A Phase 3 Randomized, Double-Masked, Placebo-Controlled Study of the Pharmacokinetics of OMS302 and the Effect of OMS302 on Intraoperative Pupil Diameter and Early Postoperative Pain in Subjects Undergoing Intra Ocular Lens Replacement with Phacoemulsification.

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The co-primary objectives of this study are to evaluate the effect of OMS302 compared to placebo when administered in irrigation solution during phacoemulsification and intraocular lens replacement on: • Intraoperative pupil diameter.• Pain during...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Anterior eye structural change, deposit and degeneration
Study type	Interventional

Summary

ID

NL-OMON37657

Source
ToetsingOnline

Brief title
ILR4

Condition

- Anterior eye structural change, deposit and degeneration
- Eye therapeutic procedures

Synonym

Cataract, Intra Ocular Lens Replacement with Phacoemulsification

Research involving
Human

Sponsors and support

Primary sponsor: Omeros Corporation
Source(s) of monetary or material Support: Omeros Coorporation

Intervention

Keyword: Cataract, ILR, Lens Replacement, OMS302

Outcome measures

Primary outcome

Change in pupil diameter over time from surgical baseline (immediately prior to surgical incision) to the end of the surgical procedure (wound closure) determined by video capture during ILR.

Postoperative pain as measured by the Visual Analog Scale (VAS) at 2, 4, 6, 8 and 10-12 after ILR surgery.

Secondary outcome

Postoperative pain as measured by the Visual Analog Scale (VAS) at 24 and 48 hours, and Days 3-7 and 14 after ILR surgery

Safety as assessed by the incidence of adverse events (AE) and serious adverse events (SAE) through Day 90.

Proportion of subjects having a pupil diameter >= 6mm at cortical clean -up.

Proportion of subjects having a pupil diameter < 6mm anytime during surgery.

Proportion of subjects reporting moderate -to-severe pain (VAS >= 40) at any timepoints during 12 hours postoperatively.

Proportion of subjects reporting no pain (VAS=0) at all timepoints during 12

hour postoperatively.

Photophobia as measured by the photophobia scale of the NRS at 2, 6, 24, and 48 hours, and 7 and 14 days after surgery.

Best-corrected visual acuity (BCVA) as measured using the Early Treatment Diabetic Retinopathy Study (ETDRS) method at 24 and 48 hours, and 7 and 14 days after surgery.

Postoperative inflammation as measured using the SOIS at 24 and 48 hours, and 7and 14 days after surgery.

Pharmacokinetics will be evaluated using plasma concentrations of PE and KE.

Study description

Background summary

Cataract is the leading cause of blindness. Epidemiological models estimate that there are between 27-35 one million blind people in the world, of whom 50 percent are blind due to cataract. Surgical removal of the cataract remains the primary treatment for cataracts with deterioration of visual acuity.

The preferred method for removing is extracapsular cataract extraction, usually by phacoemulsification, currently used in over 90% of cataract surgeries performed in America.

Improvement of visual acuity after cataract extraction and replacement of lenses (CELR) has shown encouraging results in a major international multi-center study.

Although preoperative ocular comorbidity can have a significant effect on the outcome of cataract surgery, complications (although rare) that relate to CELR play a role in the outcomes.

Refractive Lens Exchange (RLE) is an identical surgical technique used for the correction of refractive errors. The number of procedures is increasing rapidly. The avoidance of ocular complications of this procedure is crucial because patients preoperatively have a good BCVA.

A prerequisite for safe intraocular lens surgery is an adequately dilated pupil. The mechanism of mydriasis depends on the agent used and usually there is a disturbance of the parasympathetic activity of the iris or the stimulus of sympathetic activity.

Pain and inflammation are most common in patients undergoing lens extraction surgery to which various topical non-steroidal anti-inflammatory drug (NSAID)-containing ophthalmic agents are approved.

Ketolorac tromethamine during the eyechirgurgie directly and continuously supplied in the front room and will deliver directly to the tissues at the time of injury. This can block preventive anti-inflammatory pathways, to reduce surgically induced inflammation and pain, and postoperative care for an immediate and sustained benefit in less pain and inflammation.

Omeros is developing a mydriatic / NSAID combination product indicated OMS302. OMS302 contains phenylephrine HCl (PE), an α1-adrenergic receptor agonist and NSAID ketorolac tromethamine (KE), a non-selective COX-1/COX-2 inhibitor.

This study examines the effect of OMS302 on the pupil diameter and pain and also to the discomfort and inflammation endpoints in Intraocular Lens Replacement Surgery

Study objective

The co-primary objectives of this study are to evaluate the effect of OMS302 compared to placebo when administered in irrigation solution during phacoemulsification and intraocular lens replacement on:
• Intraoperative pupil diameter.
• Pain during the early postoperative period.

The secondary objectives of this study are to evaluate the effect of OMS302 compared to placebo when administered in irrigation solution during phacoemulsification and intraocular lens replacement on:
• Postoperative photophobia as measured by the photophobia subscale of the Numerical Rating System (NRS).
• Postoperative best-corrected visual acuity (BCVA).
• Postoperative inflammation as measured by Summed Ocular Inflammation Score (SOIS).
• Pain after the early postoperative period.
• Safety as measured by adverse events.
• Systemic pharmacokinetics of PE and KE.

Study design

This Phase 3 study is a randomized, parallel group, double-masked,

placebo-controlled study of OMS302 in subjects undergoing intraocular lens replacement (ILR) using a coaxial phacoemulsification process with insertion of an acrylic lens. Administration of test irrigation solutions will take place in a double-masked fashion. Subjects will be randomized 1:1 to OMS302 or placebo. Subjects undergoing ILR defined as cataract extraction and lens replacement (CELR) or refractive lens exchange (RLE) will be eligible.
Randomization to treatment arm will be stratified within site by cataract Lens Opacities Classification System II (LOCS II) grade. A total of approximately 400 subjects will be randomized.

Intervention

Standard intraocular surgical techniques for ILR will be used. For the purposes of this study, the following procedures are to be executed:
1. The surgeon will utilize the test irrigation solutions at all times during the operation.
2. Should the subject at any stage fail to have adequate anesthesia, the surgeon may inject preservative-free lidocaine 1% into the anterior chamber.
3. At the start of the procedure, after the subject has been prepared in the site*s standard manner, the surgeon will make the initial incision by means of a clear cornea incision.
4. If necessary, the operating microscope light may be turned down to the lowest level in order not to harm the eye. In subjects undergoing video recording, sufficient light needs to pass to allow the video photography to be visible.
5. The surgeon may use pharmacologic or mechanical means to manage a pupil that fails to maintain a pupil size adequate once surgery has started. Any additional medicines or mechanical techniques will be recorded.
6. The initial and primary viscoelastic device will be standardized to DuoVisc® (Alcon). Additional viscoelastic devices, if used, should not contain carboxy-methyl cellulose. The type of any additional viscoelastic or intracameral agent will be recorded.
7. The surgeon will proceed with the operation using his/her usual technique for capsulorhexis. Hydrodissection will be performed using the 3 mL test irrigation solution drawn up in the syringe (Protocol Section 10.1.2.2.3, #3). If necessary, replenishment of an emptied syringe will use the same test irrigation solution from the set-aside material (Protocol Section 10.1.2.2.3, #2). The volume used will be recorded. Note that the volume used for hydrodissection is at the discretion of the surgeon. The surgeon will use his/her standard approach to remove the cataract and insert the intraocular lens (IOL).
8. At the end of the procedure the surgeon will use the 1 mL test irrigation solution in the syringe for filling the anterior chamber (Protocol Section 10.1.2.2.3, #4). The volume used will be at the surgeon*s discretion.
9.The total phacoemulsification energy and duration will be recorded in the subject*s CRF.
10.The IOLs will be standardized to those made of acrylic material. The type of

IOL will be recorded.
11.The surgeon will make use of his/her preferred technique of corneal closure. The method will be recorded.
12.The duration of the operation from first incision to wound closure will be recorded.
13. Should any complications occur during the procedure, the complication and its management will be recorded.
14. At the end of the procedure, if miosis is needed the surgeon will use Miochol®-E according to the instructions for the product.

Study burden and risks

The burden for the subject are three additional visits to the hospital, completion of diaries during 7 days and the use additional eye drops for 7 days. With the exception of the use of another rinsing fluid during the surgery and the DVD recording during the procedure, otherwise exactly the same procedure is followed as during a normal cataract surgery.

Sometimes an allergic drug reaction happens. Some things that happen during an allergic reaction are:
• a rash
• having a hard time breathing
• wheezing
• a sudden drop in blood pressure (causing dizzyness or lightheaded)
• swelling around the mouth, throat, or eyes
• a fast pulse
• sweating

During this study subjects will also receive Vigamox®, an antibiotic. Some people who have received Vigamox® had the following side effects:
• Inflammation and/or redness of the outer part of the eye or eye lid
• Decreased vision
• Eye discomfort, itching, or dryness

During this study acetaminophen will also be given against the eye pain after the surgery.

What are the risks of other study procedures?
• Slit-lamp photography: The camera flash is bright and may cause temporary discomfort.
• Eye examinations: The risks and discomforts of eye examinations are similar to those of eye examinations you may have had in the past. Medications used may cause temporary discomfort.
• Intra Ocular Pressure: The instrument used to measure the pressure of the eye could scratch the outside of your eye.

The normal risk associated with surgery.

Some people who have received phenylephrine HCl in their eyes had the following side effects:
• Heart palpitations or a fast heartbeat
• Headache
• Paleness
• Trembling
• Sweating
• High blood pressure
Some people who have received ketorolac tromethamine in their eyes had the following side effects:
• Stinging or burning
• Bleeding in the eye
• Slow wound healing
• Inflammation of the cornea, the front part of the eye
• Increased eye pressure

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

Subjects may be included in the study only if they meet the following criteria within 28 days prior to the day of surgery:
- Are 18 years of age or older at the time of surgery.
- Are to undergo unilateral primary CELR or RLE, under topical anesthesia, with a coaxial phacoemulsification device with insertion of an acrylic lens.
- Have a best-corrected visual acuity (BCVA) of 20/400 or better in the non-study eye.
- Have an intraocular pressure (IOP) between 5 mm Hg and 22 mm Hg, inclusive, in the study eye.
- For women of childbearing potential, have a negative urine pregnancy test. Women of childbearing potential (i.e., not surgically sterilized nor post-menopausal longer than 1 year) must agree to use a medically reliable form of contraception throughout the study as necessary. Acceptable methods of contraception include a reliable intrauterine device, hormonal contraception or a spermicide in combination with a barrier method.

Exclusion criteria

- Hypersensitivity to phenylephrine, ketoprofen, or other NSAIDs, including aspirin.
- Hypersensitivity to moxifloxacin (Vigamox®) or any other fluoroquinolone.
- Hypersensitivity to tetracaine, lidocaine, Duovisc® or latex.
- Women who are nursing a child or plan to nurse a child during the study.
- Presence of clinically significant gastrointestinal, cardiovascular, hepatic, renal, hematological, endocrine, neurological, psychiatric, respiratory or other medical condition as determined by the Investigator.
- Presence of any connective tissue disorder (e.g., lupus, rheumatoid arthritis, fibromyalgia).
7. Presence of systolic blood pressure of >=160 mmHg or <=90 mmHg, or diastolic blood pressure of >=110 mmHg or <=40 mmHg at the screening visit.
- Use of phenylephrine (other than for the screening ophthalmological examination) or NSAIDs, including ketorolac, or cyclosporine within 7 days prior to the day of surgery.
- Use of topical, inhaled or oral corticosteroids within 7 days prior to surgery, or depot corticosteroids within 30 days of surgery.
- Use of monoamine oxidase inhibitors within 21 days prior to the day of surgery.
- Use of ocular mast cell stabilizers within 7 days prior to surgery (Appendix 19.2).
- Repeated use of pilocarpine in the study eye within 6 months prior to the day of surgery.
- History of use of an alpha -1- adrenergic antagonist, such as tamsulosin (Flomax®), silodosin (Rapaflo®), prazosin (Minipress®, Hypovase®), alfuzosin (Uroxatral®), doxazosin (Cardura®) or terazosin (Hytrin®) (Appendix 19.2).
- Presence of narrow-angle glaucoma or unstable glaucoma.
- Glaucoma being treated with prostaglandins or prostaglandin analogues such as Xalatan®, Lumigan®, Travatan®, and Rescula®, or Alphagan® (brimonidine tartrate) in either eye during the 7 days prior to screening and for the duration of the study (Appendix 19.2).

- Anticipated to require the use of other topical ocular medications in either eye during the trial except prophylactic antibiotics, topical lid care, allowed glaucoma medications or non-prescription tear replacement solutions.
- Presence of pseudo-capsular exfoliation in either eye.
- History of iritis, or of any ocular trauma with iris damage in the study eye.
- Presence of uncontrolled chronic ocular diseases in either eye that could affect pupil dilation or confound the analysis of pain.
- Presence of active corneal pathology or active scarring noted in either eye (except superficial punctate keratopathy in the non-study eye). Healed peripheral corneal incisions performed during prior refractive surgical procedures are not considered scars.
- Presence of extraocular/intraocular inflammation in either eye.
- Presence of active bacterial and/or viral infection in either eye.
- Participating in any investigational drug or device trial within the 30 days prior to the day of surgery.
- History of intraocular non-laser surgery in the study eye within the 3 months prior to the day of surgery, or intraocular laser surgery in the study eye within 30 days prior to the day of surgery.
- Presence of any condition that the Investigator believes would put the subject at risk or confound the interpretation of the study data.
-Investigators, employees of the investigative site, and their immediate families. Immediate family is defined as the Investigator's or employees* current spouse, parent, natural or legally adopted child (including a stepchild living in the Investigator*s household), grandparent, or grandchild.

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):	27-08-2012

Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Phenylephrine and Ketorolac trometamol
Generic name:	Phenylephrine and Ketorolac trometamol

Ethics review

Approved WMO Date:	08-05-2012
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	23-07-2012
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	18-04-2013
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)

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	EUCTR2012-000867-25-NL
CCMO	NL40276.075.12