Safety and Efficacy with Twice Daily Brinzolamide 1% / Brimonidine 0.2% (SIMBRINZA) as an Adjunctive Therapy to Travoprost 0.004% / Timolol 0.5% (DUOTRAV)

Published: 11-10-2016
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To demonstrate the additive IOP lowering effect of SIMBRINZA (dosed BID) when added to DUOTRAV solution in subjects with open-angle glaucoma or ocular hypertension.

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

Summary

ID

NL-OMON46879

Source
ToetsingOnline

Brief title
Maximal Medical Therapy Achieved with SIMBRINZA and DUOTRAV

Condition

- Glaucoma and ocular hypertension

Synonym
ocular hypertension, open-angle glaucoma

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma

Intervention

Keyword: adjunctive therapy, ocular hypertension, open-angle glaucoma

Outcome measures

Primary outcome

Change from baseline in diurnal IOP (mean of changes at 09:00 and11:00 time

points) at Week 6.

Secondary outcome

Secondary Efficacy:

* Diurnal IOP at Week 6.

* Percentage change from baseline in diurnal IOP at Week 6.

* IOP change from baseline at Week 6 at 11:00 hrs.

* Percentage change from baseline in IOP at Week 6 at 11:00 hrs.

IOP change from baseline at Week 6 at 09:00 hrs.

* Percentage change from baseline in IOP at Week 6 at 09:00 hrs.

Exploratory Efficacy:

* Difference between treatments in IOP at Week 6 for each time point.

* Percentage of subjects achieving diurnal IOP targets (* 12,13,14...,25) at

Week 6.

* Difference between treatments in Ocular perfusion pressure at week 6 (Diurnal

and individual time points).

* Mean diurnal IOP, change in diurnal IOP, and percentage change in diurnal IOP

at week 6 within subsets of : a. Baseline IOP: 19-24 mmHg, >24-28 mmHg // b.

Age category: < 50, 50-65, > 65; sex; race (Caucasian, Black, Asian, Hispanic,

Other), region (EMEA, Asia, LACAR).

Study description

Background summary

Open-angle glaucoma and ocular hypertension are eye conditions associated with abnormal high fluid pressure in the eye (intraocular pressure/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.

SIMBRINZA is a fixed combination therapy. This product contains two glaucoma medications in the same bottle (Brimonidine Tartrate Ophthalmic Solution 0.2% and Brinzolamide 1%). Brimonidine Tartrate belongs to a class of drugs used to treat ocular hypertension known as alpha 2 adrenergic agonists. It has been shown that Brimonidine Tartrate lowers IOP by both decreasing the production of fluid (aqueous humor) as well as increasing the rate the fluid (aqueous humor) drains from the eye. Brinzolamide belongs to a class of drugs used to treat glaucoma and ocular hypertension, known as carbonic anhydrase inhibitors (CAI). CAI reduces increased intraocular pressure (IOP) by decreasing the production of fluid (aqueous humor) in the eye.
DUOTRAV is a fixed dose combination eye drop containing a topical prostaglandin analogue, travoprost 0.004%, and a topical beta-adrenergic receptor blocking agent, timolol 0.5 %, which reduces increased intraocular pressure (IOP) by complementary mechanisms of action.

This combination of medications may expand the treatment options available to both clinicians and subjects in whom DUOTRAV alone does not provide sufficient IOP lowering. It gives clinicians the option to manage the disease with 4 classes of medications (PGAs, beta blockers, CAIs and alpha agonists) using 3 drops/day.

Study objective

To demonstrate the additive IOP lowering effect of SIMBRINZA (dosed BID) when added to DUOTRAV solution in subjects with open-angle glaucoma or ocular hypertension.

Study design

It concerns a multicenter, randomized, double-masked, parallel-group study. Duration of the treatment is about 42 days, divided into 2 sequential phases for a total of 5 study visits.
Phase I of the study is open-labeled, which includes a Screening Visit followed by 2 Eligibility Visits.
Phase II of the study is the randomized, double-masked treatment phase which includes 2 visits: Visit 4 (at Week 2) and Visit 5 (Week 6, Exit Visit).

At the Screening Visit, the PI will confirm that subjects have been on continuous morning or evening DUOTRAV therapy for at least 28 days. If qualified, each subject will continue with open label study DUOTRAV for the duration of the study. After randomization (randomized in a 1:1 manner), subjects will receive treatment with either SIMBRINZA or Vehicle adjunctively to their DUOTRAV therapy.

Intervention

Not applicable.

Study burden and risks

The subjects will be asked to return the clinic up to 5 times. In 3 of the 5 visits an IOP measurement will take place at 2 different time points (around 9:00 and11:00). These 3 visits takes approximately 3 hours. During these visits, the subjects are allowed to leave the clinical center.

Also see question E4 and E9.

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. Subjects 18 years of age or older, of any race, diagnosed with either open-angle glaucoma (including pseudo exfoliation or pigment dispersion glaucoma) or ocular hypertension
2. Subjects currently on treatment with Travoprost 0.004% / Timolol 0.5% prescribed as approved in the country, on morning or evening dosing for at least 28 days prior to screening and that in the opinion of the Investigator may benefit from further IOP lowering
3. Qualifying mean IOP measurements at both the Eligibility 1 and Eligibility 2 visits, in at least 1 eye (the same eye(s) * 19 and * 28 mmHg at 9:00 while on a Travoprost 0.004% / Timolol 0.5% solution)
4. Must be able to understand and sign an informed consent form that has been approved by an Institutional Review Board/Ethics Committee
5. Willing and able to attend all study visits

Exclusion criteria

1. Women of childbearing potential (WOCBP), defined as all women who are not postmenopausal for at least 1 year or less than 6 weeks since sterilization, are excluded from participation if: a. they are currently pregnant, or // b. have a positive result on the urine pregnancy test at Screening, or // c. intend to become pregnant during the study period, or // d. are breast-feeding, or // e. are not in agreement to use adequate birth control methods to prevent pregnancy throughout the study.
All women of childbearing potential are required to use adequate birth control methods which are summarized as follows: a. Total abstinence (when this is in line with the preferred and usual lifestyle of the subject). Periodic abstinence (eg, calendar, ovulation, symptothermal,

postovulation methods) and withdrawal are not acceptable methods of contraception. // b. Female sterilization (have had surgical bilateral oophorectomy with or without hysterectomy) or tubal ligation at least 6 weeks before Baseline. In case of oophorectomy alone, only when the reproductive status of the woman has been confirmed by follow up hormone level assessment. // c. Male sterilization (at least 6 months prior to Baseline). For female subjects in the study, the vasectomized male partner should be the sole partner for that subject. // d. Use of oral, injected or implanted hormonal methods of contraception or other forms of hormonal contraception that have comparable efficacy (failure rate < 1%), for example hormone vaginal ring or transdermal hormone contraception. // e. Placement of an intrauterine device (IUD) or intrauterine system (IUS).;2. Subjects with any form of glaucoma other than open-angle glaucoma or ocular hypertension.
3. Subjects with central cornea thickness (CCT) greater than 620 *m as measured by pachymetry in either eye.
4. Subjects with Schaffer angle Grade < 2 in either eye, as measured by gonioscopy (extreme narrow angle with complete or partial closure).
5. Subjects with cup/disc ratio greater than 0.80 (horizontal or vertical measurement) in either eye.
6. Subjects with severe central visual field loss in either eye or field loss threatening fixation in either eye.
7. Subjects with chronic, recurrent or severe inflammatory eye disease (eg, scleritis, uveitis, herpes keratitis) in either eye.
8. Subjects with ocular trauma in either eye within the past 6 months prior to the Screening visit.
9. Subjects with ocular infection or ocular inflammation in either eye within the past 3 months prior to the Screening visit.
10. Subjects with clinically significant or progressive retinal disease such as retinal degeneration, diabetic retinopathy, or retinal detachment in either eye.
11. Subjects with best-corrected visual acuity score worse than 55 ETDRS letters (equivalent to approximately 20/80 Snellen, 0.60 logMAR or 0.25 decimal) in either eye.
12. Subjects with other ocular pathology (including severe dry eye) in either eye that may, in the opinion of the Investigator, preclude the safe administration of any study medication.
13. Subjects with intraocular surgery in either eye within the past 6 months prior to the Screening visit.
14. Subjects with ocular laser surgery in either eye within the past 3 months prior to the Screening visit.
15. Subjects with any abnormality preventing reliable applanation tonometry in either eye.
16. Any other conditions including severe illness which would make the subject, in the opinion of the Investigator, unsuitable for the study.
17. Subjects with recent (within 4 weeks of the Eligibility 1 Visit) use of high dose (> 1 gm daily) salicylate therapy.
18. Subjects with 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 alpha-adrenergic agonist or carbonic anhydrase inhibitor in the opinion of the Investigator.
19. Subjects with current or anticipated treatment with any psychotropic drugs that augment an adrenergic response (eg, desipramine, amitriptyline).

20. Concurrent use of a monoamine oxidase inhibitor.
21. Study participants with asthma, history of asthma, or severe chronic obstructive pulmonary disease.
22. Therapy with another investigational agent within 30 days prior to the Screening Visit.
23. Subjects with 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 (eg, *-adrenergic blocking agents). The dosing regimen of these medications should not change during the study.
24. Subjects with hypersensitivity to alpha-adrenergic agonist drugs, topical or oral CAIs, PGAs, timolol, sulfonamide derivatives, or to any component of the study medications in the opinion of the Investigator.
25. Use of any additional topical or systemic ocular hypotensive medication in either eye during the study.
26. Subjects who cannot safely discontinue all glucocorticoids administered by any route prior to the Eligibility Visit 1 and continue to not use during the study. Steroid washout duration: a. Chronic therapy * 4 weeks // b. Intermittent therapy - 2 weeks.
27. Mean IOP > 28 mmHg at any time point during the Screening/Eligibility Phase.

Study design

Design

Study phase:	4
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):	24-06-2016
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Brinzolamide 1%/Brimonidine 0.2% suspension
Generic name:	SIMBRINZA
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Travoprost 0.004%/Timolol 0.5% solution
Generic name:	DuoTrav
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	11-10-2016
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	28-12-2016
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	07-06-2017
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	08-06-2017
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	EUCTR2016-000176-20-NL
ClinicalTrials.gov	NCT02730871
CCMO	NL58266.068.16

Study results

Date completed: 30-07-2018

Actual enrolment: 0

Summary results
Trial is onging in other countries