A Clinical Safety and Efficacy Comparison of NEVANAC® 0.1% to Vehicle Following Cataract Surgery in Diabetic Retinopathy Patients

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Demonstrate superiority of NEVANAC® (nepafenac ophthalmic suspension) 0.1% relative to nepafenac vehicle based on the percentage of diabetic retinopathy patients who develop macular edema (defined as >=30% increase from pre-operative baseline in...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Congenital eye disorders (excl glaucoma)
Study type	Interventional

Summary

ID

NL-OMON35481

Source
ToetsingOnline

Brief title
Macular Edema Incidence/Severity Reduction with NEVANACÂ®

Condition

- Congenital eye disorders (excl glaucoma)

Synonym
A Clinical Safety and Efficacy Comparison of NEVANAC® 0.1% to Vehicle Following Cataract Surgery in Diabetic Retinopathy Patients

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Diabetic Retinopathy, Macular Edema, NEVANAC®, Safety and Efficacy Comparison

Outcome measures

Primary outcome

Percentage of patients who develop macular edema (defined as >=30% increase from

pre-operative baseline in central subfield macular thickness) within 90 days

following cataract surgery

Secondary outcome

Key Secondary Efficacy:

Percentage of patients with a best-corrected visual acuity (BCVA) decrease of

>5 ETDRS letters from the Day 7 postoperative visit

Safety:

• adverse events

o incidence of adverse events

o targeted adverse events

• intraocular pressure

• slit-lamp parameters

o inflammatory cells

o aqueous flare

o corneal edema

o bulbar conjunctival injection

o corneal epithelium integrity [as assessed by corneal fluorescein staining]

• dilated fundus parameters

o retina/macula/choroid

o optic nerve

Study description

Background summary

Clinical Study C-09-003 is designed to evaluate the safety and efficacy of NEVANAC® (nepafenac ophthalmic suspension) 0.1% for extended use in diabetic retinopathy patients following cataract surgery.

Study objective

Demonstrate superiority of NEVANAC® (nepafenac ophthalmic suspension) 0.1% relative to nepafenac vehicle based on the percentage of diabetic retinopathy patients who develop macular edema (defined as >=30% increase from pre-operative baseline in central subfield macular thickness) within 90 days following cataract surgery.

Study design

Prospective, multicenter, double-masked, randomized, parallel group, placebo controlled study.
The study population will consist of approximately 260 (130 per treatment group) to obtain 222 patients who are evaluable per protocol (111 per treatment group).

Patients will be randomized 1:1 to receive either NEVANAC® or nepafenac ophthalmic suspension vehicle at the preoperative baseline visit via an interactive voice response system (IVRS). Additionally, the randomization will be stratified based on retinopathy severity as defined by the International Clinical Diabetic Retinopathy Severity Scale. Approximately 50% of diabetic retinopathy patients receiving cataract surgery who are randomized to each treatment group will have mild NPDR and approximately 50% will have moderate or severe NPDR. Patients will be followed for 90 days after surgery. All sites will be certified for the performance of visual acuity, fundus photography and SD-OCT (Spectralis, Heidelberg Engineering).

Patients will be treated in the operative eye for approximately 92 days with 1 drop 3-times-daily (TID) of either NEVANAC® or nepafenac vehicle. Dosing will start 1 day prior to surgery, and will continue on the day of surgery and for 90 days following surgery. An additional 1 drop of the study medication will be administered 30 to 120 minutes prior to surgery. All patients will be treated in the operative eye for 2 weeks with 1 drop QID of Tobradex® starting at their first dosing time after surgery, with the option to continue beyond 2 weeks as needed based on the medical judgment of the investigator.

Intervention

Not Applicable

Study burden and risks

Every participant has an equal chance of receiving either one of the two study drugs NEVANAC® 0.1% or Nepafenac ophthalmic suspension vehicle (placebo). The current approved dose for NEVANAC® 0.1% is one drop, three times daily, beginning one day prior to cataract surgery, continuing on the day of surgery and for two weeks postoperatively. In this study, NEVANAC® will be given three times daily, beginning one day prior to cataract surgery, continued on the day of surgery and continuing for approximately 90 days after the surgery.
All participants in the study will have their cataracts removed in the same manner, using their study doctor*s standard surgical procedures and standard surgical equipment and medications. However, the study eye drop medication will replace the anti-inflammatory medication usually prescribe. Additionally, the study doctor will prescribe Tobradex® (tobramycin and dexamethasone) eye drops, which will be instilled (1 drop) four times daily for the first 2 weeks following surgery.

There are no experimental procedures or equipment involved in this study. The extended dosing of NEVANAC® 0.1% ophthalmic suspension and nepafenac ophthalmic suspension vehicle (placebo) for 90 days after surgery is the only experimental part in this research study.

The potential risks:
The most common side effects (occurring between 1% to 10% of patients) reported in clinical studies with the use of NEVANAC® 0.1% include:
$ Headache
$ Itchy eyes
$ Foreign body sensation in eyes
$ Decreased visual acuity (vision problems)
$ Cloudiness of vision
$ Swelling of the conjunctiva (outer membrane covering the eye)

All other side effects reported in clinical studies with the use of NEVANAC®

0.1% occurred in less than 1% of patients. Some of these events may be related to the surgical procedure. Unforeseen side effects may occur.

As with any drug, it is possible that the patient could experience an allergic reaction to any of the drugs or combination of the drugs used in this study. Symptoms of any allergic reaction can include a rash, hives, itching, and/or difficulty breathing, closing of the throat, swelling of the lips, tongue or face, and-rarely-death. You will be monitored carefully after administration of the study drug for signs of an allergic reaction.

The use of NEVANAC® 0.1% during intraocular surgery may not decrease the chance of inflammation. Each patient will also be getting Tobradex® for two weeks after surgery to prevent post-surgical inflammation.

The Fluorescein Sodium Sterile Ophthalmic Strip may, if used, cause eye irritation.

The risks of drawing blood from a vein or finger stick include discomfort at the site of the needle stick, possible bruising and swelling around the site of the needle stick, rarely an infection, and uncommonly feeling faint from the procedure.

For the eye examination, your pupil(s) will be dilated. Dilation of the pupil may cause light sensitivity and slight blurring of vision for up to 4 hours after testing. Wearing sunglasses for several hours after dilation can help reduce the discomfort of light sensitivity. Also, driving may be difficult so it is advisable to arrange for transportation home, particularly on the Baseline visit when both eyes will be dilated.

There are risks associated with all surgeries including this type of surgery (cataract removal and intraocular lens implantation).

Contacts

Public
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Scientific
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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 must be 18 years of age and older, of any race and either sex, who have a cataract, and are planning to undergo cataract extraction by phacoemulsification with the implantation of a posterior chamber intraocular lens into the lens capsule
2) History of Type 1 or Type 2 diabetes
3) NPDR (mild, moderate or severe) in the study eye as defined by the International Clinical Diabetic Retinopathy Disease Severity Scale
4) Patients must be able to understand and sign an informed consent that has been approved by an Institutional Review Board (IRB)
5) Central subfield macular thickness <= 320 µm in the study eye prior to cataract surgery as determined by SD-OCT and confirmed by the reading center
6) Absence of CME or cystoid abnormalities in the study eye as detected by SD-OCT and confirmed by the reading center
7) Absence of clinically significant macular edema (CSME) in the study eye as detected by clinical exam

Exclusion criteria

1) Signs of vitreomacular traction or epiretinal membrane in the study eye as detected by reading center or investigator
2) Current or previous ocular disease in the study eye that in the opinion of the investigator may confound assessment of the macula, the retina, or central vision, other that diabetic retinopathy
3) Focal photocoagulation for the treatment of diabetic macular edema in the study eye within 6 months of the pre-operative baseline visit (Note: peripheral retina treatment for

retinal tear or lattice degeneration is permitted)
4) Prior panretinal photocoagulation in the study eye
5) Planned multiple procedures for study eye during the cataract/IOL implantation surgery (e.g., trabeculectomy, corneal transplant)
6) Patients who have received corneal transplants in the study eye
7) Patients whose baseline cumulative corneal fluorescein staining score (i.e., sum of scores for all 5 corneal regions) for the study eye is graded as >=5, or whose baseline corneal fluorescein staining score in any single region for the study eye is graded as >=3
8) Patients with history of iris atrophy or current or history of chronic or recurrent ocular infections or inflammation in the study eye.
9) Patients with a visually nonfunctional fellow eye based upon the assessment by the investigator.
10) Patients who are immunocompromised (e.g., patients receiving chemotherapy irradiation therapy, patients with AIDS, leukemia, or cachexia) or patients receiving dialysis
11) Patients, who in the opinion of the investigator, might be at increased risk of complications from topical NSAIDs or steroids including those with current or history of keratoconjunctivitis sicca (dry eye syndrome), neurotrophic keratopathy, corneal or scleral thinning and collagen vascular disease, contact lens users, and those with known bleeding tendencies.
12) Patients with current or history of asthma, urticaria, or acute rhinitis in whom attacks are precipitated by acetylsalicylic acid or other NSAIDs
13) Use of medications known to affect the macula, including hydroxychloroquinine (Plaquenil) and phenothiozines (e.g., thioridazine [Mellaril], chloropromazine [Thorazine]) or supplemental niacin >=3 grams/day
14) Use of daily doses of systemic steroids and NSAIDS within 7 days prior to surgery (through study exit). Daily doses of aspirin, up to 325 mg, will be permitted.
15) Use of daily doses of topical ocular steroids and NSAIDs in the nonstudy eye through study exit (Note: All topical ocular steroids and NSAIDs must be discontinued 1 day prior to surgery)
16) Use of topical ocular NSAIDS and steroids, in the study eye, within 7 days prior to surgery
17) Treatment with intraocular or periocular steroids in the study eye within 4 months prior to surgery
18) Patients with a known hypersensitivity to NSAIDs or steroids or any component of the study medication including Tobradex
19) Use of a topical ophthalmic prostaglandin (e.g., TRAVATAN, XALATAN) within 4 days of surgery through study exit
20) The Alcon Medical Monitor may declare any patient ineligible for a valid medical reason.
21) Participation in any other clinical study within 30 days of the Baseline examination
22) Each patient will have only one eye enrolled in the study
23) Females of childbearing potential (those who are not surgically sterilized or post-menopausal) may not participate in the study if any of the following conditions exist:
they are breast-feeding; they have a positive urine pregnancy test at screening; they are not willing to undergo a urine pregnancy test upon entering or exiting the study; they intend to become pregnant during the study; or, they do not agree to use adequate birth control methods for the duration of the study (adequate birth control methods are: hormonal - oral, implantable, transdermal, or injectable contraceptives; mechanical - spermicide in conjunction with a barrier such as condom or diaphragm; IUD; or, surgical sterilization of

partner)

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:	Recruitment stopped
Start date (anticipated):	20-04-2010
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nepafenac ophthalmic suspension 0,1%
Generic name:	nepafenac ophthalmic suspension 0,1%
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	13-07-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	18-01-2010
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-03-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-03-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-06-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-08-2010
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	EUCTR2009-010536-17-NL
CCMO	NL28483.078.09