NCT 04465630

A PROSPECTIVE, MULTICENTER STUDY OF THE OMNI® SURGICAL SYSTEM IN PSEUDOPHAKIC EYES WITH OPEN ANGLE GLAUCOMA (ORION)

PROTOCOL ID #:	#06807
CURRENT REVISION:	Rev C
REVISION DATE:	June 4, 2020
SPONSOR:	Sight Sciences, Inc. 4040 Campbell Avenue Suite 100 Menlo Park, CA 94025 877-266-1144

Agreement of Principal Investigator

I, _____ agree to conduct this trial in accordance with this clinical protocol and any amendments.

_____ _____

Signature Date

_____ _____

Center Name City, State, Country

This protocol contains confidential information for use by the Investigators and their designated representatives participating in this clinical investigation. It must be held confidential and maintained in a secure location.
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Revision History

[redacted]	[redacted]	[redacted]
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1 PROTOCOL SYNOPSIS

Protocol Title	A Prospective, Multicenter Study of the OMNI® Surgical System in Pseudophakic Eyes with Open Angle Glaucoma (ORION)
Protocol ID Number	#06807
Study Device	OMNI® Surgical System
Study Objective	To prospectively assess the clinical effect of ab-interno transluminal viscoelastic delivery and trabeculotomy performed with the OMNI Surgical System in pseudophakic eyes on intraocular pressure (IOP) and the use of IOP-lowering medications in patients with open angle glaucoma (OAG).
Study Design	Prospective, multicenter, single-arm, post-market study
Primary Effectiveness Endpoint	• Proportion of eyes with a ≥ 20% decrease in unmedicated mean diurnal IOP (DIOP) at the 12-month (or 12-month washout) postoperative examination
[redacted]	[redacted]

Inclusion Criteria	**<u>Inclusion Criteria</u>** (At least one eye of each subject should pass the ocular eligibility criteria listed below. Only one eye of each subject is eligible to receive the study procedure): 1. Male or female subjects, 22 years or older at the time of surgery 2. History of uncomplicated cataract surgery and posterior chamber IOL implantation without compromise to the lens capsule, zonular dehiscence/rupture or vitreous prolapse, 6 months or more prior to Baseline Visit. 3. [redacted] 6. Scheduled for ab-interno transluminal viscoelastic delivery and trabeculotomy using the OMNI Surgical System. 7. Shaffer grade of ≥ III in all four quadrants 8. Able and willing to comply with the protocol, including all follow-up visits. 9. Understands and signs the informed consent

[1] For combination IOP-lowering medications that consist of two or more IOP-lowering drugs, each IOP-lowering drug component counts as a separate medication.

Exclusion Criteria	A subject who meets any of the criteria listed below will not receive the study procedure. Ocular criteria are applicable to study eye and non-ocular criteria are subject-related:
	
	1. Any of the following prior treatments for glaucoma:
	  ○ Laser trabeculoplasty ≤3 months prior to Baseline visit
	  ○ iStent or iStent Inject implanted ≤6 months prior to Baseline visit
	  ○ Endocyclophotocoagulation (ECP) or Micropulse laser ≤ 6 months prior to Baseline visit
	  ○ Trabeculectomy or other bleb forming procedure including Xen, Express, glaucoma draining device/valve
	  ○ Prior canaloplasty, goniotomy, or trabeculotomy
	  ○ Hydrus microstent
	  ○ Suprachoroidal stent (e.g. Cypass, iStent Supra)
	2. Acute angle closure, traumatic, congenital, malignant, uveitic or neovascular glaucoma
	3. Concurrent IOP-lowering procedure other than use of the OMNI Surgical System at the time of surgery (e.g. ECP, CPC, etc.)
	4. In the Investigator's judgement, predisposed to significant risk because of washout of ocular hypotensive medications
	5. Concurrent ocular pathology or systemic medical condition which, in the Investigator's judgment, would either place the subject at increased risk of complications, contraindicate surgery, place the subject at risk of significant vision loss during the study period (e.g., wet AMD, corneal edema, Fuch's dystrophy, active intraocular infection or inflammation within 30 days prior to Screening Visit, etc.), or interfere with compliance to elements of the study protocol (e.g., returning to Investigator's office for follow-up visits).
	6. History of penetrating keratoplasty or another corneal transplant
	7. BCVA of logMAR 1.0 (20/200) or worse in the fellow eye not due to cataract

	8. BCVA of logMAR 0.4 (20/50) or worse in the study eye not due to posterior capsular opacification (uneventful Nd:YAG laser capsulotomy 6 months prior to baseline is permitted only if there is no vitreous present in or in front of the iris plane at the time of baseline). 9. Participation (≤ 30 days prior to baseline) in an interventional trial which could have a potential effect on the study outcome, as determined by the study investigator 10. Women of childbearing potential if they are currently pregnant or intend to become pregnant during the study period; are breast-feeding; or are not in agreement to use adequate birth control methods to prevent pregnancy throughout the study
Number of Subjects Enrolled and Treated	[redacted]
Number of Sites	[redacted]
Study Duration for Each Subject	[redacted]
Total Study Duration	[redacted]
Schedule of Visits	[redacted]
Treatments	Ab-interno transluminal viscoelastic delivery and trabeculotomy using the OMNI Surgical System as a standalone procedure in pseudophakic eyes

2 STUDY OBJECTIVE

To prospectively assess the clinical effect of ab-interno transluminal viscoelastic delivery and trabeculotomy performed with the OMNI Surgical System in pseudophakic eyes on intraocular pressure (IOP) and the use of IOP-lowering medications in patients with open angle glaucoma (OAG).

3 BACKGROUND AND JUSTIFICATION FOR THE STUDY

Glaucoma is a progressive disease leading to irreversible damage to retinal ganglion cells with the global burden expected to rise to 111.8 million people by the year 2040.[2] OAG is the most prevalent form of glaucoma and it's proven that lowering IOP is the only efficient way to slow down the progressive optic nerve damage and visual field loss.[3] Hypotensive eye drops are commonly used as the first line clinical management for OAG.[4] Ocular side effects such as allergies, ocular surface disorders, blepharitis, pemphigoid, abnormal pigmentation etc. and systemic side effects such as bradycardia, headaches, depression, anxiety, confusion, dysarthria, hallucinations, lethargy, polyuria, weight loss, metabolic acidosis, etc. can occur during long term use of topical medications for management of OAG. [5] There is also a documented low rate of compliance and tolerability with eye drops that results in disease progression and loss of vision.[6] The cost of these chronic medications and difficulty administering drops to the eyes contributes to poor compliance.

Trabeculectomy and tube-shunt implantations remain the gold standard for surgical management of IOP.[7] These interventions are associated with a long list of potential complications such as sclero-conjunctival scarring, hypotony, hypotony maculopathy, choroidal detachment, conjunctival leak, hyphema, and bleb related complications.[8] Surgical techniques that re-establish the aqueous outflow through the physiological pathways without the need for a bleb are gaining acceptance among glaucoma surgeons.[9] Delivering viscoelastic in Schlemm's canal is one such procedure that is intended to restore the natural aqueous outflow system through microcatheterization and viscodilation of the entire length of the Schlemm's canal with a well-documented

[2] Tham YC, Li X, Wong TY, et al. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. Ophthalmology. 2014;121:2081–2090.

[3] European Glaucoma Society. Terminology and guidelines for glaucoma 4th edition Savona, Italy: Editrice PubliComm, 2014.

[4] Kass MA, Heuer DK, Higginbotham EJ, Johnson CA, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol. 2002; 120:701–713.

[5] Kenji Inoue. Managing adverse effects of glaucoma medications. Clin Ophthalmol. 2014; 8: 903–913. Published online 2014 May 12. doi: 10.2147/OPTH.S44708.

[6] Newman-Casey PA, Robin AL, Blachley T, Farris K, Heisler M, Resnicow K, Lee PP. The Most Common Barriers to Glaucoma Medication Adherence: A Cross-Sectional Survey. Ophthalmology. 2015 Jul; 122(7):1308-16.

[7] Gedde SJ, Singh K, Schiffman JC, Feuer WJ. The Tube Versus Trabeculectomy Study: interpretation of results and application to clinical practice. Curr Opin Ophthalmol. 2012 Mar; 23(2):118-26.

[8] Zahid S, Musch DC, Niziol LM, Lichter PR, Collaborative Initial Glaucoma Treatment Study Group. Risk of endophthalmitis and other long-term complications of trabeculectomy in the Collaborative Initial Glaucoma Treatment Study (CIGTS). Am J Ophthalmol. 2013 Apr; 155(4):674-680, 680.e1.

[9] American Academy of Ophthalmology. Preferred practice pattern®. Primary open-angle glaucoma. San Francisco, CA. 2015.

safety and efficacy profile in reducing IOP.[10,11] Trabeculotomy is another such procedure that relieves the resistance to aqueous flow by cleaving the trabecular meshwork and the inner wall of Schlemm's canal.[12]

The OMNI™ Surgical System (Sight Sciences Inc, Menlo Park, CA) is a 510K-cleared manually operated device indicated for the delivery of small amounts of viscoelastic fluid and to cut trabecular meshwork tissue during trabeculotomy procedures. The OMNI™ Surgical System allows doctors to perform viscodilation of Schlemm's canal in conjunction with trabeculotomy through single clear corneal incision.[13,14,15]

This prospective, multicenter, single-arm, post-market clinical study will evaluate the impact of ab-interno transluminal viscoelastic delivery and trabeculotomy using OMNI™ Surgical System on IOP and the use of hypotensive medications in pseudophakic eyes with mild to moderate open angle glaucoma.

4 STUDY DEVICE

4.1 INDICATIONS FOR USE

The OMNI Surgical System has been 510k cleared by the US Food and Drug Administration (FDA) for the following indication for use:

> The OMNI™ Surgical System is a manually operated device for delivery of small amounts of viscoelastic fluid, for example Healon® or Healon GV® from Abbott Medical Optics (AMO), Amvisc® from Bausch & Lomb, or PROVISC® from Alcon, during ophthalmic surgery. It is also indicated to cut trabecular meshwork tissue during trabeculotomy procedures.

[10] Klink T, Sauer J, Körber NJ, et al. Quality of life following glaucoma surgery: canaloplasty versus trabeculectomy. Clin Ophthalmol. 2014;18;9:7-16.

[11] Lewis RA, von Wolff K, Tetz M, Körber NJ, Kearney JR, Shingleton B, Samuelson TW. Canaloplasty: circumferential viscodilation and tensioning of Schlemm's canal using a flexible microcatheter for the treatment of open-angle glaucoma in adults: interim clinical study analysis. J Cataract Refract Surg 2007; 33:1217–1226

[12] Grover DS, Godfrey DG, Smith O, Feuer WJ, Montes de Oca, Fellman RL. Gonioscopy-Assisted Transluminal Trabeculotomy, A Novel Ab Interno Trabeculotomy: technique report and preliminary results. Ophthalmology. 2014; 121:855-861.

[13] Clara Martinez-Rubio, Ioan Alexandru Placinta, Rodrigo Molina-Pallete, Paula Martínez Lopez-Corell, Jorge Vila-Arteaga. OMNI-an initial experience with a new surgical glaucoma treatment device. ESCRS 2018.

[14] Iwona Grabska-Liberek, Julita Majszyk-Ionescu, Agnieszka Skowyra, Monika Rogowska, Anna Plichta, Patrycja Duda, Ingrid Kane OMNI 360TM in Open-Angle Glaucoma Treatment: A 6-month Follow-up. ESCRS 2018.

[15] Paula Martínez Lopez-Corell, Rodrigo Molina-Pallete, Clara Martinez-Rubio, Ioan Alexandru Placinta, Jorge Vila-Arteaga Procedural Steps For OMNI, A New Surgical Technique For Glaucoma Treatment, In Combination With Cataract Surgery ESCRS 2018.

4.2 DEVICE DESCRIPTION

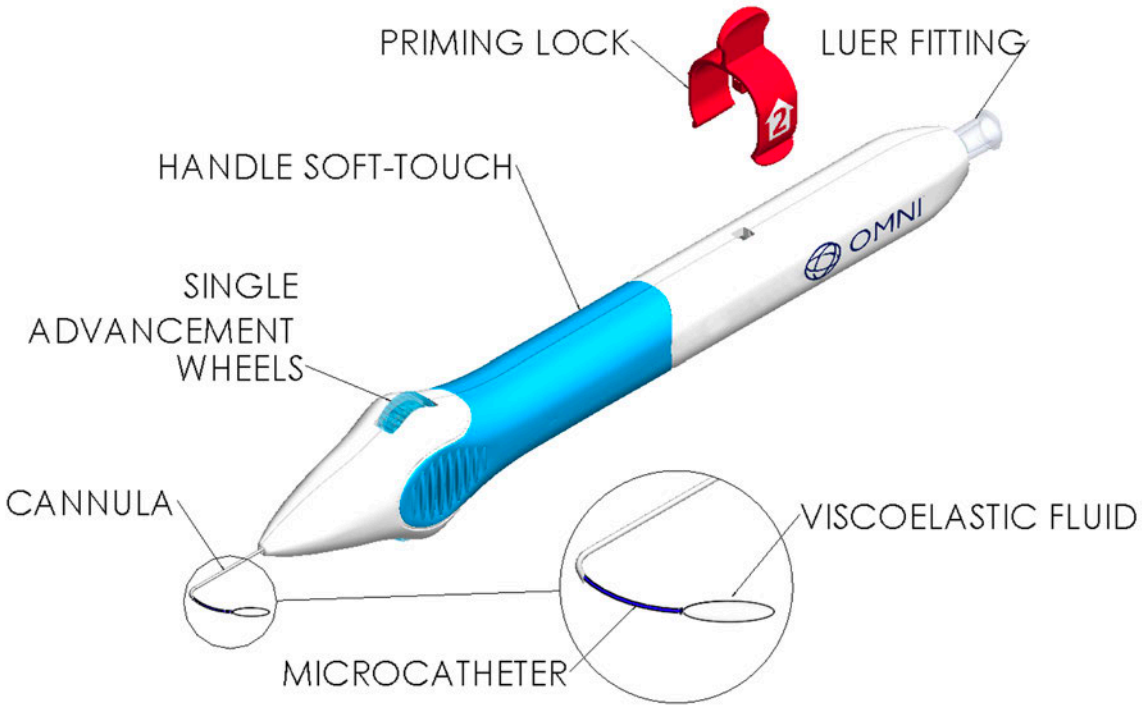
The OMNI™ Surgical System ("OMNI") is a sterile, single use, manually operated instrument used by ophthalmologists to deliver small, controlled amounts of viscoelastic into the anterior segment of the eye during ophthalmic surgery. It is also indicated to cut trabecular meshwork tissue during trabeculotomy procedures.

The OMNI is designed to function with commonly used viscoelastic fluids made commercially available by companies such as Abbott Medical Optics (AMO), Bausch & Lomb, and Alcon. The OMNI dispenses fluid on the principle of exchanging volumes much like a syringe. The handheld instrument includes a cannula, microcatheter, internal reservoir and plunger tube, and finger wheels. The finger wheels on the handle of the device are used to advance and retract the microcatheter. In addition, when the device is being used to deliver viscoelastic, retraction of the microcatheter causes the plunger tube to advance into the viscoelastic fluid reservoir thereby dispensing viscoelastic fluid.

The microcatheter can be advanced/retracted up to 20 mm per cycle. The microcatheter can be fully advanced/retracted up to 5 times (i.e. 5 full cycles of 20 mm each). Dispensation of viscoelastic can only occur during the first two 20-mm cycles.

One finger wheel is located on the top and bottom of each device handle. This allows the OMNI device to be used in either eye (OD or OS) and in either hand of the surgeon (left or right), by turning the device 180 degrees along its vertical axis.

Figure 1: OMNI Surgical System



4.3 TRAINING

Investigators participating in the study must be experienced in using the OMNI 2.0 (OMNI NextGen) Surgical System. All study staff will receive training on the protocol and execution of the study according to applicable regulations and Good Clinical Practices.

5 PRIOR INVESTIGATIONS

Several case-series studies have been performed to evaluate the results of ab-interno transluminal viscoelastic delivery and trabeculotomy performed with the OMNI device in patients with open angle glaucoma. These prior investigations were not conducted in the same subject population as defined in this protocol. Thus, the data presented here will not be used for making assumptions for the current study.

Grabska-Liberek, et al reported on 15 eyes (13 patients) with open angle glaucoma.[16] Eight eyes were treated with OMNI surgery alone and 7 eyes underwent OMNI surgery plus cataract extraction (OMNI + CE). Preoperative mean IOP was 20.13 ± 4.44 mmHg (min IOP=13 mmHg, max IOP=38 mmHg). Postoperative IOP decreased to a mean of 13.90 ± 4.45, 14.07 ± 2.52, 13.43 ± 2.95, 13.71 ± 2.58, 12.73 ± 2.00, 12.67 ± 3.32 and 12.67 ± 1.75 mmHg at 1 week, 1 month, 3 months, 6 months, 1 year, 18 months and 2 years. The number of anti-glaucoma medications dropped from a mean of 2.60 preoperatively to 0.07, 0.20, 0.29, 0.43, 0.82, 1.22 and 1.33. Complications were limited to IOP-spikes (nine eyes), hyphema (six eyes) and fibrin in the anterior chamber (five cases) that were resolved in the first week after surgery. 3 eyes underwent anterior chamber lavage for removal of blood- these patients didn't receive tranexamic acid during the surgery.

Martinez-Rubio, et al[17] reported early safety and efficacy of transluminal viscoelastic delivery and trabeculotomy using the OMNI Surgical System in 20 eyes with primary open angle glaucoma, 13 of which were treated with the OMNI device and cataract surgery and 7 who were only treated with the OMNI device. Mean pre-operative IOP was 24.2 ± 6.3 mmHg and the mean number of preoperative antiglaucoma drugs used by patients was 2.7. At 6 months, pressure had been reduced to an average of 15.9 ± 3.3 and medications were reduced to an average of 1.1. Early postoperative complications included one case of transient toxic anterior segment syndrome (TASS) and one case of transient hyphema. Early follow-up data showed a reduction of IOP, with medication reduction, in treatment of moderate glaucoma in adults.

[16] Grabska-Liberek I, et al. OMNI 360 in Open-Angle Glaucoma Treatment: A 24-Month Follow-Up. World ophthalmology congress (WOC) 2019.

[17] Martinez-Rubio, et al. OMNI-an initial experience with a new surgical glaucoma treatment device. European Society of Cataract & Refractive Surgeons (ESCRS) 2018.

Figure 3: Results for OMNI Surgery (Martinez-Rubio et al)

6 STUDY DESIGN

This is a prospective, multicenter, single-arm, post-market study.

6.1 STUDY DEVICE

The study device is the OMNI 2.0 (OMNI NextGen) Surgical System. Subjects enrolled in the study will undergo ab-interno transluminal viscoelastic delivery and trabeculotomy using the OMNI Surgical System.

6.2 STUDY SITES

This study will be conducted at up to 10 sites in the United States.

7 STUDY ENDPOINTS

7.1 EFFECTIVENESS ENDPOINTS

The **Primary effectiveness endpoint** is:

- Proportion of eyes with a ≥ 20% decrease in unmedicated mean diurnal IOP (DIOP) at the 12-month (or 12-month washout) postoperative examination

[redacted]

7.2 [redacted]

[redacted]

8 STUDY SELECTION CRITERIA

8.1 INCLUSION CRITERIA

At least one eye of each subject should pass the ocular eligibility criteria listed below. Only one eye of each subject is eligible to receive the study procedure:

1. Male or female subjects, 22 years or older at the time of surgery
2. History of uncomplicated cataract surgery and posterior chamber IOL implantation without compromise to the lens capsule, zonular dehiscence/rupture or vitreous prolapse, 6 months or more prior to Baseline Visit.
3. [redacted]

4. [redacted]
6. [redacted]
7. [redacted]
8. Able and willing to comply with the protocol, including all follow-up visits.
9. Understands and signs the informed consent

8.2 EXCLUSION CRITERIA

A subject who meets any of the criteria listed below will not receive the study procedure. Ocular criteria are applicable to study eye and non-ocular criteria are subject-related:

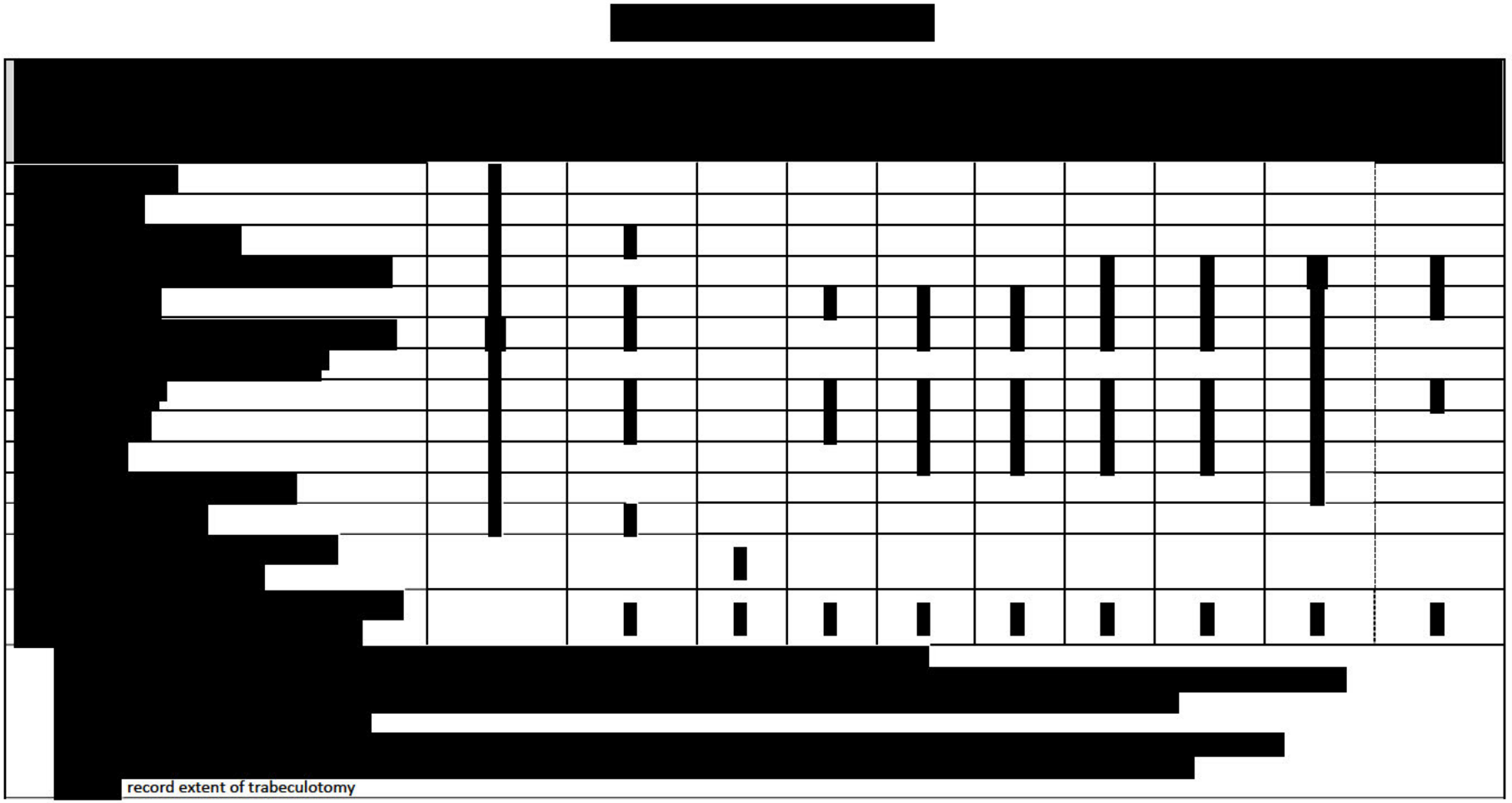
1. [redacted]
2. Acu e angle closure, traumatic, congenital, malignant, uveitic or neovascular glaucoma
3. Concurrent IOP-lowering procedure other than use of the OMNI Surgical System at the time of surgery (e.g. ECP, CPC, etc.)
4. In the Investigator's judgement, predisposed to significant risk because of washout of ocular hypotensive medications
5. Concurrent ocular pathology or systemic medical condition which, in the Investigator's judgment, would either place the subject at increased risk of complications, contraindicate surgery, place the subject at risk of significant vision loss during the study period (e.g., wet AMD, corneal edema, Fuch's dystrophy, active intraocular infection or inflammation within 30 days prior to Screening Visit, etc.), or interfere with compliance to elements of the study protocol (e.g., returning to Investigator's office for follow-up visits).
6. History of penetrating keratoplasty or another corneal transplant

[18] For combination IOP-lowering medications that consist of two or more IOP-lowering drugs, each IOP-lowering drug component counts as a separate medication.

7. BCVA of logMAR 1.0 (20/200) or worse in the fellow eye not due to cataract
8. BCVA of logMAR 0.4 (20/50) or worse in the study eye not due to posterior capsular opacification (uneventful Nd:YAG laser capsulotomy 6 months prior to baseline is permitted only if there is no vitreous present in or in front of the iris plane at the time of baseline).
9. Participation (≤ 30 days prior to baseline) in an interventional trial which could have a potential effect on the study outcome, as determined by the study investigator
10. Women of childbearing potential if they are currently pregnant or intend to become pregnant during the study period; are breast-feeding; or are not in agreement to use adequate birth control methods to prevent pregnancy throughout the study

9 STUDY PROCEDURES

[redacted]



9.2 NUMBER OF SUBJECTS, DURATION OF FOLLOW-UP AND STUDY DURATION

[redacted] in the study will take approximately 9 months. Including the 13-month follow-up period, the study is expected to last 22 months.

9.3 INFORMED CONSENT AND POINT OF ENROLLMENT

The IRB-approved informed consent will be presented and explained to each prospective subject by the investigator or a trained clinical professional. Once the subject has had ample time to read the consent form, has been informed of all aspects of the study, and has had an opportunity to ask questions, the subject will be given a choice to voluntarily confirm his or her participation in the study as documented by completion of the Informed Consent. After signing the Informed Consent and the HIPAA (Health Insurance Portability and Accountability Act) authorization, the subject can then proceed with the screening visit. The subject has the right to withdraw from the study at any time without consequences, as indicated in the Informed Consent Document.

The subject's signed and dated informed consent must be obtained before conducting any study specific procedures that are not part of the standard of care. Subjects are enrolled upon signing the ICD even if they subsequently fail to meet the eligibility criteria.

The principal investigator(s) must retain the original, signed written Informed Consent Document. A copy of the written Informed Consent Document must be given to the subject.

9.4 SCREENING VISIT

After obtaining an understanding of the purpose of this study, then reviewing and signing the Informed Consent Document, all potential subjects will undergo an initial screening examination in order to determine their eligibility for the study. Exams and tests listed in the Screening column of Table 1 should be performed. Refer to Appendix A for instructions for performing the exams.

If a subject does not meet the inclusion/exclusion criteria, he/she may be re-screened after 30 calendar days. Subject should be exited from the study and assigned another subject identification number at the second screening.

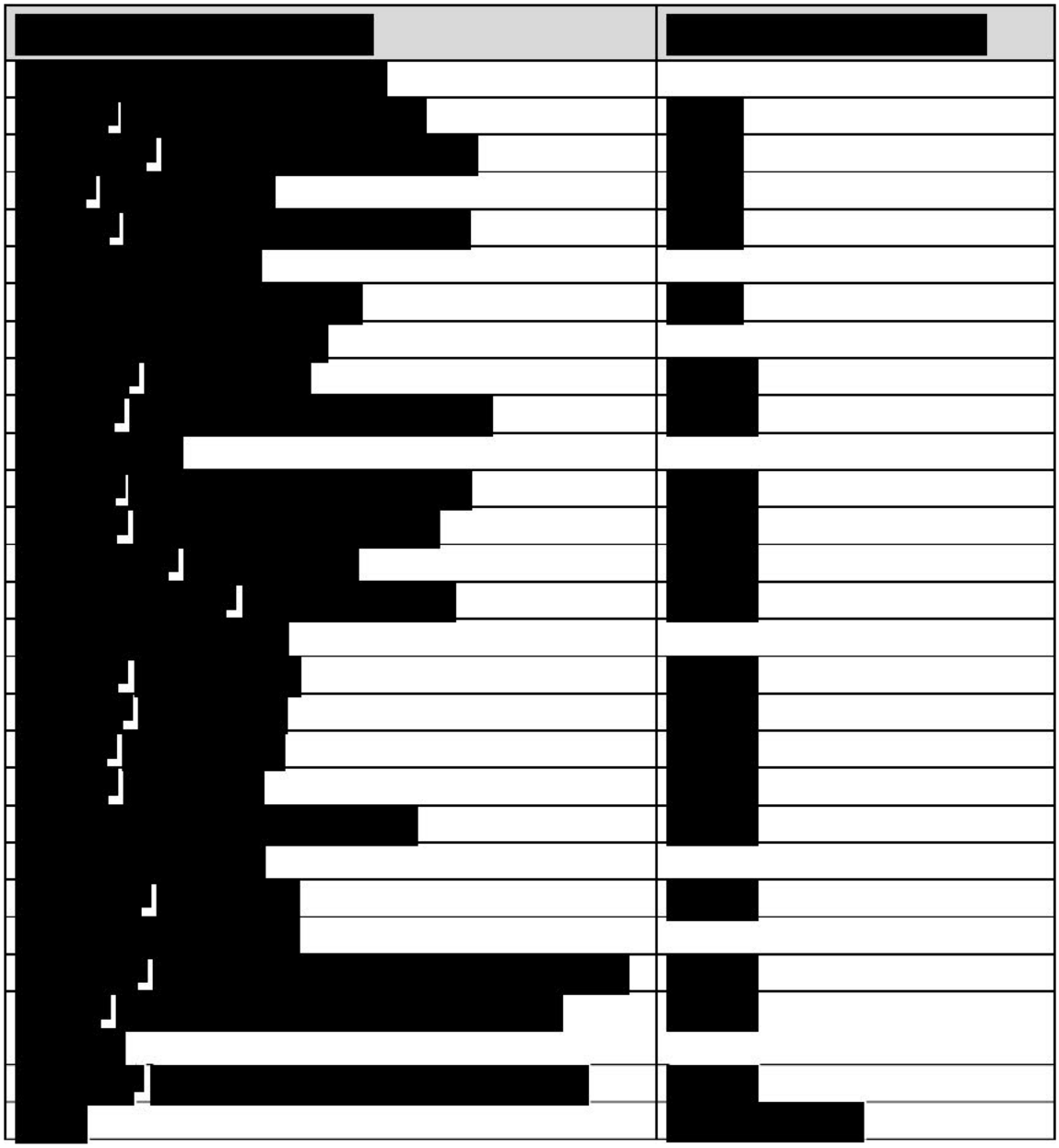
Exam data collected on subjects prior to enrollment as part of the routine clinical practice may serve as Screening data as long as it was collected within 15 days prior to the visit. The only exceptions to this are:

- IOP and IOP-lowering medications. These data must be collected at the Screening visit.
- Visual field: Visual Fields conducted per the protocol method (Humphrey 24-2 SITA standard) within 6 months of the screening visit will be acceptable.

9.5 WASHOUT OF HYPOTENSIVE MEDICATIONS

Subjects on ocular hypotensive medication who meet all eligibility criteria at the screening visit will be instructed to discontinue their ocular hypotensive medication regimen, and to return for a Baseline visit after completing the appropriate washout period. The final eligibility assessment will happen at baseline visit.

Table [redacted]



9.6 BASELINE VISIT

After appropriate washout during the Baseline visit, the exams and tests listed in the Baseline column of Table 1 should be performed in order to determine final eligibility for the study. If both eyes meet the applicable inclusion and exclusion criteria, the eye with higher IOP will be included in the study. In case of both eyes with same IOP at baseline, investigator will select the study eye. The other eye will be excluded based on the first eye already being included in the study.

Refer to Appendix A for instructions for performing the exams.

9.7 SURGICAL PROCEDURE

[redacted]

Eyes with complications related to previous glaucoma implants (such as displacement of implant) or IOL (such as posterior capsular rent or vitreous presentation) should be exited from the study. The region where the trabeculotomy procedure is performed (e.g. superior hemisphere) and the extent of trabeculotomy should be recorded on the case report forms.

Surgeons should follow their standard intra-operative and peri-operative medication regimen.

9.8 FOLLOW-UP VISITS

Follow-up visits should be performed according to the schedule provided in Table 1. All attempts should be made to conduct each follow-up visit within the time interval specified in Table 1. Evaluations conducted outside the prescribed time period will be considered protocol deviations.

9.9 MANAGEMENT OF IOP AFTER SURGERY

This protocol recommends that no IOP-lowering medications should be administered to subjects after the surgery (0 meds on postop day 1) unless medically warranted. Investigators should use their clinical judgement and best practices in determining when and why IOP-lowering medications should be reintroduced and if a subject requires surgical re-intervention to manage IOP.

In the event of a steroid response (IOP increase), the Investigator should use his/her standard of care to treat an increase in IOP; however, hypotensive medications should be discontinued once the topical steroid has been discontinued within the reasonable timeframe as deemed appropriate by the investigator.

If a pressure rise is observed, a paracentesis may be performed as necessary. If a paracentesis is performed and there is no protocol-defined adverse event, the paracentesis will be documented in the subject's medical record, the applicable visit CRF and the Ocular Procedures log. If, however, the paracentesis is performed in conjunction with an AE, then the AE is recorded as such, and the paracentesis is also recorded on the AE CRF as a treatment for the protocol-defined AE (as well as the other CRFs mentioned above).

Medications which have been re-started by the investigator may be discontinued if the investigator's judgment is that the target intraocular pressure has been reached and the continued use of some or all of the therapy may not be required. Discontinuation of medications after re-introduction is recommended to be in the reverse order of re-

introduction. The rationale for discontinuation should also be documented in the study record by the investigator.

A record of all ocular hypotensive medications added, discontinued or changed will be documented on the appropriate Case Report Form for each scheduled visit or on a Case Report Form for an Unscheduled Visit, if necessary.

Another potential reason for intervention is hypotony. Intervention should only be considered if the hypotony has caused or is likely to cause sequelae such as a flat chamber or retinal detachment. No intervention is indicated when the vision is unchanged from screening, there is no persistent choroidal detachment, the anterior chamber is not flat with lens corneal touch, or the patient is asymptomatic. No intervention should be undertaken for hypotony which is not causing, or threatening to cause, a reduction in vision.

Secondary IOP-Lowering Interventions to Control IOP

If the subject requires another glaucoma procedure to control their IOP, the subject should continue to be followed according to standard of care until the adverse event resolves or 1 month post-re-intervention, whichever is longer. Following this, the subject should be withdrawn from the study.

Subjects who have a secondary IOP-lowering intervention will be considered treatment failures for the purpose of the endpoint analyses. These subjects will be included in the Safety Endpoint analyses through their withdrawal from the study.

9.10 WITHDRAWAL AND DISCONTINUATION

All subjects have the right to withdraw at any point during the study without prejudice. The investigator can discontinue any subject at any time at his/her discretion, or if continued participation in the study would result in harm to the subject. All efforts should be made by the investigator to retain the subject in the study. If a subject withdraws prematurely from the study, a genuine effort must be made to determine the reason(s) the subject discontinued the study. The reason must be recorded in the subject's file and on the Study Exit Form.

9.11 SUBJECTS LOST TO FOLLOW-UP

Subjects who do not show up for a follow-up must be contacted to attempt to have them come for the follow-up. For those subjects who cannot be reached every attempt should be made and documented. If a subject misses two consecutive follow-up visits without any contact with the study staff, the subject will be considered lost-to-follow-up unless there is a further communication by the subject.

10 ADVERSE EVENTS (AEs)

Adverse Events are defined below. Adverse events that occur in the eye during the trial, whether they are considered to be device related or not, must be documented in the subject's records. Date of the event, its severity, treatment (if any) and the assessed relationship of the event to the study device will be recorded on the Adverse Event Form. Conditions which exist at the time the subject is enrolled do not need to be recorded as adverse events unless they increase in severity during the study. Sites should document any known existing medical and ophthalmic conditions at the time of screening.

10.1 DEFINITIONS OF AE, SAE, SADE, USADE

Adverse Event	Any untoward medical occurrence in a subject who has been treated with the device that does not necessarily have causal relationship with the treatment.
Adverse Device Effect	Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease that is possibly related to the study device.
Serious Adverse Event (SAE)	Any untoward medical occurrence that: • Results in death • Is life-threatening • Requires in-patient hospitalization or prolongs existing hospitalization • Necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure • Sight threatening
Unanticipated Adverse Device Effect	Any serious adverse effect on health or safety, any life-threatening problem or death caused by, or associated with a device if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the clinical investigational plan; or any other serious problem associated with a device that relates to the rights, safety, or welfare of subjects (21 CFR 812.3(s)). Any sight-threatening event, whether listed in the protocol or not, is considered to be reportable as a UADE

10.2 LIST OF ANTICIPATED POTENTIAL ADVERSE EVENTS

Anticipated potential adverse events listed below include those that might reasonably be expected to occur in this study because they are associated with glaucoma, ab-interno transluminal viscoelastic delivery, trabeculotomy, and/or the risk analysis for OMNI System. Adverse events may occur intra-operatively or post-operatively.

[19] To avoid double counting an event, events of IOP ≥ 10 mmHg above baseline IOP at ≥1 month visit that require management with systemic medication or secondary surgical intervention should be reported as "IOP increase requiring management with systemic medication at ≥1 month visit" or "Need for secondary surgery intervention to manage IOP," respectively.

[20] Hypotony is defined as "early" if it occurs within 2 weeks of surgery and "late" if it occurs more than 2 weeks after surgery

10.3 REPORTING ADVERSE EVENTS AND UNANTICIPATED ADVERSE DEVICE EFFECTS

Identification, collection and reporting of adverse event information is the responsibility of the principal investigator. The investigator records the date of the event, its severity, treatment (if any) and the assessed relationship of the event to the study device on the Adverse Event Case Report Form (AE CRF).

Any ocular-related **serious adverse event** (SAE) should be reported to the study sponsor within one business day of learning of the event. Non-ocular-related SAEs should be reported to the study sponsor within two working days of learning of the event. Email the AE CRF to OMNIsafety@sightsciences.com.

Any **unanticipated adverse device effects (UADE)** must be reported to the following two entities:

1. The study sponsor – Within one working day of the investigator first learning of the event, e-mail the AE CRF to OMNIsafety@sightsciences.com; and
2. The reviewing IRB – As soon as possible, but no later than 10 working days after the investigator first learns of the event, report per the IRB's instructions.

The sponsor will conduct an evaluation of unanticipated adverse device effects. If the sponsor determines that an unanticipated adverse device effect presents an unreasonable risk to subjects, parts of the investigation presenting risks will be terminated. Termination will occur no later than 5 working days after the sponsor

makes such a determination and no later than 15 working days after the sponsor first received notice of the effect.

11 STATISTICAL CONSIDERATIONS

11.1 SAMPLE SIZE CALCULATION

The sample size calculation is based on the following statistical hypotheses and assumptions for the primary and secondary effectiveness endpoints.

Primary Effectiveness Endpoint

The statistical hypotheses for the primary effectiveness endpoint, proportion of eyes with a $\geq$ 20% reduction in unmedicated mean diurnal IOP at the 12-month postoperative examination (P1), are H0: P1 $\leq$ 0.4 and Ha: P1 > 0.4. The performance goal of 0.4 is based on Ahmed et al.[21] that 56% of Hydrus pseudophakic eyes had an outcome of 0 medications and 20% IOP reduction and 11% of 2-iStent eyes had the same outcome. The average of these two reported rates of 0 medications with IOP reduction of $\leq$ 20%, 33.5%, was used for determining the performance goal of this study. However, the article mentioned that 20% of 2-iStent eyes did not have the terminal hypotensive medications washout. As such, the rate of 11% of the 2 iStent eyes might be an under-estimation of the true rate of unmedicated IOP reduction of $\leq$ 20%. Therefore, a performance goal of 40% (the closest integer larger than 33.5%) is used as the performance goal of the primary effectiveness endpoint of the study.

Based on the adjusted normal distribution approach with a one-sided significance level of 0.025 (or two-sided 0.05), a sample size of **91** eyes with evaluable data at 12 months provides a statistical power of 80% at a true P1 = 0.55.

Only the study results demonstrate that the device is effective based on the primary effectiveness endpoint (i.e. one-sided p-value < 0.025), the formal statistical and clinical conclusions for the secondary effectiveness endpoints will be performed. Therefore, the overall two-sided significance level for the secondary effectiveness endpoints will be 0.05.

[redacted]

[redacted]

[21] Iqbal Ike K. Ahmed, MD, Antonio Fea, MD, PhD, Leon Au, MBBS, et al. A Prospective Randomized Trial Comparing Hydrus and iStent Microinvasive Glaucoma Surgery Implants for Standalone Treatment of Open-Angle Glaucoma, The COMPARE Study. *Ophthalmology*. 2020 Jan;127(1):52-61.

[redacted]

11.2 ANALYSIS POPULATIONS

The intent-to-treat (ITT) analysis population includes all subjects who are enrolled and treated, regardless of whether or not they have a protocol deviation. The per-protocol analysis population (PP) is a subset of ITT, which includes all subjects who have ab-interno transluminal viscoelastic delivery and trabeculotomy, 12 month IOP (or hypotensive medications washed out IOP if the medications can be washed out) and medication data, and have no clinically significant protocol deviations. It should be noted that the ITT subjects with an uneventful study procedure but with SSIs before the 12-month visit will be included in the PP population even if they do not have the 12-month IOP and medication data. The primary analyses on the primary and secondary endpoint analyses will be carried out on the per-protocol population.

The safety data will be summarized based on the ITT population. The primary and secondary endpoint analyses will also be performed on the ITT population.

11.3 DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Demographic variables gender, race, ethnicity, and age will be summarized for all enrolled subjects treated with OMNI Surgical System, along with medical history. Descriptive statistical summaries of pre-treatment parameters (min, max, median, mean, standard deviation) will also be provided. The same analyses will be performed for the ITT and PP populations.

11.4 EFFECTIVENESS ENDPOINTS AND ANALYSIS METHODS

Descriptive statistics on continuous variables will include mean, standard deviation, median, minimum, and maximum. Confidence intervals for change from baseline will be included for selected endpoints. Categorical variables will be summarized using frequency counts and percentages. Exact confidence intervals for point estimates may be provided. Statistical testing will be one-sided with a significance level of 0.025 or two-sided significance level of 0.05 unless specify otherwise. Data listings of individual subject data may be provided.

As described above, the primary analyses of the primary and secondary effectiveness endpoints will be based on the PP population, although the analyses will also be performed on the ITT population. The safety data will be summarized based on the ITT population.

11.4.1 PRIMARY EFFECTIVENESS ENDPOINT

Proportion of eyes with a ≥ 20% decrease in unmedicated mean diurnal IOP at the 12-month postoperative examination compared to baseline will be calculated. The binomial distribution will be used to derive the exact 95% confidence interval of the percent. The

proportion will be compared against the performance goal of 0.4 (or 40%) based on binomial distribution.

[redacted]

For the analyses based on the ITT population, the following imputation for subjects with missing 12-month data but without SSI may be performed:

- The within-eye worst IOP (collected after 3 months postoperatively or IOP at baseline for the subjects with no data after postoperative 3 months) for the missing 12-month IOP and worst number of IOP lowering medications (collected after 3 months postoperatively or IOP-lowering medication data at baseline for the subjects with no data after postoperative 3 months) for the missing 12-month number of IOP-lowering medications.
- The worst IOP (collected after 3 months postoperatively or IOP at baseline for the subjects with no data after postoperative 3 months) during the study for the missing 12-month IOP and worst number of IOP-lowering medications (collected after 3 months postoperatively or IOP-lowering medication data at baseline for the subjects with no data after postoperative 3 months) during the study for the missing 12-month number of IOP-lowering medications.
- The mean IOP during the study for the missing 12-month IOP and mean number of IOP-lowering medications during the study for the missing 12-month number of IOP-lowering medications.
- The last-observed-carried-forward approach.

11.4.2 [redacted]

[redacted]

11.4.3 COVARIATE ANALYSIS

The following variables will be examined for their prognostic value to the primary and secondary effectiveness endpoints using the PP population with the imputation used for the IOP-related SSIs:

- Age group (based on observed quartiles)
- Gender (male and female)
- Race (White and non-White)
- Ethnicity
- Baseline IOP group (based on observed quartiles)
- Screening Number of IOP-lowing medications (0, 1, 2, 3 and 4)
  Note: the grouping of medication number may be changed based on the observed data.
- Study site

For the primary effectiveness endpoint and the second secondary effectiveness endpoint, Fisher's test will be performed. For the first secondary effectiveness endpoint, one-way ANOVA with one of the factors listed above will be used to check the possible covariate effects. A p-value of 0.15 will be used for evaluating the possible covariate effects.

11.4.4 Other Important Clinical Effectiveness Outcomes

The analysis will be based on the PP Population.

For subjects treated with hypotensive medications at Screening Visit, the change in number of hypotensive medications from Screening to 12 Month (before washout if it is needed) will be calculated. For subjects treated with SSIs the change in number of hypotensive medications will be assumed to be 0. The descriptive statistics such as mean, standard deviation, median, minimum, and maximum will be used to summarize the change in number of hypotensive medications used at 12 months from Screening. The 95% confidence interval of the mean change will be calculated based on the t-distribution.

The percent change in unmedicated DIOP from baseline to 12 months will be calculated for each eye in the PP population. For eye treated with SSI, the baseline unmedicated DIOP will be used to impute the 12 month unmedicated IOP (i.e. 0% change). The descriptive statistics such as mean, standard deviation, median, minimum, and maximum will be used to summarize the percent change in unmedicated DIOP at 12 months. The 95% confidence interval of the mean percent change will be calculated based on the t-distribution.

11.4.5 [redacted]

11.5 Safety Analysis

All safety analyses will be performed on the ITT population based on all available data descriptively.

11.5.1 Adverse Event

Adverse events (AEs) will be classified as pretreatment, intraoperative or postoperative. The number and the percent of eyes reporting at least 1 adverse event of a given type will be summarized. Additionally, the number of reports of each type of AEs will be provided.

For each AE, the number and the percent of eyes reported with the event will be summarized by the severity level. For eyes with multiple reports of the same type of AE, the maximum severity will be used. Similarly, the AE relationship to the procedure will be summarized. For eyes with multiple reports of the same type of AE, the closest relationship to the procedure will be used.

11.5.2 Best Corrected Visual Acuity (BCVA)

The number and percent of eyes reporting with BCVA of 20/20 or better, 20/25 or better, 20/32 or better, 20/40 or better, worse than 20/40 to 20/80, worse than 20/80

to 20/200, and worse than 20/200 at each visit will be summarized. The number and percent of eyes reporting BCVA of increase ≥ 10 letters, increase 10 letters, increase ≥ 5 letters to < 10 letters, within 5 letters change, decrease ≥ 5 letters to < 10 letters, decrease 10 letters, and decrease ≥ 10 letters at each postoperative visit will be calculated.

[redacted]

[redacted]

[redacted]

11.6 INTERIM ANALYSIS

The primary analysis for this study will occur after the final subject reaches their 12-month follow-up. Endpoints listed below will be analyzed at an interim analysis performed when 80% of subjects reach 6 months follow up. No device effectiveness will be claimed based on the interim analysis outcomes.

Effectiveness outcomes up to 6 months will be summarized descriptively:

1. Percent of eyes with a ≥20% reduction in IOP with no increase in IOP-lowering medications compared to screening visit
2. Percent of eyes with IOP between 6 and 18 mmHg with no increase in IOP-lowering medications compared to screening visit
3. Percent of eyes with IOP between 6 and 21 mmHg with no increase in IOP-lowering medications compared to screening visit
4. Reduction in mean IOP from screening visit; and
5. Reduction in mean number of IOP-lowering medications from screening visit for the subjects who are on medications at the screening visit

[redacted]

[redacted]

11.7 DEVIATION FROM THE STATISTICAL PLAN

Any deviations from the statistical plan will be noted in the final report.

12 MONITORING PROCEDURES

Sight Sciences or contract research organization (CRO) personnel will monitor the study in a manner consistent with FDA regulations, good clinical practices and the clinical research standards adopted by Sight Sciences. Study monitoring will be executed using on-site visits, via remote means, or a combination of both, and will involve the following elements:

- Site Qualification: Sight Sciences or CRO personnel will meet with investigators and clinical study staff prior to the initiation of the study in order to review the adequacy of the subject population, facilities, and equipment with respect to the needs of the study, and to familiarize the investigator with the study protocol. If Sight Sciences or the CRO have recently been involved with an investigator for another study, a site qualification visit may not be necessary.
- Site Initiation: Sight Sciences and/or CRO personnel will meet with the investigator(s) and clinical study staff when the site is ready to begin enrolling subjects in order to train them in how to properly select subjects, perform the study procedure, and record study data. This visit will include, but not be limited to a review of the following:
  - Detailed review of the protocol
  - Informed consent procedures
  - Instructions for the surgical procedure
  - Records and reports
- Interim Monitoring: Sight Sciences or CRO personnel will conduct routine visits either remotely or in-person, during the course of the study to review charts, perform source document verification, ensure proper adherence to the study protocol, and to review regulatory documents. Interim monitoring visits and telephone consultation will occur as necessary during the course of the study to ensure the proper progress and documentation of the study findings.
- Study Close Out Visit: At the conclusion of the trial there will be a study closure visit during which several actions, including but not limited to the following, will be performed:
  - A final inspection of the study binder
  - Accountability and return of all devices and non-consumable ancillary study supplies to the sponsor
  - Discussion of record retention requirements with the investigator
  - Close-out notification to the IRB

13 DATA AND QUALITY MANAGEMENT

13.1 DATABASE MANAGEMENT

The study database will be designed using an electric data capture (EDC) system that is compliant with 21 CFR Part 11 and relevant guidance documents. The EDC will be developed and maintained by an independent, qualified data management firm.

The database will incorporate time-stamped audit trails, protection of human subjects, restricted access, and data security at the component level. Each database module, including each individual eCRF, will be validated by conducting a series of standard tests that demonstrate usability and correctness of the database system. The database will be maintained on an ongoing basis and will be routinely backed up.

13.2 SUBJECT IDENTIFICATION

The subjects will be identified by a six-digit subject number composed of a double-digit study identification number, a two-digit center identification number followed by a two to three-digit sequential subject number. A subject identification number will be assigned after informed consent is obtained. This will ensure that subject information contained in the study records is de-identified of personal information and kept confidential.

13.3 SUBJECT ACCOUNTABILITY

All subjects enrolled and treated in this clinical investigation shall be monitored for the duration of the investigation. The clinical investigation shall be considered completed when all subjects that have been enrolled in the investigation have reached the final reporting period, excluding subjects who were withdrawn.

13.4 CONFIDENTIALITY

All medical records associated with the clinical investigation will be made available for review by Sight Sciences personnel, its contract research organization (CRO) and governmental/regulatory agencies involved. The results of the study may be published in the future for scientific and marketing purposes, but the identity of each subject will not be revealed. All records will be stored in a secure area at the investigator's facility, the CRO, the data management firm and at Sight Sciences, Inc per each organization's own SOPs.

13.5 SOURCE DATA AND CASE REPORT FORMS

Source data will be entered into a validated electronic system at each site by trained personnel in accordance with 21 CFR Part 11 requirements. Electronic entries will be

100% verified against corresponding source data at the sites and queried/corrected if needed to the extent possible. Medical site records serve as source data. In addition, data that are collected exclusively for the purpose of this study and not normally recorded in the subjects' medical records can be collected directly on the study worksheets provided by the sponsor and these study worksheets will serve as the source data.

Source data and study worksheets are to be maintained at the site in the subject records or in the medical records. All data entries must be made in accordance with ALCOA standards and GDP.

13.6 Retention Period

Clinical sites are to retain any and all clinical trial material (documentation, photographs, etc.) for a period of two years from the date a marketing application is approved or two years after the investigation has been discontinued, or as directed by their institutional document retention requirements, whichever is the longest. After that time, the items must be returned to Sight Sciences for archiving.

14 Protocol Modifications and Deviations

Protocol modifications may occur during the study. Each will be approved by the sponsor before implementation. Each will undergo Institutional Review Board (IRB) review and approval, as necessary.

Any deviations from this protocol intended to protect the life or physical well-being of a subject in an emergency are to be reported to Sight Sciences, Inc. as well as the IRB as soon as possible, and no later than 5 working days after the emergency occurred.

All protocol deviations will be documented using the Protocol Deviation form.

15 Device Failures and Malfunctions

All device failures or malfunctions should be recorded on the Customer Experience Form and reported to Sight Sciences Customer Service (877-266-1144).

16 Ethical Considerations

16.1 Declaration of Helsinki

This study shall be conducted in accordance with the Declaration of Helsinki (Appendix D).

16.2 INSTITUTIONAL REVIEW BOARDS (IRB)

The study shall not begin at a site until approval has been obtained from the reviewing IRB. It is the Investigators' responsibility to obtain and maintain written approval of the study protocol and Informed Consent documents from the appropriate IRB. It is also the Investigators' responsibility to notify that body about any amendments to these documents and to follow the IRBs rules regarding the reporting of Adverse Events and Protocol Deviations related to the device and/or this study. Copies of all written approvals (identifying the study, the submitted and approved documents and the date reviewed) and the approved versions of the documents must be provided to Sight Sciences or its CRO.

The Investigators must file all correspondence with the IRB and forward copies of such correspondence to Sight Sciences.

16.3 INFORMED CONSENT DOCUMENT (ICD)

An Informed Consent template that covers all protocol procedures and follows GCP Guidelines will be prepared by Sight Sciences and made available to each Investigator. The Investigator may adapt these templates to the requirements of the local IRB and of the institution where the study is conducted, but any revisions made to the ICD must be submitted to the sponsor for review prior to submission to the IRB. A copy of each IRB-approved ICD version is to be made available to Sight Sciences and its CRO. The approved, IRB-stamped ICD is to be kept in its full length in the study Regulatory Binder. Original, signed ICDs are to be maintained in study records and must be made available for monitoring review.

16.4 PUBLIC LISTING OF STUDY

The study will be listed on the NIH website www.clinicaltrials.gov.

17 STUDY ADMINISTRATION

17.1 EARLY TERMINATION OR SUSPENSION OF THE STUDY OR AN INVESTIGATIONAL SITE

Sight Sciences may terminate the study, in which case the investigators and associated IRBs will be notified in writing. Possible reasons for study termination include but are not limited to:

- The discovery of an unexpected, significant, or unacceptable risk to the study subjects implanted with the device
- Withdrawal of FDA clearance of the OMNI device.
- Insufficient enrollment in the study

- The Sponsor determines that enough data has been collected for the study, and no further data are needed.

Sight Sciences reserves the right to stop the study at a particular site any time after the initiation visit if there have been no subject enrollments or if there have been significant protocol deviations/violations at the site.

Likewise, a principal investigator may terminate the study at his/her institution. This decision must be followed by written notification to Sight Sciences within five working days, stating the reasons for termination.

If the study is terminated, every effort should be made to obtain final follow-up from all subjects.

In the event that there are significant human use issues with the device, the investigator will be consulted to make a determination of whether the study should be terminated or not.

17.2 INVESTIGATOR RESPONSIBILITIES

17.2.1 GENERAL RESPONSIBILITIES OF INVESTIGATORS

An Investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations, for protecting the rights, safety, and welfare of subjects under the Investigator's care, and for the control of devices under investigation. An Investigator also is responsible for ensuring that informed consent is obtained in accordance with 21 CFR part 50.

17.2.2 SPECIFIC RESPONSIBILITIES OF INVESTIGATORS

1. Awaiting approval - An Investigator may determine whether potential subjects would be interested in participating in an investigation, but shall not request the written informed consent of any subject to participate, and shall not allow any subject to participate before obtaining IRB approval.
2. Subject Qualification -The Investigator is responsible for ensuring that all subjects entering the study conform to the subject selection criteria.
3. Compliance - An Investigator shall conduct an investigation in accordance with the signed agreement with the Sponsor, the investigational plan, all applicable FDA regulations, and any conditions of approval imposed by an IRB.

17.2.3 INVESTIGATOR RECORDS

A participating Investigator shall maintain the following accurate, complete, and current records relating to the Investigator's participation in an investigation for the period specified in Section 13.6:

1. All correspondence with another Investigator, an IRB, the Sponsor, a clinical research associate (CRA) or monitor, or FDA, including required reports.
2. Records of each subject's case history and exposure to the device. Case histories include the study CRF's/worksheets and supporting data including, for example, signed and dated consent forms and medical records. Such records shall include:
    a) Documents evidencing informed consent.
    b) All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.
3. The protocol, with documents showing the dates and reasons for each deviation from the protocol.
4. Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

17.2.4 INVESTIGATOR REPORTS

An Investigator shall prepare and submit the following complete, accurate, and timely reports:

1. Unanticipated Adverse Device Effects - An Investigator shall submit to the Sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the Investigator first learns of the effect.
2. Withdrawal of IRB Approval - An Investigator shall report to the Sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the Investigator's part of an investigation.
3. Progress - An Investigator shall submit progress reports on the investigation to the Sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly.
4. Deviations from the Investigational Plan - An Investigator shall document and report to the Sponsor any deviation from the investigational plan.
5. Informed Consent - If an Investigator enrolls a subject without obtaining informed consent, the Investigator shall report such use to the Sponsor and the reviewing IRB within 5 working days after the use occurs.

6. Final Report - An Investigator shall, within 3 months after termination or completion of the investigation or the Investigator's part of the investigation, submit a final report to the Sponsor and the reviewing IRB.
7. Other - An Investigator shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

17.3 INVESTIGATOR AGREEMENT

The principal investigators in each center shall agree to the clinical protocol and any amendments and indicate their approval and agreement by signing and dating the cover page of the study protocol and the Investigator Responsibility Agreement.

18 PUBLICATION POLICY

Sight Sciences recognizes the value of disseminating research results. It is understood that the Study is part of the Multi-Center Clinical Trial and publication of results is expected. This publications policy applies to journal articles, conference abstracts, and conference presentations (posters and slides) covering Sight Sciences-sponsored clinical studies. This policy is in addition to any arrangement contained in the Clinical Trial Agreement between Sight Sciences and the investigator.

Multi-Site Data

Clinical site investigators are encouraged to propose publications and abstracts that include clinical or research data from multiple clinical sites; such projects will be coordinated by Sight Sciences. Authorship of papers and abstracts resulting from these projects will be determined collaboratively according to the following guidelines:

- The first author on such publications will be the person who primarily wrote the paper and took the lead on the research. In the case of clinical trial papers where all authors contributed equally, authorship order may be based on site enrollment or other criteria at Sight Sciences' discretion.
- Other authors include those who significantly contributed to the specific work.
- At least one person from each clinical site whose study subjects appear in the work will be acknowledged in the manuscript/presentation in some way, either as an author group member, a non-author contributor, or listed in the acknowledgements, depending on the particular policies of the journal or conference.

Single Site Data

After publication of the multi-center study results in a peer-reviewed journal, or if Sponsor has not submitted a manuscript for publication in a peer-reviewed journal within twelve (12) months after the study has been completed, whichever occurs first, Investigators may publish the results of the Study generated by the Investigator, subject

to the obligations of the Clinical Trial Agreement between Sight Sciences and the Investigator, and the prior approval of Sponsor in writing.

Publications Review Policy

Investigators must submit all presentations, posters, abstracts and manuscripts pertaining to this study to Sight Sciences for review in advance of their submission. Sight Sciences conducts this review to protect its proprietary rights to information, inventions, or products developed under the Study. Please use the following guideline to determine the absolute minimum advance time for submitting an item to Sight Sciences for review:

- Presentations/Posters: 5 business days in advance of presentation
- Abstracts: 5 business days in advance of submission
- Manuscripts: 30 calendar days in advance of submission for publication

In accordance with the Clinical Trial Agreement, these items must receive written approval from Sight Sciences in order for them to be submitted or presented. If an item is not received in the timeframe listed above, approval may not be granted due to insufficient time for considered review. In addition, since most of our Clinical Trial Agreements require that Sight Sciences has 60 days to review publications, Sight Sciences reserves the rights granted in those Agreements if circumstances require a longer review.

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20 APPENDIX A – METHODS FOR EXAMS, TESTS AND QUESTIONNAIRES

20.1 LIST OF STUDY PROCEDURES

1. Informed Consent
2. Demographics, Medical & Ocular History
3. Medication Log
4. [redacted]
5. BCVA
6. [redacted]
7. IOP (Goldmann Tonometry)
8. Unmedicated Diurnal IOP
9. Slit Lamp Exam
10. Gonioscopy
11. Dilated Fundus Exam/C:D Ratio
12. Eligibility Assessment
13. [redacted]
14. AE Assessment

[redacted]

[redacted]

1. [redacted]

4. [redacted]

7. [redacted]

6. [redacted]

Calibration and Documentation

The calibration of the tonometer will be checked at least once every three months with the weight system at 0, 2, and 6 grams as supplied by the manufacturer. When the calibration steps provide readings within ± 2 mmHg of the target value for each weight, the tonometer is considered adequately calibrated. However, if the variation exceeds this amount, a different adequately calibrated instrument should be used for IOP measurements.

The investigator must maintain written documentation in a log (hardcopy or electronic format acceptable) of the calibration of each tonometer used at the beginning and throughout the study period, and make these records available to study monitors for review. Documentation must describe the unit (by model and serial number or other permanent identifier), the date of each calibration, the name or initials of the person performing the calibration, and an indication as to whether or not the unit passed the calibration. If not calibrated successfully, a note should be entered in the log about contacting the authorized manufacturer's representative for repair and what repairs were required. Following any repair, another calibration should be documented prior to clinical use.

[redacted]

20.5 VISUAL FIELD EXAMINATION

[redacted]

Visual fields are to be performed with a non-dilated pupil unless, in the opinion of the investigator, the pupil is so miotic that dilation is required (e.g., < 3mm). If dilation was

performed at screening, it should be performed at all subsequent visual field examinations. However, dilation should not be performed before the IOP measurement on the appropriate visits.

[redacted]

20.6 DILATED FUNDUS EXAMINATION

A mydriatic should be used to dilate the pupil so that an examination of the fundus can be conducted with an indirect ophthalmoscope and slit lamp biomicroscopy (with contact lens, Hruby lens or 60-, 66-, 78-, or 90 diopter lens). The appearance of the optic disc, macula, vessels and periphery should be evaluated and reported on the Baseline form. A measurement of the cup to disc ratio should be made and reported.

20.7 SLIT LAMP EXAMINATION

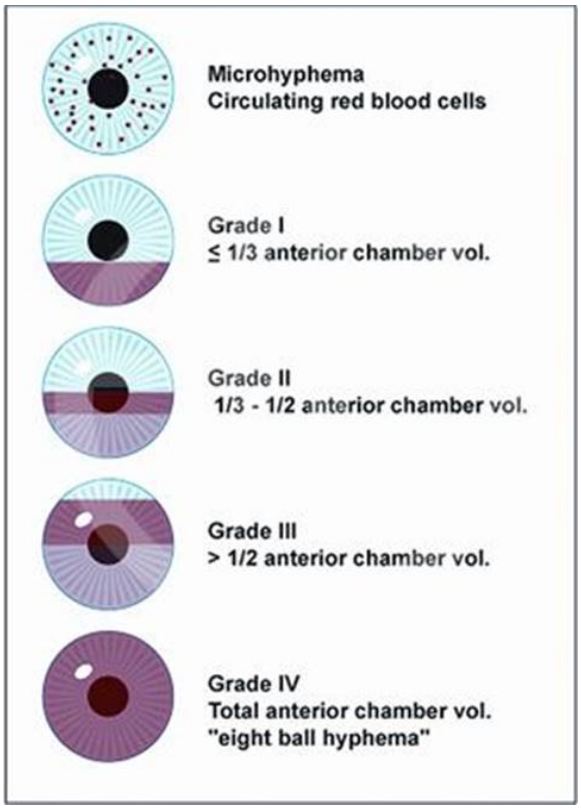
The clinician will examine the conjunctiva, cornea, anterior chamber, lens and anterior vitreous of the eye with the aid of a slit lamp, which is a table-mounted binocular microscope. Fluorescein dye will be instilled into the ocular cul-de-sac to facilitate this examination. In addition to the following, any evidence of pigment dispersion visible in slit lamp examination should be evaluated and noted.

[redacted]

Severe (+3) Marked fluorescein staining or epithelial loss

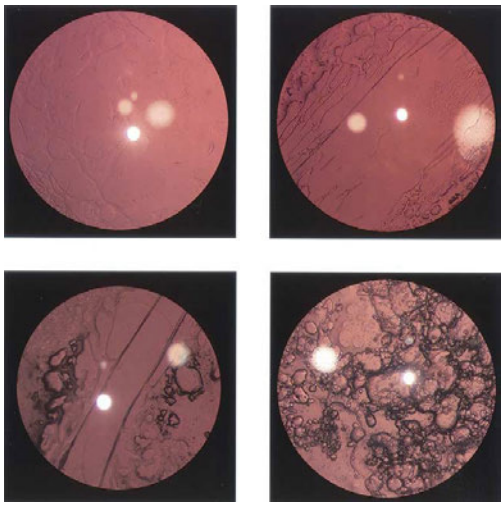
The presence of hypopyon is recorded separately. The presence of "microhyphema" or "layered hyphema" in the anterior chamber should also be recorded. Layered hyphema will be graded using the following scale (If Grade 1, also record size in mm on the CRF).[22]

[22] http://www.aao.org/image/hyphema-grading-system-2



Posterior Capsule Opacification

As a routine part of the slit lamp examination, posterior capsule opacification (PCO) will be evaluated using the following scale:



NONE

Minimal (Top left image)

Mild (Top right image)

Moderate (bottom left image)

Severe (bottom right image)

Other Slit Lamp Findings (complete for each finding)

- Trace
- Mild
- Moderate
- Severe

[redacted]

[redacted]

20.9 OCULAR HYPOTENSIVE MEDICATIONS

Each ocular hypotensive medication will be recorded on the study record. If subjects are taking combination medications such as Cosopt this is to be counted as two medications even though this is only in 1 bottle.

21 APPENDIX B - DECLARATION OF HELSINKI

I. PREAMBLE

1. The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data.

   The Declaration is intended to be read as a whole and each of its constituent paragraphs should be applied with consideration of all other relevant paragraphs.

2. Consistent with the mandate of the WMA, the Declaration is addressed primarily to physicians. The WMA encourages others who are involved in medical research involving human subjects to adopt these principles.

II. GENERAL PRINCIPLES

1. The Declaration of Geneva of the WMA binds the physician with the words, “The health of my patient will be my first consideration,” and the International Code of Medical Ethics declares that, “A physician shall act in the patient's best interest when providing medical care.”

2. It is the duty of the physician to promote and safeguard the health, well-being and rights of patients, including those who are involved in medical research. The physician's knowledge and conscience are dedicated to the fulfilment of this duty.

3. Medical progress is based on research that ultimately must include studies involving human subjects.

4. The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best proven interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality.

5. Medical research is subject to ethical standards that promote and ensure respect for all human subjects and protect their health and rights.

6. While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects.

7. It is the duty of physicians who are involved in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects. The responsibility for the protection of research subjects must always rest with the physician or other health care professionals and never with the research subjects, even though they have given consent.

8. Physicians must consider the ethical, legal and regulatory norms and standards for research involving human subjects in their own countries as well as applicable international norms and standards. No national or international ethical, legal or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration.

9. Medical research should be conducted in a manner that minimizes possible harm to the environment.

10. Medical research involving human subjects must be conducted only by individuals with the appropriate ethics and scientific education, training and qualifications. Research on patients or healthy volunteers requires the supervision of a competent and appropriately qualified physician or other health care professional.

11. Groups that are underrepresented in medical research should be provided appropriate access to participation in research.

12. Physicians who combine medical research with medical care should involve their patients in research only to the extent that this is justified by its potential preventive, diagnostic or therapeutic value and if the physician has good reason to believe that participation in the research study will not adversely affect the health of the patients who serve as research subjects.

13. Appropriate compensation and treatment for subjects who are harmed as a result of participating in research must be ensured.

III. RISKS, BURDENS AND BENEFITS

- In medical practice and in medical research, most interventions involve risks and burdens.

  Medical research involving human subjects may only be conducted if the importance of the objective outweighs the risks and burdens to the research subjects.

- All medical research involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and groups involved in the research in comparison with foreseeable benefits to them and to other individuals or groups affected by the condition under investigation.

  Measures to minimize the risks must be implemented. The risks must be continuously monitored, assessed and documented by the researcher.

- Physicians may not be involved in a research study involving human subjects unless they are confident that the risks have been adequately assessed and can be satisfactorily managed.

  When the risks are found to outweigh the potential benefits or when there is conclusive proof of definitive outcomes, physicians must assess whether to continue, modify or immediately stop the study.

IV. VULNERABLE GROUPS AND INDIVIDUALS

- Some groups and individuals are particularly vulnerable and may have an increased likelihood of being wronged or of incurring additional harm.

  All vulnerable groups and individuals should receive specifically considered protection.

- Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research.

V. SCIENTIFIC REQUIREMENTS AND RESEARCH PROTOCOLS

- Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, as appropriate, animal experimentation. The welfare of animals used for research must be respected.

- The design and performance of each research study involving human subjects must be clearly described and justified in a research protocol.

  The protocol should contain a statement of the ethical considerations involved and should indicate how the principles in this Declaration have been addressed. The protocol should include information regarding funding, sponsors, institutional affiliations, potential conflicts of interest, incentives for subjects and information regarding provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study.

  In clinical trials, the protocol must also describe appropriate arrangements for post-trial provisions.

VI. RESEARCH ETHICS COMMITTEES

- The research protocol must be submitted for consideration, comment, guidance and approval to the concerned research ethics committee before the study begins. This committee must be transparent in its functioning, must be independent of the researcher, the sponsor and any other undue influence and must be duly qualified. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as

applicable international norms and standards but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration.

The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events. No amendment to the protocol may be made without consideration and approval by the committee. After the end of the study, the researchers must submit a final report to the committee containing a summary of the study's findings and conclusions.

VII. PRIVACY AND CONFIDENTIALITY

- Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information.

VIII. INFORMED CONSENT

- Participation by individuals capable of giving informed consent as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no individual capable of giving informed consent may be enrolled in a research study unless he or she freely agrees.

- In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information.

  After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed.

  All medical research subjects should be given the option of being informed about the general outcome and results of the study.

- When seeking informed consent for participation in a research study the physician must be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In such situations the informed consent must be sought by an appropriately qualified individual who is completely independent of this relationship.

- For a potential research subject who is incapable of giving informed consent, the physician must seek informed consent from the legally authorized representative. These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the group represented by the potential subject, the research cannot instead be performed with persons capable of providing informed consent, and the research entails only minimal risk and minimal burden.

- When a potential research subject who is deemed incapable of giving informed consent is able to give assent to decisions about participation in research, the physician must seek that assent in addition to the consent of the legally authorized representative. The potential subject's dissent should be respected.

- Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research group. In such circumstances the physician must seek informed consent from the legally authorized representative. If no such representative is available and if the research cannot be delayed, the study may proceed without informed consent provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee. Consent to remain in the research must be obtained as soon as possible from the subject or a legally authorized representative.

- The physician must fully inform the patient which aspects of their care are related to the research. The refusal of a patient to participate in a study or the patient's decision to withdraw from the study must never adversely affect the patient-physician relationship.

- For medical research using identifiable human material or data, such as research on material or data contained in biobanks or similar repositories, physicians must seek informed consent for its collection, storage and/or reuse. There may be exceptional situations where consent would be impossible or

impracticable to obtain for such research. In such situations the research may be done only after consideration and approval of a research ethics committee.

IX. USE OF PLACEBO

- The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best proven intervention(s), except in the following circumstances:

  Where no proven intervention exists, the use of placebo, or no intervention, is acceptable; or

  Where for compelling and scientifically sound methodological reasons the use of any intervention less effective than the best proven one, the use of placebo, or no intervention is necessary to determine the efficacy or safety of an intervention

  and the patients who receive any intervention less effective than the best proven one, placebo, or no intervention will not be subject to additional risks of serious or irreversible harm as a result of not receiving the best proven intervention.

  Extreme care must be taken to avoid abuse of this option.

X. POST-TRIAL PROVISIONS

- In advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial. This information must also be disclosed to participants during the informed consent process.

XI. RESEARCH REGISTRATION AND PUBLICATION AND DISSEMINATION OF RESULTS

- Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject.

- Researchers, authors, sponsors, editors and publishers all have ethical obligations with regard to the publication and dissemination of the results of research. Researchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. All parties should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results must be published or otherwise made publicly available. Sources of funding,

institutional affiliations and conflicts of interest must be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication.

XII. UNPROVEN INTERVENTIONS IN CLINICAL PRACTICE

In the treatment of an individual patient, where proven interventions do not exist, or other known interventions have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician's judgment it offers hope of saving life, re-establishing health or alleviating suffering. This intervention should subsequently be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information must be recorded and, where appropriate, made publicly available.