. History of any substance abuse (excessive or habitual use of alcohol and/or

drug including
nicotine) and not willing to abstain from these substance(s) during the 4-year study period.
17. Female subjects who are pregnant, nursing, or plan to become pregnant at any time during the
study.
18. Employees of the study site and their family members are not permitted to participate as
subjects in the study. Immediate family is defined as a spouse, parent, child, or sibling,
whether biological or legally adopted.
19. Current or history of significant or severe damage to the cornea.

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:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-04-2019
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Not applicable
Generic name:	Atropine Sulfate Ophthalmic Solution

Ethics review

Approved WMO Date:	25-06-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-10-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-03-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-04-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-10-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-12-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-02-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	04-03-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-05-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-05-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-09-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-10-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-10-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-02-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-03-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	24-10-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-12-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-04-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-06-2022
Application type:	Amendment
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	EUCTR2018-001077-24-NL

Register	ID
ClinicalTrials.gov	NCT03350620
CCMO	NL65901.078.18