A 3 Month, Multicenter, Double-Masked Safety and Efficacy Study of Travoprost Ophthalmic Solution, 0.004% Compared to Timolol (0.5% or 0.25%) in Pediatric Glaucoma Patients

Published: 25-02-2013
Last updated: 24-04-2024

The primary objective of this study is to demonstrate that the IOP-lowering efficacy of Travoprost Ophthalmic Solution, 0.004% (preserved with POLYQUAD) is noninferior to Timolol Ophthalmic Solution (0.5% or 0.25%) in pediatric glaucoma patients.

Ethical review	Not approved
Status	Will not start
Health condition type	Glaucoma and ocular hypertension
Study type	Interventional

Summary

ID

NL-OMON38960

Source
ToetsingOnline

Brief title
Travoprost 0.004% in Pediatric Glaucoma Patients

Condition

- Glaucoma and ocular hypertension

Synonym
raised intra-ocular pressure with optic nerve damage

Research involving
Human

Sponsors and support

Primary sponsor: Alcon Laboratories
Source(s) of monetary or material Support: Alcon Research Ltd.

Intervention

Keyword: glaucoma, pediatric, Travatan

Outcome measures

Primary outcome

IOP change from baseline at Month 3

Secondary outcome

Not Applicable

Study description

Background summary

Glaucoma is an eye condition associated with an abnormally high pressure in the eye (called intraocular pressure or IOP). If left untreated, elevated IOP may eventually cause damage to the optic nerve and a loss of vision. Treatment for glaucoma is aimed at lowering pressure in the eye and there are different types of medications that can be used for this; Among the pharmacological treatments, the most commonly used are eye drops containing drugs of different classes.

Studies describing off-label use of Travoprost Solution, 0.004% (preserved with BAK) or latanoprost 0.005% in pediatric glaucoma populations suggest that prostaglandin analogs generally confer significant IOP-lowering efficacy, are well tolerated with few systemic side effects, and provide a long duration of action with convenience through once daily administration (Yanovitch 2009, Helmanova 2007). These studies suggest that statistically significant and clinically meaningful IOP reductions in pediatric populations were observed when Travoprost was used either as a monotherapy or adjunctive to other topical ocular hypotensive medications. Ocular side effects associated with Travoprost or the prostaglandin analogue class such as conjunctival injection and ocular irritation were generally mild and transient. No evidence of iris pigmentation changes was noted and no clinically relevant systemic side effects were reported. Therefore, Travoprost Ophthalmic Solution, 0.004% preserved with POLYQUAD is the most appropriate formulation to evaluate in the pediatric

glaucoma population.

Study objective

The primary objective of this study is to demonstrate that the IOP-lowering efficacy of Travoprost Ophthalmic Solution, 0.004% (preserved with POLYQUAD) is noninferior to Timolol Ophthalmic Solution (0.5% or 0.25%) in pediatric glaucoma patients.

Study design

Approximately 4 months during, multicenter, double-masked, randomized study with a parallel-group.
Patients will be randomized in a 1:1 manner to receive treatment with Travoprost Ophthalmic Solution, 0.004% or Timolol Ophthalmic Solution, 0.5% (or 0.25% for children < 3 years of age), respectively.

Intervention

Not applicable

Study burden and risks

In a period of 4 months, patients need to come to the hospital 5 times for an ophthalmic examination. Each visit will take approximately 1 to 2 hours of their time. None of the tests are experimental.

Participation in this trial may cause little risk/ discomfort:
If the child is currently using medication to control the pressure in his/her eyes, an increase in the pressure could occur during this study. This may occur at any time during the study and particularly when they stop the drops they are taking before beginning the study (washout period). An increase in the pressure in the eye can result in damage to the optic nerve and consequently cause loss of vision and, depending on the severity and duration of the high pressure, may result in blindness. If the pressure in the child*s eyes increases, the child*s study doctor will determine whether they should continue in the study or be removed from the study. In addition, the study doctor will discuss alternative therapies for the child.

The tests used in the examinations should cause little discomfort. The eye-pressure test involves the placement of eye drops containing a small amount of a numbing drop into the eye.

It is important that the child not rub his/her eyes for at least 15 minutes after the drops are put in the eye since small particles or dust in the eye might scratch the cornea and the numbing drop would make the child temporarily

unable to feel the pain. Minor scratching of the corneal surface may rarely occur when the pressure in the eye is measured and usually heals very quickly.

The eye drops put into the child*s eye to dilate (enlarge) the pupil to allow for a better view of the inside and back of the eye may cause his/her vision to be blurred for a few hours and may also cause the child to be more sensitive to bright light until the medication wears off. While your child*s eyes are dilated, they should be protected from bright light. Wearing sunglasses for several hours after dilation can help reduce the discomfort of light sensitivity.

Both of the medications tested in this study can cause side effects.
Travoprost is currently marketed (TRAVATAN®) to reduce pressure in the eyes of adult patients with open-angle glaucoma or ocular hypertension. A common side effect reported with the use of Travoprost has been color changes in the iris (eye color) causing blue eyes to turn brown. Also color changes in the eyelids have been reported as well as increased eye lash length, thickness, color and/or number of lashes. These changes may be permanent. In other Travoprost clinical studies, the most common side effect observed was red eyes (hyperemia) in 30-50 percent of the subjects. Other events reported in 5-10 percent of the subjects were a decrease in vision, eye discomfort, a feeling of something in the eye or itchy eyes (pruritus).
Side effects reported with the use of timolol eye drops include dizziness, decreased heart rate, decreased blood pressure, and shortness of breath. Allergic reactions to the study eye drops are usually local (affecting the eye with itching, redness, etc.) rather than generalized (throughout the body). Allergic reactions can make the eye itch and cause eye redness.

Due to the nature of this research study and the unknown side effects of the study drug on pregnant women, fetuses, unborn children, and nursing infants, your child is not permitted to participate in this study if she is pregnant, at risk of becoming pregnant, or a nursing mother. If your child is a female able to bear children she must have a negative urine pregnancy test before participating in the study and she must agree to use an a highly effective form of contraception during the course of this study if she is sexually active. Adequate birth control methods include: (A) true abstinence; (B) hormonal methods: implantable chemical contraceptives; or (C) mechanical methods: intrauterine device (IUD) with progestogen; or (D) surgical sterilization of partner. The child must also agree to avoid becoming pregnant during the course of the study, and must immediately stop taking the study drops and inform your study doctor should she become pregnant.

If the child is a male whose partner is of childbearing potential, he should make sure that a partner uses a reliable means of birth control (such as IUD with progestogen to avoid fathering a child while taking part in this study. This is because the effects of the study drug on the development of an unborn

child are not known.

Contacts

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Alcon Laboratories

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

1. Patients 2 months to <18 years of age
2. Diagnosis of pediatric glaucoma.
3. Patients with conditions requiring chronic treatment with glucocorticoids resulting in steroid induced glaucoma may be enrolled as long as the patient has been on a stable dose of steroids for at least 30 days prior to the Screening Visit.
4. Qualifying mean IOP at the Eligibility Visit in at least one eye must be:

* * 20 mmHg at the 9 AM (± 60 minutes) time point
Note: Mean IOP is the average of 2 successive IOP measurements in the same eye, as described in the Manual of Procedures. A third measurement is required if the first 2 measurements differ by more than 4 mmHg.
5. Aphakic patients with contact lenses may be enrolled. If study drops are to be instilled with lens in place, patient will be provided with a contact lens to be used during the study.
6. Written informed consent, including assent when applicable, MUST be obtained from the parent or legally authorized representative prior to any procedure specified in the protocol, including screening procedures.

Exclusion criteria

1. Females of childbearing potential are excluded from participation in the study if they meet any of the following conditions:
a. They are currently pregnant
b. They have a positive result on a pregnancy test at the Screening Visit
c. They intend to become pregnant during the study period
d. They are breast feeding
e. They are not using any of the following highly effective birth control
measures:
* True abstinence * when this is in line with the preferred and usual lifestyle of the subject. If subjects become sexually active, they must agree to use one of the birth control methods (hormonal, mechanical, or surgical) listed below for the remainder of the study.
* Hormonal * implanted contraceptives.
* Mechanical *IUD with progestogen.
* Surgical * vasectomized partner (must be * 6 months post vasectomy).
Note: All females of childbearing potential must consent to a urine pregnancy test at the Screening Visit and upon exiting the study.
Note: Females of childbearing potential will be instructed to immediately inform the Investigator if they become pregnant during the study. Should this occur, the Investigator shall immediately contact the Sponsor).
2. Patients who have previously failed long-term treatment with a prostaglandin analog or timolol to control IOP or patients in which reasonable IOP control would not be expected from pharmacological treatment.

3. History of chronic, recurrent or severe inflammatory eye disease (ie, scleritis, uveitis, herpes keratitis).
4. Ocular trauma requiring medical attention within the past 3 months prior to the Screening Visit.
5. Ocular infection or ocular inflammation within the past 30 days prior to the Screening Visit.
6. Clinically significant or progressive retinal disease such as retinal degeneration, diabetic retinopathy, or retinal detachment in the study eye.
7. Severe ocular pathology (including severe dry eye) in the opinion of the Investigator that would preclude the administration of a topical prostaglandin analog or a topical beta-blocker.
8. Intraocular surgery within the past 30 days in the study eye prior to the Screening Visit.
9. Any abnormality preventing reliable applanation tonometry, including a history of penetrating keratoplasty.
10. Patients with a history of previous cyclodestructive procedure.
11. Any other conditions including severe illness which would make the patient, in the opinion of the Investigator, unsuitable for the study.
12. Hypersensitivity to any component of the study medications, including medications administered during study exams, in the opinion of the Investigator.
13. History of congenital cardiovascular anomalies or abnormalities which would preclude the safe administration of a topical beta-blocker. In the event that the effects of the study medications are unclear, the patient may participate with written approval from the patient*s cardiologist.
There is a potential for additive effects resulting in hypotension and/or marked bradycardia when eye drops with timolol are administered concomitantly with oral calcium channel blockers, quanethidine or beta-blocking agents, antiarrhythmics, digitalis glycosides or parasympathomimetics.
The hypertensive reaction to sudden withdrawal of clonidine or can be potentiated when taking beta-blockers. Potentates systemic beta-blockade (e.g. decreased heart rate) has been reported during combined treatment with CYP2D6 inhibitors (e.g. quinidine, cimetidine) and timolol. Beta-blockers may increase the hypoglycemic effect of anti-diabetic agents. Beta-blockers can mask the signs and symptoms of hypoglycemia.
Investigators must use their clinical judgment regarding the use of these products during the study.
14. Use of any additional topical or systemic ocular hypotensive medication during the study.
15. Less than 30 days stable dosing regimen before the Screening

Visit of any medications (excluding the IOP-lowering treatments) or substances administered by any route and used on a chronic basis that may affect IOP (ie, * adrenergic blocking agents). The dosing regimen of these medications should not change during the study.
16. Therapy with another investigational agent or device within 30 days prior to the Screening Visit.
17. Patients with reactive airway disease including bronchial asthma or a history of bronchial asthma, severe chronic obstructive pulmonary disease; sinus bradycardia; sick sinus syndrome, sino-atrial block, second or third degree atrioventricular block not controlled with pace-maker; overt cardiac failure; and cardiogenic shock.
18. Patients with severe allergic rhinitis.
19. Patients with corneal dystrophies.

Study design

Design

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	5
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	TIMOLOL MALEATE Ophthalmic Solution USP, 0.25%

Generic name:	TIMOLOL MALEATE Ophthalmic Solution USP, 0.25%
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	TIMOLOL MALEATE Ophthalmic Solution USP, 0.50%
Generic name:	TIMOLOL MALEATE Ophthalmic Solution USP, 0.50%
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	TRAVOPROST 0.004%
Generic name:	TRAVOPROST 0.004%
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	25-02-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Not approved Date:	08-05-2013
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	EUCTR2012-001324-34-NL
ClinicalTrials.gov	NCT01652664
CCMO	NL43025.078.13