Efficacy and Safety of Brinzolamide 10 mg/ml / Brimonidine 2 mg/ml Eye Drops, Suspension Compared to Brinzolamide 10 mg/ml Eye Drops, Suspension plus Brimonidine 2 mg/ml Eye Drops, Solution in Patients with Open-Angle Glaucoma or Ocular Hypertension.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glaucoma and ocular hypertension
Study type	Interventional

Summary

ID

NL-OMON36182

Source
ToetsingOnline

Brief title
Brinz/Brim BID versus Brinzolamide + Brimonidine BID in OAG or OHT

Condition

- Glaucoma and ocular hypertension

Synonym
raised intra-ocular pressure with optic nerve damage, raised intra-ocular pressure without

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: - Brinz/Brim fixed combination, - IOP control

Outcome measures

Primary outcome

Primary Efficacy:

• Mean diurnal IOP Change from Baseline at Month 3 (patient IOP change from

baseline averaged over the 9 AM and +2 hrs time points)

Secondary outcome

There are no secondary efficacy endpoints.

Study description

Background summary

Open-angle glaucoma and ocular hypertension are eye conditions associated with abnormally high fluid pressure in the eye (called intraocular pressure of IOP). If left untreated, elevated IOP may eventually cause damage to the optic nerve and a loss of vision. Treatment for both open-angle glaucoma and ocular hypertension 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;
Among several possible drugs available for the treatment of elevated eye pressure, the two that will be used in this study are *brinzolamide* (AZOPT®, Brinzolamide 10mg/ml, Eye Drops, Solution) and *brimonidine* (Brimonidine Tartrate 2 mg/ml, Eye Drops, Solution, available on the market in several countries with different trade names, eg., ALPHAGAN). Brinzolamide belongs to

a class of drugs known as carbonic anhydrase inhibitors (CAI) that reduce eye pressure by decreasing the production of fluid (aqueous humor) in the eye. Brimonidine is an alpha 2 adrenergic agonists and can decrease the production of fluid (aqueous humor) and also increase the rate it drains from the eye. Both products are currently available and can be used alone or in combination with other products when the treatment with only one drug is not sufficient to decrease the eye pressure as desired.

Patients may already use both medications at the same time as directed by their eye doctor; however, the combination of these two drugs in a single bottle would be a more convenient way to use the medication, making it easier to follow dosing instructions, and consequently, better maintain the eye pressure levels.

Study objective

The purpose of this research study is to demonstrate that the fixed combination brinz/brim used twice daily has a similar effect (both in terms of reduction of the eye pressure and possible side effects) as brinzolamide and brimonidine used twice daily as separate medications in concomitant administration.

Study design

Approximately 7 months (inclusive wash-out period), 2 arms, parallel groeps, multicenter, double-masked, randomised, active-controlled study:
- Brinzolamide 10 mg/ml / Brimonidine 2 mg/ml eye drops suspension (+ for masking: Vehicle eye drops, solution) (2X per day)
- Brinzolamide 10 mg/ml eye drops, suspension (2X per day) and Brimonidine 2 mg/ml eye drops, solution (2X per day)

Intervention

Not applicable

Study burden and risks

In a period of 6 months, patients need to come to the hospital 7 times for an ophthalmic examination. each visit will take approximately 90 minutes of their time. None of the tests are experimental.

All the patients will receive both brinzolamide and brimonidine, either as separate medications or together in the same bottle. Like with all medicines, these medications can cause side effects, although not everyone gets them. It is expected that the possible side effects will be very similar in the two groups and will be reflective of the side effects reported with brimonidine and brinzolamide described below

The common side effects observed with brinzolamide:
In the body: include general side effects like a bitter or unusual taste in the mouth (dysgeusia), headache, and dry mouth,
In the eye like blurred vision, eye irritation, eye pain, eye discharge, itchy eye, dry eye, a feeling of something in the eye (foreign body sensation), red eye, inflammation of the eyelid (blepharitis)

The most common side effects seen with brimonidine:
In the body: dry mouth, tiredness/drowsiness, headache, dizziness, abnormal taste or general weakness.
In the eye: allergic reactions in the eye, follicles or white spots on the see-through layer which covers the surface of the eye (conjunctival follicles), blurred vision, red eyes, burning, stinging, a feeling of something in the eye (foreign body sensation), itchy eyes, changes to the surface of the eye, inflammation of the eyelid, inflammation of the see-through layer which covers the surface of the eye, abnormal vision, sticky eyes, swelling of the eyelid or see-through layer which covers the surface of the eye, sensitivity to light (photophobia), irritation, eyelid redness, pain, dryness, erosion on the surface of the eye and staining, tears or whitening of the see-through layer which covers the surface of the eye.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1) Patients 18 years of age or older, of either gender, and any race/ethnicity, diagnosed with open-angle glaucoma or ocular hypertension who in the opinion of the investigator are insufficiently controlled on monotherapy or are currently on multiple IOP-lowering medications.
2) Mean IOP measurements in at least one eye, the same eye(s), must be:
• >= 24 mmHg and <= 36 mmHg at the 9 AM time point and
• >= 21 mmHg and <= 36 mmHg at the 11 AM time point ,
at both Eligibility 1 and Eligibility 2 Visits, following wash-out of any IOP-lowering medication. Mean IOP must not be > 36 mmHg at any time point.
3) Must be able to understand and sign an informed consent form that has been approved by an Independent Ethics Committee

Exclusion criteria

1. Women of childbearing potential (who are not postmenopausal for at least 1 year or surgically sterile) are excluded from participation if they are currently pregnant, have a positive result on the urine pregnancy test at Screening, or intend to become pregnant during the study period; are breast-feeding; are not in agreement to use adequate birth control methods (see the Manual of Procedures) to prevent pregnancy throughout the study.
2. Schaffer angle Grade < 2 as measured by gonioscopy (extreme narrow angle with complete or partial closure).
3. Cup/disc ratio (C/D) greater than 0.80 (horizontal or vertical measurement).
4. Severe central visual field loss. Severe central visual field loss is defined as a sensitivity of less than or equal to 10 dB in at least 2 of the 4 visual field test points closest to the point of fixation.
5. Patients who cannot safely undergo the initial wash-out period discontinuing all IOP-lowering ocular medication(s) for a minimum of 5 (± 1) to 28 (± 1) days prior to E1 Visit.
6. Chronic, recurrent or severe inflammatory eye disease (ie, scleritis, uveitis, herpes keratitis).
7. Ocular trauma within the past 6 months.
8. Ocular infection or ocular inflammation within the past 3 months.
9. Clinically significant or progressive retinal disease such as retinal degeneration, diabetic retinopathy, or retinal detachment.
10. Best-corrected visual acuity (BCVA) score worse than 55 ETDRS letters (equivalent to approximately 0.60 logMAR, 20/80 Snellen, or 0.25 decimal).

11. Other ocular pathology (including severe dry eye) that may, in the opinion of the Investigator, preclude the administration of α-adrenergic agonist and/or topical carbonic anhydrase inhibitor (CAI).
12. Intraocular surgery within the past 6 months.
13. Ocular laser surgery within the past 3 months.
14. Any abnormality preventing reliable applanation tonometry.
15. Any other conditions including severe illness which would make the patient, in the opinion of the Investigator, unsuitable for the study.
16. History of active, severe, unstable or uncontrolled cardiovascular (eg, coronary insufficiency, hypertension, Raynaud*s phenomenon, orthostatic hypotension, thromboangiitis obliterans), cerebrovascular (eg, cerebral insufficiency), hepatic, or renal disease that would preclude
the safe administration of a topical α-adrenergic agonist or CAI in the opinion of the investigator.
17. Recent (within 4 weeks of the E1 Visit) use of high-dose (>1 g daily) salicylate therapy.
18. Current or anticipated treatment with any psychotropic drugs that augment adrenergic response (eg, desipramine, amitriptyline).
19. Concurrent use of monoamine oxidase inhibitors (MAOI).
20. Concurrent use of glucocorticoids administered by any route.
21. Therapy with another investigational agent within 30 days prior to the Screening Visit.
22. Hypersensitivity to α-adrenergic agonist drugs, topical or oral CAIs, sulfonamide derivatives, or to any component of the study medications in the opinion of the Investigator.
23. Less than 30 days stable dosing regimen before the Screening Visit of any medications or substances administered by any route and used on a chronic basis that may affect IOP, including but not limited to β-adrenergic blocking agents.
24. Use of any additional topical or systemic ocular hypotensive medication during the study.

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:	Recruitment stopped
Start date (anticipated):	11-08-2011
Enrollment:	36
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Brimonidine 2 mg/ml eye drops, solution
Generic name:	Brimonidine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Brinzolamide 10 mg/ml / Brimonidine 2 mg/ml eye drops, suspension
Generic name:	Brinzolamide / brimonidine
Product type:	Medicine
Brand name:	Brinzolamide 10 mg/ml eye drops, suspension
Generic name:	AZOPT
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	09-05-2011
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	22-06-2011
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	03-08-2011

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	07-09-2011
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	08-09-2011
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	16-09-2011
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	07-03-2012
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-04-2012
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	24-04-2012
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	EUCTR2010-024513-31-NL
ClinicalTrials.gov	NCT01309204
CCMO	NL36677.008.11