IVANTIS®

# Hydrus® Microstent
# Instructions for Use

**CAUTION: Federal Law restricts this device to sale by or on the order of a physician.**

## INSTRUCTIONS FOR USE TABLE OF CONTENTS



## 1. DEVICE DESCRIPTION

The Hydrus® Microstent is a crescent-shaped implantable **microstent** pre-loaded onto a hand-held **delivery system**.

The microstent (**Figure 1**) is composed of nitinol, a metal alloy of nickel (Ni) and titanium (Ti). Nitinol has been used extensively in a variety of implantable devices for its proven properties of flexibility, strength and biocompatibility. As a shape memory alloy, nitinol has super-elastic properties making it suitable as a support structure in Schlemm's canal. The implant is laser cut from nitinol tubing to a proprietary design with alternating “spines” for structural support and “windows” to provide outflow pathways for aqueous humor. After laser cutting, the shape of the implant is heat-set to a curvature that matches the curvature of Schlemm’s canal and is electro-polished to create a smooth biocompatible surface. The microstent is approximately 8mm in overall length with major and minor axes of 292µm and 185µm, respectively. The length and curvature of the implant are designed to occupy approximately 90° or 3 clock hours of Schlemm’s canal. The implant is designed to have adequate structural thickness to support the tissue of the canal while providing maximum open flow areas through the canal, with the proximal portion of the implant exiting the canal through the trabecular meshwork to allow inflow of aqueous humor from the anterior chamber.

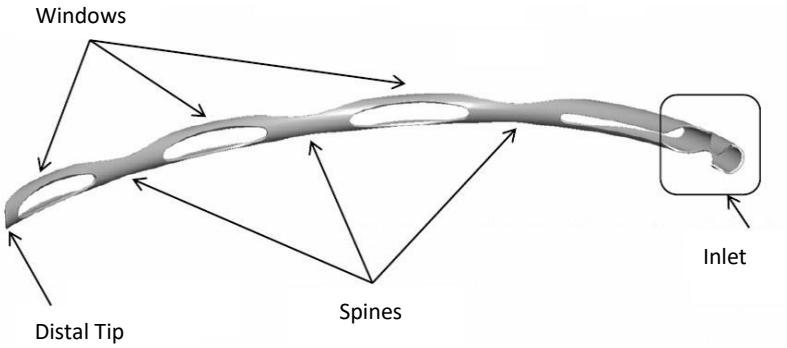


***Figure 1: Hydrus Microstent Implant***

The microstent is implanted into the eye using a hand-held delivery system (**Figure 2**) that provides for delivery of the implant through a stainless steel cannula into the target site in the eye. The delivery system was designed to provide smooth tracking and controlled delivery of the microstent into Schlemm's canal. The delivery system is an ergonomic design for use in either the right or left hand, allowing for surgeon individual preference and hand position. To accommodate a wide range of hand positions, a rotatable sleeve at the distal end allows positioning and alignment of the cannula by the surgeon to direct the implant into Schlemm's canal. The tracking wheel on the delivery system serves as the control mechanism to advance the implant into the canal or retract the implant into the cannula.

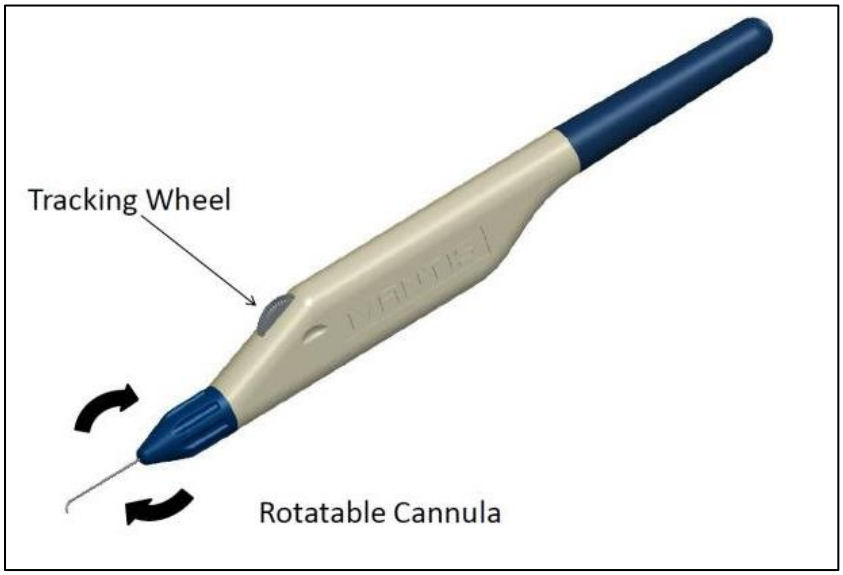


***Figure 2: Hydrus Microstent Delivery System***

To deliver the microstent into Schlemm's canal, the cannula of the delivery system is inserted through a clear corneal incision (approximately 1.5 mm in length). The cannula tip is then advanced through the trabecular meshwork until it enters Schlemm's canal and the entry point into the meshwork is coincident

with the end of the cannula bevel. The target tissue is visualized using a gonioscopic prism. After observing that the distal cannula tip is properly positioned through the trabecular meshwork into Schlemm's canal, the tracking wheel on the delivery system is used to advance and release the microstent.

The Hydrus Microstent is packaged in sterile-barrier packaging and provided sterile by gamma irradiation.

**2. INDICATIONS FOR USE:**

The Hydrus Microstent is indicated for use in conjunction with cataract surgery for the reduction of intraocular pressure (IOP) in adult patients with mild to moderate primary open-angle glaucoma (POAG).

**3. CONTRAINDICATIONS:**

The Hydrus Microstent is contraindicated under the following circumstances or conditions:

1. In eyes with angle closure glaucoma.
2. In eyes with traumatic, malignant, uveitic, or neovascular glaucoma or discernible congenital anomalies of the anterior chamber (AC) angle.

**4. WARNINGS**

1. Clear media for adequate visualization is required. The following conditions may prohibit sufficient visualization of the angle required for safe and successful implantation of the Hydrus Microstent: corneal haze, corneal opacity, or any other conditions that may inhibit gonioscopic view in the intended implant location.
2. The surgeon should perform gonioscopy prior to surgery to exclude congenital anomalies of the angle, peripheral anterior synechiae (PAS), angle closure, rubeosis and any other angle abnormalities that could lead to improper placement of the stent and pose a hazard.
3. The surgeon should monitor the patient postoperatively for proper maintenance of IOP. If IOP is not adequately maintained after surgery, the surgeon should consider appropriate additional therapy to maintain target IOP.
4. The surgeon should periodically monitor the status of the microstent with gonioscopy to assess for the development of PAS, obstruction of the inlet, migration, or device-iris or device-cornea touch. Baseline photo-documentation of the device placement is recommended. In the pivotal trial, obstruction with or without PAS was observed postoperatively as soon as 1 week up to 24 months.
5. The Hydrus Microstent is intended for implantation in conjunction with cataract surgery, which may impact corneal health. Therefore, caution is indicated in eyes with evidence of corneal compromise (e.g., Fuch’s dystrophy, corneal guttae or low endothelial cell density) or with risk factors for corneal compromise following cataract surgery (e.g., advanced age, dense nuclear sclerosis).
6. The Hydrus device consists of nickel-titanium (nitinol) alloy, which is generally considered safe. Persons with allergic reactions to nickel may have an allergic response to this device, especially those with a history of metal allergies. Some subjects may develop an allergy to nickel if this device is implanted. Certain allergic reactions can be serious. While devices that release nickel are not expected to result in symptoms such as difficulty in breathing or inflammation of the face or throat, if these types of allergic reactions occur, subjects should be instructed to seek immediate medical attention. Some forms of nickel have also been associated with carcinogenicity (ability to cause cancer) in animal models; it is unknown whether nickel released from implants will increase a patient's cancer risk.

## 5. PRECAUTIONS

1. The safety and effectiveness of the Hydrus Microstent has not been established in patients with the following circumstances or conditions:
    - Age 21 years or younger
    - Eyes with significant prior trauma
    - Eyes with abnormal anterior segment
    - Eyes with chronic inflammation
    - Eyes with glaucoma associated with vascular disorders
    - Eyes with preexisting pseudophakia
    - Eyes with uveitic glaucoma
    - Eyes with pseudoexfoliative or pigmentary glaucoma
    - Eyes with other secondary open angle glaucomas
    - Eyes that have undergone prior incisional glaucoma surgery or cilioablative procedures
    - Eyes that have undergone argon laser trabeculoplasty (ALT)
    - Eyes with unmedicated IOP < 22 mmHg or > 34 mmHg
    - Eyes with medicated IOP > 31 mmHg
    - Eyes requiring > 4 ocular hypotensive medications prior to surgery
    - In the setting of complicated cataract surgery with iatrogenic injury to the anterior or posterior segment.
    - When implantation is without concomitant cataract surgery with IOL implantation
2. The safety and effectiveness of use of more than a single Hydrus Microstent has not been established.
3. The Hydrus Microstent has not been established as an alternative to the primary treatment of glaucoma with medications.
4. If excessive resistance is encountered during the insertion of the microstent at any time during the procedure, discontinue use of the device. Continuing to insert the microstent against resistance during the insertion process may result in injury to the patient or damage to the microstent.
5. Some anatomical restrictions may not be overcome by repositioning and further attempts at implantation should cease.
6. Inspect each sterile package and Hydrus Microstent prior to use in order to verify that the device and packaging are not damaged. Do not use the product if the device or packaging has been compromised.
7. The Patient Information Card included in the package is to be given to the patient, together with instructions to keep the card as a permanent record to be shown to any health care practitioner that the patient consults in the future.

## 6. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of potential adverse effects (AEs) that may be associated with the use of the Hydrus Microstent in conjunction with cataract removal surgery. Adverse effects that occurred in the pivotal clinical trial are indicated with an asterisk (*****) and additional information regarding these adverse effects is summarized in the section, **Pivotal Clinical Trial Results.**

**Potential intraoperative adverse effects may include but are not limited to:** Choroidal detachment, choroidal hemorrhage or effusion, corneal abrasion*, corneal edema, cyclodialysis*, Descemet's membrane detachment*, device malposition*, difficulty with microstent implantation, or inability to

implant the microstent*, hyphema obscuring the surgeon's view*, inadvertent perforation of the sclera, inadvertent loss of vitreous not associated with cataract removal, iridodialysis*, iris prolapse/wound incarceration*, posterior capsular rupture, significant corneal damage, significant iris injury or trauma, vitreous in AC*, vitreous loss not associated with the cataract procedure and zonular dialysis.

**Potential postoperative adverse events may include but are not limited to:** Angle recession, anterior uveitis/iritis*, atrophy/phthisis, choroidal detachment, hemorrhage, or effusion, chronic pain in the implanted eye*, circulating blood in the AC*, corneal edema*, corneal opacification or decompensation, elevated IOP requiring treatment with oral or intravenous medications or with surgical intervention*, endophthalmitis, flat or shallow AC with lens/corneal touch, inadvertent bleb, increase in vertical cup-to-disc ratio (C/D) and/or worsening of visual field*, layered hyphema*, loss of best corrected visual acuity (BCVA)*, maculopathy, including hypotony maculopathy*, microstent-cornea or microstent-iris touch, microstent explantation, microstent malposition, dislodgement, or movement, microstent obstruction (partial or complete with blood or inflammatory material)*, peripheral anterior synechiae (PAS) formation with or without microstent obstruction*, persistent hypotony, presence of a shallow AC with peripheral iridocorneal apposition, ptosis*, retinal complications (dialysis, flap tears, retinal detachment* or proliferative vitreoretinopathy), scleral ectasia, significant foreign body sensation*, unplanned secondary ocular surgical re-intervention*, vitreous in AC*, vitreous hemorrhage associated with hyphema* and wound dehiscence (persistent aqueous leak or fistula formation).

## 7. DIRECTIONS FOR USE

**Surgical Procedure:**

The desired implant location should be assessed prior to making the clear corneal incisions for cataract surgery. Consult **Figure 4** for placement of the corneal incision to achieve implant position in the nasal hemisphere, utilizing an incision at least 1.5 mm in size for device implantation.

The microstent implantation procedure should be performed after completion of cataract extraction and intraocular lens implantation. It is important to completely remove OVD from inside the bag and from behind the iris before proceeding with Hydrus implantation.

1. Position the patient's head and microscope for use of direct gonioprism lens as shown in **Figure 3**.

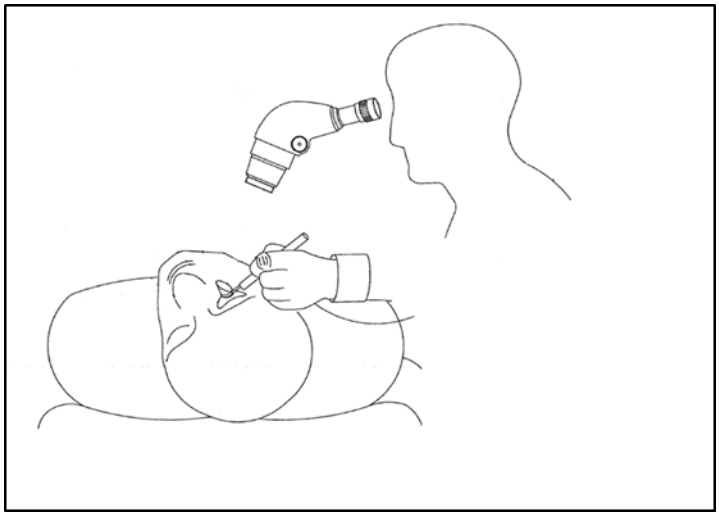

***Figure 3: Patient Positioned for Implantation Procedure***

2. Place gonioprism lens on the eye to establish a view of the angle. Use saline or ophthalmic viscoelastic as a coupling agent. Verify angle structures including scleral spur and trabecular meshwork to determine target location. Remove gonioprism lens.
3. Use of an intracameral miotic is recommended to achieve the desired visibility of implantation locations.
4. Create a corneal incision at one of the recommended incision locations as follows (refer to **Figure 4**):
    - In the right eye, for 3:00 to 12:00 clock hour location of the microstent, the incision should be made at the 7:00 clock hour position. (Figure 4 right eye)
    - In the left eye, for 9:00 to 6:00 clock hour location of the microstent, the incision should be made at the 1:00 clock hour position. (Figure 4 left eye)

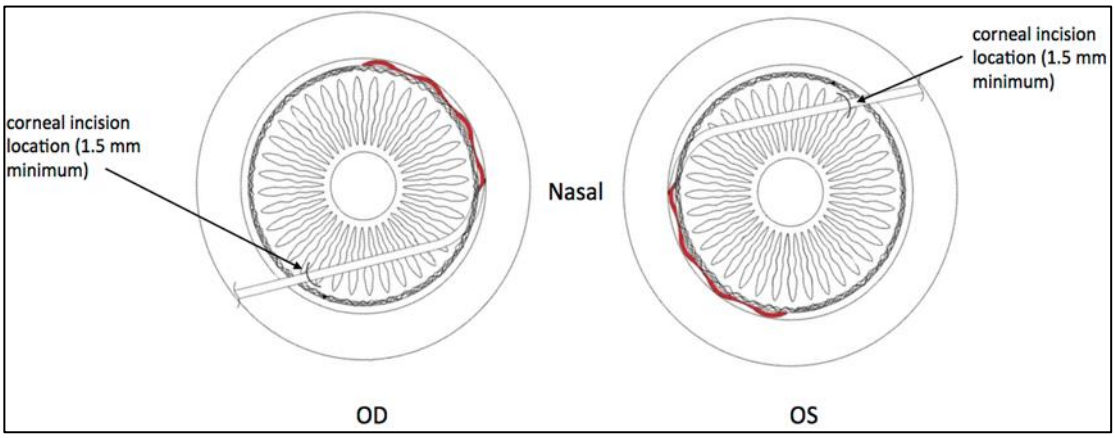


***Figure 4: Preferred Position of Incisions and Target Placement of the Microstent***

**Caution:** Superior temporal placement in either the right or left eye should be avoided, since this placement area might interfere with the ability to perform a trabeculectomy or glaucoma device surgery later with a different device (e.g., aqueous shunt).

5. Inject ophthalmic viscoelastic into the anterior chamber, unless enough viscoelastic remains from cataract procedure. A high molecular weight cohesive viscoelastic is recommended. Verify eye is firm but do not overinflate. The anterior chamber should be maintained at moderate AC pressure (approximately 15 – 20 mmHg) for an optimal view and microstent delivery.
6. Remove the Hydrus Microstent from the packaging, remove the cannula protector and adjust the cannula orientation for proper hand position.
7. Advance the microstent slightly out of the cannula then retract the implant back into the cannula to position the implant just behind the cannula opening.
8. Insert the cannula through the corneal incision as shown in **Figure 4**.
9. Replace the gonioprism lens onto the cornea to establish view of the anterior chamber angle and the cannula tip. Target the trabecular meshwork four clock hours counter clockwise from the entry point for right-handed access (opposite for left-handed access). The approach of the

delivery cannula to the target tissue area should be lateral and not across the pupil, so that the cannula angle of approach is not steep. **(Figure 4**)

10. Pierce the trabecular meshwork by aiming the cannula tip at a slight angle anteriorly (approximately 15 degrees) toward the target. After piercing the TM, the cannula tip should slide gently into Schlemm's canal. Care should be taken with cannula tip approach to fully incise the TM and position the cannula against the posterior wall of Schlemm's canal.
11. When the cannula tip is in the canal and the first window of the microstent is visible, align the cannula to be parallel with the iris. Continue to advance the microstent by rolling the wheel slowly. If resistance is felt, stop advancement, retract if necessary and readjust the position of the cannula.
12. Visually confirm the windows of the microstent entering the canal. The windows should be visible during advancement. The microstent should appear "dull" during advancement and behind the TM. A shiny stent appearance means the microstent is in front of the TM and not in Schlemm's canal. If the microstent cannot be visualized during delivery, the microstent may be posterior to Schlemm's canal. Retract the implant and redeliver the microstent.
13. Continue to advance the microstent until a physical stop is felt and the interlock releases the microstent. Verify that the inlet of the microstent is positioned in the anterior chamber.
14. If repositioning of the microstent is desired, recapture the microstent by engaging the inlet onto the interlock and reversing the wheel. Alternatively, a Kuglen hook or micro-forceps may be used to reposition the microstent.
15. If the interlock does not appear to release the microstent, slightly withdraw the cannula tip from the TM. After this cannula tip adjustment, the microstent should release.

    ***Caution:*** *If the microstent does not release from the interlock, or if the microstent cannot be retracted into the cannula, withdraw the entire delivery system from the eye.*
16. After release of the microstent from the delivery system, take care to remove the cannula tip from the eye without contacting the microstent.
17. Completely irrigate and aspirate the viscoelastic from the anterior segment.
18. Close the corneal incision according to normal practice and verify the eye has been re-pressurized.

After implantation of the Hydrus Microstent, patients should be monitored for IOP changes that may occur as possible sequelae following intraocular surgery in patients with glaucoma.

**Figure 5** shows the microstent positioned in Schlemm's canal with the proximal end (i.e., the inlet) protruding slightly into the anterior chamber for inflow of aqueous humor.

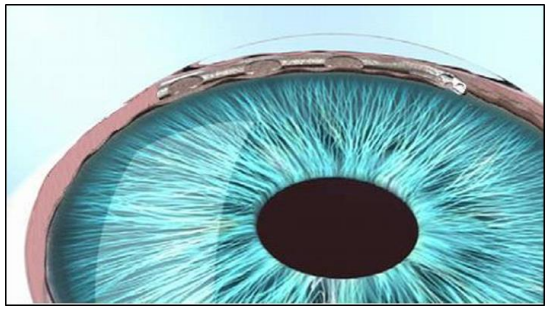

***Figure 5: Microstent in Schlemm's Canal***
**(Proximal end at right accessing aqueous humor from the anterior chamber)**

**Caution:** The Hydrus Microstent procedure requires use of an ophthalmic viscoelastic agent and anti-inflammatory steroids. These agents are known to cause IOP increases in some patients in the immediate postoperative period. Care should be taken intraoperatively to completely remove viscoelastic to decrease the risk of IOP spikes. In the postoperative period, use of hypotensive medications within the first month after surgery may become necessary. Medications should be used at the discretion of the physician.

**Caution:** If recapturing and repositioning the microstent is deemed necessary, use caution when re-engaging the interlock with the microstent. Take care to avoid inadvertent capture of tissue between the interlock and the microstent during reverse rotation of the tracking wheel.

**Postoperative Hydrus Microstent Removal**

Postoperative explantation of the microstent should be considered under the following conditions:

- Microstent contact, either continuous or intermittent, with the corneal endothelium
- Persistent uncontrolled uveitis attributable to the implant with significant anterior chamber reaction not responsive to corticosteroid therapy (topical, sub-Tenon or oral).
- Persistent hyphema due to the implant, with elevated IOP in the presence of maximum hypotensive medications.
- Microstent migration with potential threat to vision.

In the immediate postoperative period, the microstent may be removed via a clear corneal incision. To remove the Hydrus Microstent, use a gonioprism for visualization. Instill OVD to pressurize the anterior chamber; gently grasp the inlet with micro forceps and slide the implant out of the canal and the anterior chamber. In the event that the surrounding tissue is adherent to the implant, tissue separation and/or dissection may be required to facilitate removal.

## 8. ADVERSE EVENT REPORTING

Adverse events and/or potentially sight-threatening complications that may reasonably be regarded as related to the Hydrus Microstent must be reported to Ivantis, Inc.

Ivantis, Inc.
38 Discovery
Suite 150
Irvine, CA 92618 USA
+1 949 600-9650
+1 866-Ivantis (1 866 482 6847) Toll free

## 9. HOW SUPPLIED

The Hydrus Microstent is supplied sterile and non-pyrogenic in sealed inner and outer trays. The product is placed in a unit box containing product labeling and product information. The Hydrus Microstent has been sterilized using radiation.

The Hydrus Microstent is designed for single use only, and is intended to be used only on a single patient. The safety and effectiveness of cleaning, re-sterilization and/or reuse has not been evaluated and may adversely impact device integrity and patient safety.

The Hydrus Microstent and manufacturing processes do not contain latex.

Used delivery systems should be discarded only in a suitable, biohazardous sharps container.

## 10. STORAGE REQUIREMENTS

The Hydrus Microstent should be stored at room temperature in the range of 55-85°F.

## 11. EXPIRATION DATE

The sterility expiration date (year, month and day) is clearly indicated both on the outer tray and the outside of the unit box. Sterility is assured until the expiration date as long as the packaging is not punctured or otherwise damaged. The Hydrus Microstent should not be used past the expiration date.

## 12. MRI SAFETY INFORMATION


### MR Conditional

Non-clinical testing demonstrated that the Hydrus Microstent is MR Conditional. A patient with this device can be scanned safely in an MR system under the following conditions:

- Static magnetic field of 3-Tesla or less
- Maximum spatial field gradient of 4,000-gauss/cm (40-T/m)
- Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 4-W/kg in the First Level Controlled Operating Mode

Under the scan conditions defined above, the Hydrus Microstent is expected to produce a maximum temperature rise of 2.2˚C after 15-minutes of continuous scanning.

In non-clinical testing, the image artifact caused by the Hydrus Microstent extends approximately 2-mm from the microstent when imaged using a gradient echo pulse sequence and a 3-Tesla MR system.

## 13. RETURNED GOODS POLICY

In the United States, returned product will only be accepted in exchange for other products, not credit. All returns must be accompanied by an Ivantis, Inc. Return Authorization (RA) Number and be shipped via traceable means. A return authorization number is obtained by contacting the Ivantis, Inc., Customer Service Department. Issuance of this number does not constitute final acceptance of the returned products. For detailed policy guidelines, including exchange, please contact your Sales or Customer

## 14. PIVOTAL CLINICAL TRIAL RESULTS

The pivotal study for the Hydrus Microstent, known as the HORIZON Study (Hydrus 4 Trial), was a prospective, randomized, controlled, multicenter investigation conducted in the United States and other countries. A total of 556 subjects from 38 sites were randomized in a 2:1 fashion to undergo either implantation of the Hydrus Microstent after uncomplicated cataract surgery (Hydrus group) or to undergo cataract surgery without implantation of the Hydrus Microstent (control group). A total of 369 subjects were randomized to the Hydrus group and 187 subjects were randomized to the control group. In each subject, only one eye was designated as the study eye. Enrollment in the study began in February 2012, and the last study subject was randomized in May 2015. Randomized subjects were followed for 2 years postoperatively.

To participate in the study, subjects were required to have a diagnosis of POAG in the study eye treated with 1 to 4 hypotensive medications, optic nerve characteristics of glaucoma, and operable age-related cataract with BCVA of 20/40 or worse. Other key inclusion criteria for the study were as follows:

- Diurnal IOP ≥ 22 mmHg and ≤ 34 mmHg after washout of ocular hypotensive medications
- IOP increase ≥ 3 mmHg after washout of ocular hypotensive medications
- Mild-to-moderate glaucoma as determined by visual field mean deviation less than 0 and greater than -12dB

Subjects could not participate in the study if they had closed angle forms of glaucoma, congenital or developmental glaucoma, or secondary glaucoma (such as neovascular, uveitic, pseudoexfoliative, pigmentary, lens-induced, steroid-induced, trauma induced, or glaucoma associated with increased episcleral venous pressure). Subjects who had previously undergone argon laser trabeculoplasty, trabeculectomy, tube shunts, or any other prior filtration or cilioablative surgery were also excluded, as were subjects with advanced glaucoma or with unacceptable risk from washout of ocular hypotensive medications. Other exclusion criteria included proliferative diabetic retinopathy, previous surgery for retinal detachment, previous corneal surgery or clinically significant corneal dystrophy, e.g., Fuch's dystrophy (>12 confluent guttae), unclear ocular media preventing visualization of the fundus or anterior chamber angle, degenerative visual disorders such as wet age-related macular degeneration, or clinically significant ocular pathology, other than cataract and glaucoma, or subjects with other clinically significant risk factors for ocular surgery.

Only subjects who underwent uncomplicated cataract surgery were randomized to Hydrus implantation or control groups.

During the HORIZON Study, the Hydrus Microstent was implanted with a delivery system slightly different than the commercially available delivery system. The delivery system in the HORIZON study had a different interlocking mechanism for attaching and releasing the microstent. Releasing the microstent for

implantation in the HORIZON study required the microstent to be advanced into Schlemm's canal and released by reversing the wheel on the delivery system. The commercially available delivery system requires that the microstent be advanced into the canal, and is released passively from the side-interlocking mechanism by advancing the wheel to its full forward position (i.e., reversing the wheel is not required). Additionally, using the commercially available delivery system, the microstent can be reattached onto the delivery system to facilitate repositioning the microstent, if required.

The mean age of the study population was 71.1 years, with the majority (78.8%) between 60 and 79 years of age at the time of enrollment. Slightly more females (55.9%) than males (44.1%) were randomized. 79.9% of the cohort was white, 10.8% black/African-American, 5.8% Asian, and 3.6% other races. Screening and baseline characteristics were balanced between the 2 study groups. The mean baseline unmedicated, diurnal IOP was 25.5±3.0 mmHg in the Hydrus group and 25.4±2.9 mmHg in the control group. 15.7% of the Hydrus group and 15.0% of the control group had prior SLT (selective laser trabeculoplasty).

**Study Endpoints**

The primary effectiveness endpoint for this study was:

- The proportion of subjects with a reduction of at least 20% (i.e., ≥ 20%) in mean diurnal IOP from baseline at 24 months following medication washout. These subjects were defined as "IOP responders"

The percentage of eyes achieving the primary effectiveness endpoint (24-month IOP responder rate) was compared between the Hydrus group (cataract surgery with Hydrus implant) and control group (cataract surgery only). The 24-month IOP responder rate of the Hydrus group was also compared to a target rate (performance goal) of 0.5 (or 50%).

Subjects were defined as non-responders if they did not achieve the primary effectiveness endpoint, if they were missing 24-month IOP assessment outcomes, if ocular hypotensive medications were not washed out at the 24-month visit, or if they underwent an IOP-affecting secondary surgical procedure (i.e., iridotomy, iridectomy, trabeculectomy, glaucoma shunt implantation, argon laser trabeculoplasty, selective laser trabeculoplasty), or other surgery that would affect IOP.

The secondary effectiveness endpoint for the study was:

- The mean change in unmedicated diurnal IOP from baseline to 24 months

Each endpoint required a comparison between the Hydrus and control groups. The primary effectiveness analysis was performed using the Intent to Treat (ITT) population, consisting of all randomized subjects grouped according to their randomization assignment.

**Effectiveness Results**

Results from the primary and secondary endpoints are shown in **Table 1**. The primary effectiveness endpoint was met, with 77.2% in the Hydrus group and 57.8% in the control group achieving a clinically significant (≥ 20%) decrease in unmedicated mean DIOP from baseline to the hypotensive medication-free 24-month postoperative examination. This difference between groups was statistically significant ($p < 0.001$).

The secondary endpoint, the mean change in unmedicated IOP between baseline and 24-month postoperative examination, was met. The mean reduction in unmedicated mean DIOP from baseline to

24 months was -7.5±4.1 mmHg in the Hydrus group compared to -5.3±3.9 mmHg in the control group ($p < 0.001$).

***TABLE 1: PRIMARY AND SECONDARY EFFECTIVENESS RESULTS***

| Effectiveness Endpoint (Evaluated at 24 Months Postoperatively) | Hydrus (N=369) | Control (N=187) | Difference (Hydrus-Control) | p-value |
|---|---|---|---|---|
| **Primary Effectiveness Endpoint** | | | | |
| Proportion of subject eyes with unmedicated mean IOP reduction ≥ 20% from baseline | 77.2% | 57.8% | 19.5% | <0.001 |
| **Secondary Effectiveness Endpoint** | | | | |
| Difference in unmedicated mean DIOP (mmHg) reduction from baseline | -7.5 | -5.3 | -2.3 | <0.001 |

A summary of IOP non-responders who did not achieve the primary endpoint (≥20% reduction in mean DIOP from baseline at 24 months) is shown in **Table 2.**

***TABLE 2: SUMMARY OF IOP NON-RESPONDER CATEGORIES***

| | Cataract Surgery with Hydrus (N=369) n (%) | Cataract Surgery Only (N=187) n (%) |
|---|---|---|
| Total Non-Responders | 84 (22.8%) | 79 (42.2%) |
| Non-Responders: 24-month unmedicated mean DIOP reductions < 20% vs. baseline | 61 (16.5%) | 54 (28.9%) |
| Non-Responders for reasons other than IOP reduction | 23 (6.2%) | 25 (13.4%) |
| Had glaucoma-related events or secondary surgical procedures[1] | 4 (1.1%) | 5 (2.7%) |
| Unable to washout glaucoma medications | 5 (1.4%) | 3 (1.6%) |
| Missed 24-month visit | 14 (3.8%) | 17 (9.1%) |

n = number of eyes meeting corresponding criteria

[1] Secondary glaucoma surgeries included laser goniosynchialysis, YAG laser membranectomy, anterior chamber paracentesis, glaucoma filtration surgery, and selective laser trabeculoplasty (SLT)

Of the participants who were responders, 82.8% in the Hydrus group (236/285) and 56.5% in the control group (61/108) were not using ocular hypotensive medications at 24 months.

**Safety Results**

**Intraoperative Adverse Events**

Implantation of the Hydrus Microstent was successful in almost all cases, with non-implantation reported in 11 eyes (3.0%). The reasons for non-implantation were anatomical restrictions (n=3), poor visualization due to hyphema (n=3), excessive movement by the subject (n=3), suboptimal placement of the device in Schlemm's canal (n=1), and difficulty viewing the target for implantation (n=1). Besides non-implantation, a total of 14 intraoperative AEs were reported in 14 of 369 Hydrus eyes (3.8%). Intraoperative AEs in the Hydrus group are shown in **Table 3**.

***TABLE 3: INTRAOPERATIVE OCULAR ADVERSE EVENTS (AVAILABLE DATA FOR SAFETY POPULATION)***

| Adverse Event | Cataract Surgery with Hydrus (N=369) n (%) |
|---|---|
| **Eyes with any Adverse Event** | **14 (3.8%)** |
| Corneal abrasion | 2 (<1.0%) |
| Cyclodialysis | 1 (<1.0%) |
| Descemet's membrane detachment | 1 (<1.0%) |
| Device malposition[1] | 1 (0.3%) |
| Hyphema obscuring surgeon's view | 4 (1.1%) |
| Iridodialysis | 1 (<1.0%) |
| Iris prolapse/wound incarceration | 3 (<1.0%) |
| Vitreous in anterior chamber | 1 (<1.0%) |

[1] Device malposition is considered an AE if there are associated clinical sequelae of secondary surgical intervention to modify device position (i.e., repositioning or explantation), corneal endothelial touch by device, central endothelial cell loss (ECL) ≥30%, device obstruction requiring secondary surgical intervention, or chronic inflammation or irritation. None of the eyes reported with device malposition required surgical intervention to remove or reposition the microstent.

**Postoperative Adverse Events**

Postoperative ocular adverse events (AEs) that occurred in either group are reported in **Table 4**. There were no reports of device migration, flat AC with lens-cornea touch or shallow AC with peripheral iridocorneal apposition, endophthalmitis, hypopyon, choroidal hemorrhage or effusion, or atrophy/phthisis.

Peripheral anterior synechiae without device obstruction was reported in 27/369 (7.3%) Hydrus-implanted eyes, although the majority of areas of synechia or iris adhesions to the device were small in size (<1mm). PAS with device obstruction was reported in 13/369 (3.5%) Hydrus-implanted eyes; a partial device obstruction of the Hydrus inlet was reported in 6 of these cases and complete device obstruction in the remaining 7 cases. Partial or complete device obstruction was reported in 27/369 (7.3%) Hydrus implanted eyes. Anterior segment inflammation resolved in 99.5% of Hydrus subjects by 3 months. Non-persistent anterior uveitis/iritis requiring a change in the standard postoperative steroid medication regimen or re-medication with steroids was reported in 19 Hydrus eyes (5.1%). These findings resolved without sequelae in all affected eyes. In the 2 Hydrus eyes with persistent inflammation (≥Grade 1+

anterior chamber cells and/or flare lasting for more than 3 months postoperatively or recurring less than 3 months after discontinuation of treatment), the anterior chamber cells resolved 6 weeks later.

Best-corrected visual acuity (BCVA) was stable throughout the postoperative period, with 1.4% of Hydrus subjects experiencing BCVA loss of 2 lines or more on ETDRS testing in the study. Based on available data, 98.6% of Hydrus subjects had BCVA of 20/40 or better at 24 months (n=352).

***TABLE 4: POSTOPERATIVE ADVERSE EVENTS (AVAILABLE DATA FOR SAFETY POPULATION)****

| Adverse Event | Cataract Surgery with Hydrus (N=369) n (%) | Cataract Surgery Only (N=187) n (%) |
|---|---|---|
| **Subjects with Any Adverse Event** | **186/369** | **62/187** |
| Anterior uveitis / iritis (non-persistent)[1] | 19 (5.1%) | 3 (1.6%) |
| Anterior uveitis / iritis (persistent)[2] | 2 (0.5%) | 4 (2.1%) |
| BCVA loss of ≥ 2 ETDRS lines ≥ 3 months | 5 (1.4%) | 3 (1.6%) |
| Choroidal detachment | 0 (0.0%) | 1 (0.5%) |
| Corneal edema | 5 (1.4%) | 1 (0.5%) |
| Conjunctivitis | 21 (5.7%) | 13 (7.0%) |
| Cystoid macular edema | 8 (2.2%) | 4 (2.1%) |
| Device malposition[3] | 5 (1.4%) | 0 (0.0%) |
| Device obstruction, partial or complete[4] | 27 (7.3%) | N/A |
| Dry eye | 14 (3.8%) | 6 (3.2%) |
| Hyphema (>2mm at >1 day) | 4 (1.1%) | 1 (0.5%) |
| Hypotony (IOP <6 mmHg ≥ 1 month) | 0 (0.0%) | 1 (0.5%) |
| IOP elevated ≥10 mmHg from baseline ≥ 1 month | 2 (0.5%) | 5 (2.7%) |
| Peripheral anterior synechiae (device implanted) | 40 (10.8%) | N/A |
| Peripheral anterior synechiae with device obstruction | 13 (3.5%) | N/A |
| Peripheral anterior synechiae without device obstruction | 27 (7.3%) | N/A |
| Peripheral anterior synechiae (no device implanted) | 2 (0.5%) | 4 (2.1%) |
| Subconjunctival hemorrhage | 9 (2.4%) | 0 (0.0%) |
| Surgical re-intervention in study eye (not paracentesis prior to 1 week postop) | 9 (2.4%) | 9 (4.8%) |
| Vitreous hemorrhage associated with hyphema | 2 (0.5%) | 0 (0.0%) |
| Worsening in visual field MD by ≥ 2.5 dB compared with preoperative | 16 (4.3%) | 10 (5.3%) |
| Worsening ocular symptoms: a 2-point worsening to severe or more ≥ 3 months postop | 16 (4.3%) | 9 (4.8%) |

*Occurring at 2% or greater in either group, or other adverse events known to be associated with glaucoma procedures or potential risks with stent implantations

[1]Anterior chamber cell and flare requiring change in steroid treatment

[2] ≥Grade 1+ anterior chamber cells and/or flare lasting for more than 3 months postoperatively or recurring less than 3 months after discontinuation of treatment (requiring change in steroid regimen)

[3] Device malposition is considered an AE if there are associated clinical sequelae of secondary surgical intervention to modify device position (i.e., repositioning or explantation), corneal endothelial touch by device, central endothelial cell loss (ECL) ≥30%, device obstruction requiring secondary surgical intervention, or chronic inflammation or irritation. None of the eyes reported with device malposition required surgical intervention to remove or reposition the microstent.

[4] In two eyes with device obstruction, three YAG laser procedures were performed on two eyes. These procedures were not successful in removing the obstruction.

In addition to the AEs reported in **Table 4**, AEs that occurred at <2% in both groups included blepharitis, blurry vision, chalazion, diplopia (monocular), ocular pain, diabetic retinopathy (non-proliferative), epiretinal membrane, retinal break, retinal detachment/repair, retinal tear with vitreous hemorrhage, retinopathy (central serous), superficial punctate keratitis and vitreous floaters.

Adverse events that occurred at <2% in the Hydrus group included age related macular degeneration (dry and wet form), anterior capsule fibrosis, asthenopia, blood reflux, central serous retinopathy, chronic pain in study eye ≥3 months, circulating blood in the anterior chamber (i.e., not yet settled inferiorly), conjunctival cyst, conjunctival injection, corneal abrasion, corneal haze, cyst, decentered IOL, dermatitis (eyelid), diabetic retinopathy (proliferative), diplopia, disc hemorrhage, dysphotopsia (including glare and intermittent flashes), eyelid edema, foreign body in eye, hordeolum, IOP <6 mmHg due to thin cornea, lacrimal obstruction, lesion on eyelid, malpositioned IOL haptic, orbital hemangioma, persistent mydriasis, photosensitivity, ptosis, punctal stenosis, pupil irregularity, retained lens fragment, retinal macroaneurysm, retinal pigment epithelial detachment, significant foreign body sensation ≥3 months, squamous cell carcinoma, vitreous in anterior chamber and vitreous opacities.

Adverse events that occurred at <2% in the control group included afferent pupillary defect, choroidal detachment, ectropion, glaucoma progression, hematoma (eyelid), hypotony (IOP <6 mmHg ≥ 1 month), increased C/D ratio ≥0.3, inflamed pterygium, keratitis (including nummular), lid myokymia, meibomian gland dysfunction, microaneurysm, neovascular glaucoma, hypertensive retinopathy, macular edema, retinal vein occlusion, vitreoretinal tuft.

**Secondary Surgical Interventions**

Secondary ocular surgeries reported through 24 months in both groups are shown in **Table 5.** Secondary ocular surgeries for IOP or glaucoma-related events occurred in 4 (1.1%) Hydrus eyes and 5 (2.7%) controls.

*TABLE 5: SECONDARY SURGICAL INTERVENTIONS (SSI) FOR ANY OCULAR ADVERSE EVENT THROUGH 24 MONTHS*

| Adverse Event | Cataract Surgery with Hydrus (N=369) n (%) | Cataract Surgery Only (N=187) n (%) |
|---|---|---|
| **Subjects with SSIs for any ocular adverse event*** | **16 (4.3%)** | **10 (5.3%)** |
| **Secondary surgeries for IOP or glaucoma-related Events** | **4 (1.1%)** | **5 (2.7%)** |
| Anterior chamber paracentesis | 1 (0.3%) | 2 (1.1%) |
| Goniosynchialysis - with laser | 1 (0.3%) | 0 (0.0%) |
| Glaucoma shunt implantation | 0 (0.0%) | 2 (1.1%) |
| Express shunt removal | 0 (0.0%) | 1 (0.5%) |
| Selective laser trabeculoplasty (SLT) | 0 (0.0%) | 1 (0.5%) |
| Trabeculectomy with Express shunt implantation | 0 (0.0%) | 2 (1.1%) |
| Tube with pars plana vitrectomy and scleral reinforcement | 0 (0.0%) | 1 (0.5%) |
| YAG membranectomy or membranotomy | 3 (0.8%) | 0 (0.0%) |
| **Other secondary surgical interventions** | **12 (3.3%)** | **5 (2.7%)** |
| Anterior chamber irrigation and aspiration | 1 (0.3%) | 0 (0.0%) |
| Canthoplasty | 1 (0.3%) | 0 (0.0%) |
| Descemet membrane endothelial keratoplasty | 1 (0.3%) | 0 (0.0%) |
| Haptic reposition | 1 (0.3%) | 0 (0.0%) |
| Orbital tumor biopsy | 1 (0.3%) | 0 (0.0%) |
| Pars plana vitrectomy with laserpexy | 0 (0.0%) | 1 (0.5%) |
| Pars plana vitrectomy with membrane peel | 1 (0.3%) | 1 (0.5%) |
| Punctoplasty | 1 (0.3%) | 0 (0.0%) |
| Retinal detachment repair - vitrectomy and/or scleral buckle | 1 (0.3%) | 2 (1.1%) |
| Retained lens material removal | 1 (0.3%) | 0 (0.0%) |
| Retinal laser | 3 (0.8%) | 3 (1.6%) |
| Vitrectomy with retinal detachment repair | 1 (0.3%) | 0 (0.0%) |

* Some subjects had multiple SSIs

**Other Postoperative Observations**

Patient-reported information on ocular symptoms was collected using a shortened (7-item) version of an 18-item questionnaire [Musch DC et al, JAMA Ophthalmol 2017;135(12):1345-1351] adapted from the 43-item glaucoma-related symptom questionnaire used in the Collaborative Initial Glaucoma Treatment Study (CIGTS) [Janz NK et al, Ophthalmology 2001;108:887-898]. The questionnaire asked participants to report on the presence of eye irritation or burning, foreign body sensation, droopy eyelids, excessive tearing, skin sensitivity around the eyes, eye pain, and red eyes. Participants were also asked to rate how bothersome the symptom was and the degree to which they attributed the symptom to glaucoma or glaucoma treatment. The majority of participants in each group did not report the presence of symptoms at baseline, postoperative month 12, and postoperative month 24 and these proportions were similar between groups. The results of the patient reported information on ocular symptoms are provided in **Tables 6**.

***TABLE 6 CIGTS SYMPTOMS IMPACT GLAUCOMA SUBSCALE: LOCAL EYE***

| Symptom | Cataract Surgery & Hydrus Implant (369 Subjects) | | | Cataract Surgery Only (187 Subjects) | | |
|---|---|---|---|---|---|---|
| | **Baseline n (%)** | **12M n (%)** | **24M n (%)** | **Baseline n (%)** | **12M n (%)** | **24M n (%)** |
| **Total** | **369** | **365** | **357** | **187** | **180** | **170** |
| **Missed Assessment** | **5** | **8** | **4** | **1** | **2** | **1** |
| **Eye Irritation Burning, N** | **364** | **357** | **353** | **185** | **178** | **169** |
| No | 296 (81.3%) | 306 (85.7%) | 311 (88.1%) | 163 (88.1%) | 141 (79.2%) | 139 (82.2%) |
| Yes | 68 (18.7%) | 51 (14.3%) | 42 (11.9%) | 22 (11.9%) | 37 (20.8%) | 30 (17.8%) |
| Bothersome[1] | | | | | | |
| A lot | 6 (8.8%) | 4 (7.7%) | 1 (2.3%) | 5 (20.8%) | 0 (0.0%) | 6 (20.0%) |
| A moderate amount | 11 (16.2%) | 7 (13.5%) | 17 (39.5%) | 3 (12.5%) | 8 (22.2%) | 6 (20.0%) |
| Some | 18 (26.5%) | 18 (34.6%) | 8 (18.6%) | 4 (16.7%) | 10 (27.8%) | 2 (6.7%) |
| A little | 20 (29.4%) | 18 (34.6%) | 10 (23.3%) | 9 (37.5%) | 14 (38.9%) | 13 (43.3%) |
| Not at all | 13 (19.1%) | 5 (9.6%) | 7 (16.3%) | 3 (12.5%) | 4 (11.1%) | 3 (10.0%) |
| Not Reported | 296 | 305 | 310 | 161 | 142 | 139 |
| **Eye Pain, N** | **364** | **357** | **353** | **186** | **178** | **168** |
| No | 344 (94.5%) | 336 (94.1%) | 327 (92.6%) | 171 (91.9%) | 163 (91.6%) | 157 (93.5%) |
| Yes | 20 (5.5%) | 21 (5.9%) | 26 (7.4%) | 15 (8.1%) | 15 (8.4%) | 11 (6.5%) |
| Bothersome[1] | | | | | | |
| A lot | 2 (9.5%) | 4 (19.0%) | 1 (3.7%) | 1 (5.9%) | 1 (7.1%) | 1 (8.3%) |
| A moderate amount | 4 (19.0%) | 1 (4.8%) | 4 (14.8%) | 5 (29.4%) | 3 (21.4%) | 3 (25.0%) |
| Some | 7 (33.3%) | 3 (14.3%) | 6 (22.2%) | 3 (17.6%) | 3 (21.4%) | 3 (25.0%) |
| A little | 6 (28.6%) | 8 (38.1%) | 11 (40.7%) | 5 (29.4%) | 6 (42.9%) | 3 (25.0%) |
| Not at all | 2 (9.5%) | 5 (23.8%) | 5 (18.5%) | 3 (17.6%) | 1 (7.1%) | 2 (16.7%) |
| Not Reported | 343 | 336 | 326 | 169 | 164 | 156 |
| **Excessive Tearing, N** | **364** | **357** | **353** | **185** | **178** | **169** |
| No | 331 (90.9%) | 320 (89.6%) | 309 (87.5%) | 172 (93.0%) | 156 (87.6%) | 151 (89.3%) |
| Yes | 33 (9.1%) | 37 (10.4%) | 44 (12.5%) | 13 (7.0%) | 22 (12.4%) | 18 (10.7%) |
| Bothersome[1] | | | | | | |
| A lot | 5 (15.2%) | 6 (16.2%) | 6 (13.3%) | 2 (14.3%) | 1 (4.3%) | 3 (16.7%) |
| A moderate amount | 3 (9.1%) | 5 (13.5%) | 8 (17.8%) | 1 (7.1%) | 6 (26.1%) | 4 (22.2%) |
| Some | 7 (21.2%) | 6 (16.2%) | 11 (24.4%) | 2 (14.3%) | 3 (13.0%) | 4 (22.2%) |
| A little | 13 (39.4%) | 9 (24.3%) | 12 (26.7%) | 8 (57.1%) | 9 (39.1%) | 5 (27.8%) |
| Not at all | 5 (15.2%) | 11 (29.7%) | 8 (17.8%) | 1 (7.1%) | 4 (17.4%) | 2 (11.1%) |
| Not Reported | 331 | 320 | 308 | 171 | 155 | 151 |
| **Droopy Eyelids, N** | **364** | **357** | **353** | **185** | **178** | **168** |
| No | 341 (93.7%) | 337 (94.4%) | 341 (96.6%) | 175 (94.6%) | 170 (95.5%) | 162 (96.4%) |
| Yes | 23 (6.3%) | 20 (5.6%) | 12 (3.4%) | 10 (5.4%) | 8 (4.5%) | 6 (3.6%) |
| Bothersome[1] | | | | | | |
| A lot | 0 (0.0%) | 2 (9.5%) | 1 (7.7%) | 3 (25.0%) | 1 (14.3%) | 1 (14.3%) |
| A moderate amount | 2 (8.7%) | 2 (9.5%) | 0 (0.0%) | 1 (8.3%) | 2 (28.6%) | 0 (0.0%) |
| Some | 5 (21.7%) | 2 (9.5%) | 2 (15.4%) | 0 (0.0%) | 0 (0.0%) | 1 (14.3%) |
| A little | 7 (30.4%) | 8 (38.1%) | 5 (38.5%) | 4 (33.3%) | 1 (14.3%) | 3 (42.9%) |
| Not at all | 9 (39.1%) | 7 (33.3%) | 5 (38.5%) | 4 (33.3%) | 3 (42.9%) | 2 (28.6%) |
| Not Reported | 341 | 336 | 340 | 173 | 171 | 161 |

| Symptom | Cataract Surgery & Hydrus Implant (369 Subjects) | | | Cataract Surgery Only (187 Subjects) | | |
|---|---|---|---|---|---|---|
| | **Baseline n (%)** | **12M n (%)** | **24M n (%)** | **Baseline n (%)** | **12M n (%)** | **24M n (%)** |
| **Total** | **369** | **365** | **357** | **187** | **180** | **170** |
| **Missed Assessment** | **5** | **8** | **4** | **1** | **2** | **1** |
| **Red Eyes, N** | **364** | **357** | **353** | **185** | **178** | **169** |
| No | 316 (86.8%) | 310 (86.8%) | 306 (86.7%) | 158 (85.4%) | 152 (85.4%) | 150 (88.8%) |
| Yes | 48 (13.2%) | 47 (13.2%) | 47 (13.3%) | 27 (14.6%) | 26 (14.6%) | 19 (11.2%) |
| Bothersome[1] | | | | | | |
| A lot | 5 (10.2%) | 2 (4.3%) | 1 (2.2%) | 5 (17.2%) | 0 (0.0%) | 1 (5.3%) |
| A moderate amount | 7 (14.3%) | 6 (12.8%) | 8 (17.4%) | 2 (6.9%) | 4 (16.0%) | 4 (21.1%) |
| Some | 9 (18.4%) | 9 (19.1%) | 7 (15.2%) | 4 (13.8%) | 8 (32.0%) | 3 (15.8%) |
| A little | 15 (30.6%) | 22 (46.8%) | 11 (23.9%) | 9 (31.0%) | 8 (32.0%) | 7 (36.8%) |
| Not at all | 13 (26.5%) | 8 (17.0%) | 19 (41.3%) | 9 (31.0%) | 5 (20.0%) | 4 (21.1%) |
| Not Reported | 315 | 310 | 307 | 156 | 153 | 150 |
| **Feeling Like Something is in Your Eye, N** | **364** | **356** | **353** | **186** | **178** | **169** |
| No | 296 (81.3%) | 280 (78.7%) | 297 (84.1%) | 143 (76.9%) | 152 (85.4%) | 131 (77.5%) |
| Yes | 68 (18.7%) | 76 (21.3%) | 56 (15.9%) | 43 (23.1%) | 26 (14.6%) | 38 (22.5%) |
| Bothersome[1] | | | | | | |
| A lot | 6 (8.7%) | 2 (2.6%) | 5 (8.9%) | 5 (11.1%) | 2 (8.0%) | 7 (18.9%) |
| A moderate amount | 7 (10.1%) | 12 (15.8%) | 4 (7.1%) | 7 (15.6%) | 4 (16.0%) | 4 (10.8%) |
| Some | 19 (27.5%) | 19 (25.0%) | 18 (32.1%) | 7 (15.6%) | 7 (28.0%) | 4 (10.8%) |
| A little | 25 (36.2%) | 31 (40.8%) | 17 (30.4%) | 19 (42.2%) | 10 (40.0%) | 18 (48.6%) |
| Not at all | 12 (17.4%) | 12 (15.8%) | 12 (21.4%) | 7 (15.6%) | 2 (8.0%) | 4 (10.8%) |
| Not Reported | 295 | 280 | 297 | 141 | 153 | 132 |
| **Skin Sensitivity or Irritation around the Eye, N** | **364** | **357** | **353** | **186** | **178** | **169** |
| No | 339 (93.1%) | 328 (91.9%) | 329 (93.2%) | 170 (91.4%) | 160 (89.9%) | 157 (92.9%) |
| Yes | 25 (6.9%) | 29 (8.1%) | 24 (6.8%) | 16 (8.6%) | 18 (10.1%) | 12 (7.1%) |
| Bothersome[1] | | | | | | |
| A lot | 2 (7.7%) | 4 (13.3%) | 0 (0.0%) | 2 (11.1%) | 3 (17.6%) | 3 (25.0%) |
| A moderate amount | 3 (11.5%) | 1 (3.3%) | 6 (23.1%) | 3 (16.7%) | 6 (35.3%) | 2 (16.7%) |
| Some | 6 (23.1%) | 10 (33.3%) | 2 (7.7%) | 3 (16.7%) | 1 (5.9%) | 1 (8.3%) |
| A little | 12 (46.2%) | 10 (33.3%) | 11 (42.3%) | 6 (33.3%) | 6 (35.3%) | 5 (41.7%) |
| Not at all | 3 (11.5%) | 5 (16.7%) | 7 (26.9%) | 4 (22.2%) | 1 (5.9%) | 1 (8.3%) |
| Not Reported | 338 | 327 | 327 | 168 | 161 | 157 |

N = number of available subjects with non-missing Yes/No response. N < number of subjects with assessment = missing response for the corresponding CIGTS symptom questionnaire. % for No or Yes = n/N x 100%.

Not reported = number of subjects who responded to the symptom questionnaire but with missing data for 'bothersome'.

[1] The denominator for the % is the number of subjects reported with the response of the corresponding sub-question (i.e., 'bothersome'). Subjects might report 'No' symptom but with a response to 'bothersome'. Also, subjects might report 'Yes' to the symptom but fail to respond to 'bothersome'. As such, the total number of subjects with the responses could be different from the total number of subjects reported with 'Yes' for the corresponding symptom.

At 24 months, no change in bothersome grade was reported 73.4% to 91.6% of the Hydrus group and 67.1% to 91% of the control group. Increase from baseline in the bothersome score of two or more grades to a “moderate amount” or “a lot” at any postoperative visit were reported as adverse events (AEs). Such AEs were reported in 4.3% (16/369) of the Hydrus group and 4.8% (9/187) of the control group. Results for worsening symptom scores by group are provided in **Table 7**.

Note that it has not been determined how well this questionnaire applies to glaucoma patients undergoing implantation of a MIGS device with or without cataract surgery. The original CIGTS questionnaire was developed with a cohort of patients who were newly diagnosed with open-angle glaucoma (primary open-angle, exfoliation, and pigmentary) and who were required to be new to IOP-lowering medication use (2 weeks of lifetime use or less) or any other glaucoma treatment as part of eligibility. These participants were randomized to treatment with topical IOP-lowering medication or trabeculectomy; cataract surgery and implantation of a MIGS device were not part of the planned interventions in the CIGTS trial. Also, the impact of symptoms on visual function or quality of life was not assessed, and the questionnaire was not administered during unscheduled visits.

***TABLE 7 OCULAR SYMPTOMS ADVERSE EVENTS***

| Worsened ≥2 grades to Bothersome Grade "A Lot" or to "A Moderate Amount" | Cataract Surgery & Hydrus Implant (369 Subjects) | | Cataract Surgery Only (187 Subjects) | |
|---|---|---|---|---|
| | 12M n/N (%) | 24M n/N (%) | 12M n/N (%) | 24M n/N (%) |
| Eye Irritation Burning | 1/365 (<1%) | 3/357 (<1%) | 1/180 (<1%) | 2/170 (1.2%) |
| Eye Pain | 0/365 (0.0%) | 1/357 (<1%) | 1/180 (<1%) | 0/170 (0.0%) |
| Excessive Tearing | 2/365 (<1%) | 3/357 (<1%) | 4/180 (2.2%) | 2/170 (1.2%) |
| Droopy Eyelids | 0/365 (0.0%) | 0/357 (0.0%) | 1/180 (<1%) | 0/170 (0.0%) |
| Red Eyes | 1/365 (<1%) | 0/357 (0.0%) | 1/180 (<1%) | 2/170 (1.2%) |
| Feeling Like Something is in Your Eye | 5/364 (1.4%) | 2/357 (<1%) | 2/180 (1.1%) | 1/170 (<1%) |
| Skin Sensitivity or Irritation around the Eye | 1/365 (<1%) | 1/357 (<1%) | 3/180 (1.7%) | 0/170 (0.0%) |
| Overall | 9/365 (2.5%) | 7/357 (2.0%) | 5/180 (2.8%) | 4/170 (2.4%) |

For each symptom, grades of 1, 2, 3, 4, and 5 were assigned to non-missing bothersome response of "not at all", "a little", "some", "a moderate amount", and "a lot", respectively. Otherwise a bothersome grade of 0 was assigned to a response of "no symptom" or a response of "symptom not due to glaucoma/treatment". Change = postop bothersome grade - baseline bothersome grade. A positive value means a worsening in the symptom.
N = number of subjects with a non-missing bothersome grade change from baseline for the corresponding symptom.
% = n/N x 100%.

**Corneal Endothelial Cell Density**

There was little difference in endothelial cell loss (ECL) between the Hydrus and control groups. At 24 months, mean central ECD in the Hydrus group (n=346) was 2060 ± 480 cells/mm$^2$ (range 539, 3471) compared to 2417 ± 390 cells/mm$^2$ (range 854, 3405) at baseline (n=363). Similarly, control group subjects, who underwent cataract surgery alone, had mean central ECD of 2183 ± 425 cells/mm$^2$ (range 678, 3204) at 24 months (n=167), compared to 2426 ± 371 cells/mm$^2$ (range 613, 3528) at baseline (n=186). Mean ECD change at 24 months in the Hydrus group was -14% ±14% (range -68%, 25%), and -10% ±11% (range -50%, 21%) in the control group. Central endothelial cell loss ≥ 30% was observed in a higher proportion in the Hydrus group: 13.6% (47/346) in the Hydrus group, and 7.2% (12/167) in the control group at 24 months. However, these cases, unless accompanied by other precipitating adverse

events, were not associated with corneal edema after 1 month, or any other clinical sequelae, including persistent BCVA loss.

ECD loss of 30% or more was observed in four of the device malposition cases. At 24 months, 1.7% (6/369) of the Hydrus group and 1.2% (2/187) of the control group experienced central ECD counts <1000. In one Hydrus and one control participant each, ECD <1000 had been observed at baseline. In the other cases, ECD was found to be <1000 at various time points, from 3 to 24 months postoperatively.

## 15. PHYSICIAN TRAINING

Physician training by certified Ivantis personnel is required prior to use of the Hydrus Microstent. Training consists of three segments: didactic session including video session; wet-lab simulation of implantation of Hydrus Microstent in human anterior segment tissue; and supervised Hydrus Microstent implantation in clinical cases until implantation proficiency is demonstrated.

Contact your Ivantis Representative for more information regarding training for Hydrus Microstent.

## 16. MANUFACTURER

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## 17. SYMBOLS GLOSSARY

**ISO 15223-1:2016**
Medical devices – Symbols to be used with medical device labels, labelling and information to be supplied – Part 1: General requirements

| Symbol | Title | Description | Reference Number |
|---|---|---|---|
|  | Caution | Indicates the need for the user to consult the instructions for use for important cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device itself. | 5.4.4 |
|  | Consult instructions for use | Indicates the need for the user to consult the instructions for use. | 5.4.3 |
|  | Manufacturer | Indicates the medical device manufacturer. | 5.1.1 |
|  | Catalogue number | Indicates the manufacturer's catalogue number so that the medical device can be identified. Synonyms for "catalogue number" are "reference number", "reorder number", and "model number". | 5.1.6 |
|  | Batch code | Indicates the manufacturer's batch code so that the batch or lot can be identified. Synonyms for "batch code" are "lot number" and "batch number". | 5.1.5 |
|  | Use-by date | Indicates the date after which the medical device is not to be used. Provided in YYYY-MM-DD format. | 5.1.4 |
|  | Sterilized using irradiation | Indicates a medical device that has been sterilized using irradiation. | 5.2.4 |
|  | Do not resterilize | Indicates a medical device that is not to be resterilized. | 5.2.6 |
|  | Do not re-use | Indicates a medical device that is intended for one use, or for use on a single patient during a single procedure. | 5.4.2 |
|  | Do not use if package is damaged. | Indicates a medical device that should not be used if the package has been damaged or opened. | 5.2.8 |
|  | Non-pyrogenic | Indicates a medical device that is non-pyrogenic. | 5.6.3 |

**ASTM F2503-13**
Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment

| Symbol | Title | Description | Reference Number |
|---|---|---|---|
|  | MR Conditional | An item with demonstrated safety in the MR environment within defined conditions. See the MRI Safety Information section. | 7.4.5 |

**Other Symbols**

| Symbol | Title | Description |
|---|---|---|
|  | Contents | Indicates the quantity of devices contained within the package. |
|  | Telephone | The manufacturer's telephone number. |
|  | Fax | The manufacturer's fax number. |