DIRECTIONS FOR USE/PACKAGE INSERT
Glaukos Corporation iStent® Trabecular Micro-Bypass Stent System

DIRECTIONS FOR USE TABLE OF CONTENTS

1. DEVICE DESCRIPTION

The iStent® Trabecular Micro-Bypass Stent (Models GTS100R and GTS100L) is an intraocular stent that is manufactured from titanium (Ti6Al4V ELI) and is heparin coated (note: the heparin is from a porcine source). The stent has a single piece design, is 1.0 mm in length, 0.33 mm in height, with a snorkel length of 0.25 mm, and a snorkel bore diameter of 120µm (**Figure 1**).

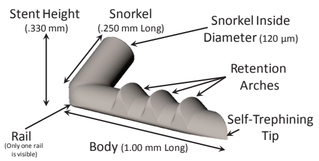


Figure 1. iStent®; front view of right stent GTS100R

The iStent® has an "L"-shaped structure with a snorkel (inlet) on the short side which resides in the anterior chamber, and which opens to the half-pipe body which resides in Schlemm's canal. The closed side of the body (**Figure 1**) sits against the inner wall of Schlemm's canal. The retention arches on the closed side of the body serve to securely fixate the device in Schlemm's canal. The open half-pipe part of the body (**Figure 2**) is against the outer wall in order to access collector channels. The rails are the edges of the open half-pipe. **Figure 2** shows a view of the stent in **Figure 1**, rotated 180 degrees, to display the open half-pipe of the stent body.

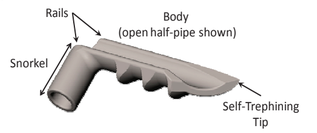


Figure 2. iStent®; view of open stent body (right stent GTS100R)

When properly implanted, the iStent® is intended to create a bypass through the trabecular meshwork to Schlemm's canal to improve aqueous outflow through the natural physiologic pathway. The implant is provided to the surgeon in a pre-loaded configuration in order to allow for precise insertion into Schlemm's canal. The inserter has been designed by Glaukos Corporation to hold the implant and to release the implant once it has been inserted within Schlemm's canal. Two model numbers of the iStent® Trabecular Micro-Bypass Stent (GTS100R and GTS100L) are available. The last digit of these model numbers (R and L) correlates to a right-flow stent and a left-flow stent, respectively. The stents are identical except the body faces opposite directions in order to facilitate nasal stent placement. Model GTS100L is designed for the left eye, and Model GTS100R is designed for the right eye (**Table 1**).

The Glaukos iStent® Trabecular Micro-Bypass Inserter (Model GTS100i) is also available in a stand-alone configuration; i.e., the Inserter (Model GTS100i) does not have an iStent® Trabecular Micro-Bypass Stent attached to the tip when packaged in this configuration. The inserter is provided as a single-use, disposable device that is able to reacquire the stent intraocularly should the surgeon determine it is necessary.

TABLE 1
Glaukos Corporation iStent® Trabecular Micro-Bypass Stent System

Catalogue #	Description
GTS100L	Left-flow iStent attached to disposable inserter, designed for left eye
GTS100R	Right-flow iStent attached to disposable inserter, designed for right eye
GTS100i	Stand-alone inserter (no stent attached)

2. INDICATIONS FOR USE

The iStent® Trabecular Micro-Bypass Stent (Models GTS100R and GTS100L) is indicated for use in conjunction with cataract surgery for the reduction of intraocular pressure (IOP) in adult patients with mild to moderate open-angle glaucoma currently treated with ocular hypotensive medication.

3. CONTRAINDICATIONS

The iStent® Trabecular Micro-Bypass Stent is contraindicated under the following circumstances or conditions:

- In eyes with primary angle closure glaucoma, or secondary angle-closure glaucoma, including neovascular glaucoma, because the device would not be expected to work in such situations
- In patients with retrobulbar tumor, thyroid eye disease, Sturge-Weber Syndrome or any other type of condition that may cause elevated episcleral venous pressure

4. WARNINGS

1. The following conditions may prohibit sufficient visualization of the angle required for safe and successful stent implantation: 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 taking a patient to surgery to exclude congenital anomalies of the angle, peripheral anterior synechiae (PAS), rubeosis, and any other angle abnormalities that could lead to improper placement of the stent and pose a hazard.
3. Regarding the Magnetic Resonance (MR) status of the implant, non-clinical testing has demonstrated that the iStent® Trabecular Micro-Bypass Stent (Models GTS100R and GTS100L) is MR Conditional. Please see the "MRI SAFETY INFORMATION" section at the end of this document for conditions for safe scanning.

5. PRECAUTIONS

1. The surgeon should inform the patient that the stent is MR-Conditional (as noted on their Patient ID card), and if the patient needs to undergo an MRI, they should let their doctor know they have an iStent® implanted in their eye.
2. After the surgery, the surgeon should give the patient the Patient ID card (enclosed in the iStent® packaging) with the appropriate information filled in, and should advise the patient to keep the card in a safe place, e.g., his or her wallet, for future reference. The surgeon should advise the patient that this Patient ID card contains important information related to the iStent® and that the card should be shown to their current and future health care providers.
3. The surgeon should monitor the patient postoperatively for proper maintenance of intraocular pressure. If intraocular pressure is not adequately maintained after surgery, the surgeon should consider an appropriate medication regimen to reduce intraocular pressure.
4. The safety and effectiveness of the iStent® Trabecular Micro-Bypass Stent has not been established as an alternative to the primary treatment of glaucoma with medications. The effectiveness of this device has been demonstrated only in patients with mild to moderate open-angle glaucoma who are currently treated with ocular hypotensive medication and who are undergoing concurrent cataract surgery for visually significant cataract.
5. The safety and effectiveness of the iStent® Trabecular Micro-Bypass Stent has not been established in patients with the following circumstances or conditions which were not studied in the pivotal trial:
   - In children
   - In eyes with significant prior trauma
   - In eyes with abnormal anterior segment
   - In eyes with chronic inflammation
   - In glaucoma associated with vascular disorders
   - In pseudophakic patients with glaucoma
   - In uveitic glaucoma
   - In patients with prior glaucoma surgery of any type including argon laser trabeculoplasty
   - In patients with medicated intraocular pressure greater than 24 mmHg
   - In patients with unmedicated IOP less than 22 mmHg nor greater than 36 mmHg after "washout" of medications
   - For implantation of more than a single stent
   - After complications during cataract surgery, including but not limited to, severe corneal burn, vitreous removal/vitrectomy required, corneal injuries, or complications requiring the placement of an anterior chamber IOL
   - When implantation has been without concomitant cataract surgery with IOL implantation for visually significant cataract
6. The safety and effectiveness of the iStent® Trabecular Micro-Bypass Stent has not been established in patients with pseudoexfoliative glaucoma and pigmentary glaucoma, because the pivotal trial was not powered to evaluate the outcomes of these groups. The safety and effectiveness of the iStent® has also not been established in patients with other secondary open-angle glaucomas.

6. ADVERSE REACTIONS

Refer to the Pivotal Clinical Trial Results section for the adverse events that occurred in the pivotal clinical trial. Additional adverse events that may be reasonably associated with the use of the device include but are not limited to the following: anterior chamber shallowing, severe, prolonged, or persistent intraocular inflammation, aqueous misdirection, choroidal effusion, choroidal hemorrhage, corneal decompensation, corneal injury, corneal opacification, cyclodialysis cleft, damage to trabecular meshwork, hyphema, hypopyon, hypotony, hypotony maculopathy, IOL dislocation, iridodialysis, loss of vitreous, perforation of sclera, posterior capsular bag rupture, proliferative vitreoretinopathy, pupillary block, pupillary membrane formation, retinal detachment, retinal dialysis, retinal flap tears, secondary surgical intervention, including but not limited to glaucoma surgery, stent inadvertently released from inserter in eye, stent dislocation, stent not retrievable, stent not visible with gonioscopy, stent malfunction, and vitreous hemorrhage.

7. INSTRUCTIONS FOR USE

Cataract Surgery

1. Cataract surgery with IOL implantation should be performed first followed by implantation of the iStent®.
2. The stent implantations are designed for nasal placement; therefore, surgery is to be performed from the temporal side of the head.
3. If the angle needs to be deepened after cataract surgery for placement of the iStent®, an intracameral miotic should be injected.

Stent Implantation

1. Select the model for implantation (i.e., Model GTS100L or Model GTS100R).
2. The peel pouch containing the iStent® Trabecular Micro-Bypass Stent System should be opened onto the sterile field. Caution: Do not use the device if the Tyvek® lid has been opened or the packaging appears damaged. In such cases, the sterility of the device may be compromised.
3. Grasp the inserter as shown in **Figure 3** with your index finger on the release button. With the release button on the inserter facing up, ensure that the orientation of the stent on the inserter is appropriate for the desired nasal implantation as shown in **Figure 4a** for the Model GTS100L and in **Figure 4b** for the Model GTS100R.

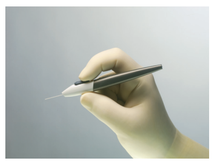


Figure 3. Hand position on inserter

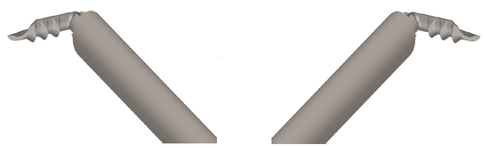


Figure 4a. Model GTS100L (top view) Stent tip is inferior and points left

Figure 4b. Model GTS100R (top view) Stent tip is inferior and points right

4. Inspect angle with a gonioprism to ensure that a good view is available at the nasal implant location.
5. Place a gonioscope on the cornea and reposition the surgical microscope as needed to visualize the trabecular meshwork, through the gonioprism, on the nasal side of the eye. Focus on the landmarks in the angle of the eye (**Figure 5**). Look up from the iris root to find the scleral spur (white line). Then look for Schwalbe's line (white line) down from the cornea. The trabecular meshwork (typically a red/brown line) is between the scleral spur and Schwalbe's line. Schlemm's canal is behind the trabecular meshwork.

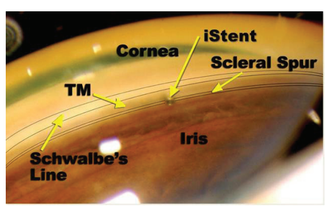


Figure 5. iStent® Implant Site

6. Insertion of stent

a. Inject viscoelastic into the anterior chamber to assist with chamber maintenance.

b. Insert the stent (which is attached to the inserter tip) through the temporal incision that was used to extract the cataract and insert the intraocular lens.

c. Traverse the anterior chamber with the inserter and position the inserter tip at approximately the pupillary margin. Place the goniopism into the desired position (see **Figure 6** for Model GTS100R).

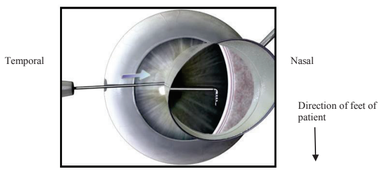


Figure 6.
Gonioscopic View of Approach to Trabecular Meshwork (right eye)

d. Locate the trabecular meshwork, and look for bifurcated areas based on asymmetric areas of pigmentation, and select an implant location below the horizontal midline of the meshwork and adjacent to any pigmented areas (which could represent collector channels).

e. Gently slide the stent tip through the trabecular meshwork and into Schlemm's canal at the nasal position (3 to 4:00 o'clock position for the right eye; 8 to 9:00 o'clock position for the left eye), with the tip of the implant directed inferiorly, i.e., towards the patient's foot: see **Figure 7** for an example of Model GTS100R insertion in a right eye. Approach the trabecular meshwork at an approximate 15º angle between the tip of the stent and the TM (**Figure 7a**). Insert the self-trephining stent tip through the trabecular meshwork and into Schlemm's canal (**Figure 7b**). A slight lifting motion may be required for insertion. The stent should be inserted so that the rails are located on the back wall of Schlemm's canal and the stent body is parallel to the iris plane (**Figures 7c and 7d**). Note: minimal blood reflux is a normal physiological response to placement of the stent, although this does not occur in all cases.

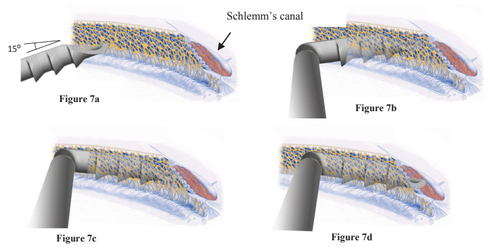


Figure 7. Insertion of Stent through Trabecular Meshwork
Figure 7a. Approach trabecular meshwork
Figures 7b-7d. Insertion through trabecular meshwork into Schlemm's Canal

If there is difficulty with insertion at the desired location, try inserting about 0.5 clock hour inferior (i.e., if the first attempt is at 3:00 in the right eye, move inferiorly to the 3:30 position; if the first attempt is at 9:00 in the left eye, move inferiorly to the 8:30 position). Continue to move inferior as needed for subsequent attempts. Note: Implanting superior to the 3:00 or 9:00 positions may prevent the tip of the device from penetrating tissue due to the circular geometry of the eye.

f. Release the stent by pushing the button on the inserter. Once the stent is in Schlemm's canal, gently tap **the side** of the snorkel with the inserter to align the body of the stent in Schlemm's canal (**Figure 8**). The body of the stent will not be aligned within Schlemm's canal without this last step.

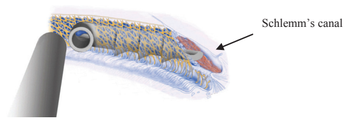


Figure 8.
Release stent and tap side with inserter to align stent in Schlemm's canal

g. Verify that the inlet of the snorkel is visible in the anterior chamber.

h. Withdraw the inserter. A view of the implanted stent with the snorkel visible is shown below in **Figure 9**.

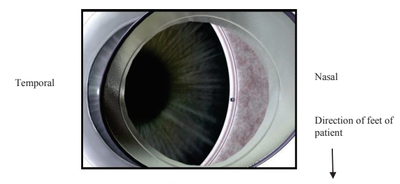


Figure 9.
Gonioscopic view of implanted stent (right eye)

7. At the end of the procedure, the following should be performed:

   a. Irrigate the anterior chamber with balanced salt solution (BSS) through the corneal wound manually, or with automated irrigation/aspiration to remove viscoelastic and refluxed blood.

   b. Inflate the anterior chamber with saline solution as needed to achieve physiologic pressure.

   c. Ensure that the corneal incision is sealed, and place 10-0 nylon suture if needed.

Postoperative Instructions

1. Patients should be managed postoperatively for IOP increases that may occur in the early postoperative period as a possible sequelae following cataract surgery in patients with glaucoma.

Retrieval of an Implanted Stent

If the surgeon determines that another inserter (Model GTS100i) is required to grasp a stent (i.e., the original inserter from the stent system is no longer available or not used), the inserter (Model GTS100i) may be used by the surgeon as follows:

1. Similar to the initial implant procedure, visualize the location of the iStent® using a goniolens.
2. Enter the eye through a clear corneal incision.
3. Advance to the location of the iStent®, and depress the inserter button to open the inserter jaws (**Figure 10a**).
4. While holding down the release button, position the snorkel of the stent in the inserter (**Figure 10b**), and then release the release button to grasp the snorkel of the stent (**Figure 10c**). Once the stent is in the inserter, it can then be implanted as described in Step 6 above, or removed from the eye. Care should be exercised when exiting the wound.

Figure 10a. Approach the stent as shown on right, and press down on the release button as shown on left.

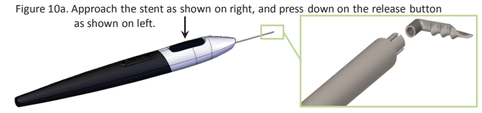


Figure 10b. While holding down the release button (left), position the snorkel of the stent in the inserter (right).

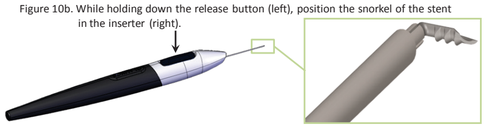
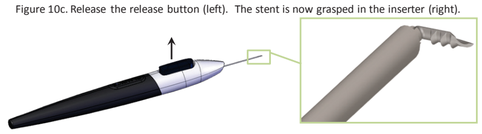


Figure 10c. Release the release button (left). The stent is now grasped in the inserter (right).



Figures 10a, 10b and 10c. Steps To Reacquire an Implanted Stent

8. ADVERSE EVENT REPORTING

Adverse events and/or potentially sight-threatening complications that may reasonably be regarded as device related must be reported to Glaukos Corporation at:

U.S. Toll Free Phone Number: 1-800-GLAUKOS (452-8567)
Alternate Phone Number: 949-367-9600

Fax Number: 949-297-4540

9. HOW SUPPLIED

Glaukos iStent® Trabecular Micro-Bypass Stent (Models GTS100R and GTS100L):

The stent is attached to the tip of a single-use inserter, and the system is provided sterile and nonpyrogenic in a blister tray. Each stent system is individually serialized, and the serial number is provided on the tray lid and unit carton. The device has been sterilized by gamma radiation.

Glaukos iStent® Trabecular Micro-Bypass Inserter (Model GTS100i):

The Glaukos iStent® Trabecular Micro-Bypass Inserter (Model GTS100i) is a stand-alone inserter; i.e., the Model GTS100i does not have an iStent® Trabecular Micro-Bypass Stent attached to the tip when packaged in this configuration. The inserter (Model GTS100i) is provided sterile and nonpyrogenic in a blister tray. Each inserter has a lot number which is provided on the tray lid and unit carton. The device has been sterilized by gamma radiation.

10. STORAGE REQUIREMENTS

The device should be stored at room temperature in the range of 15-30º C.

11. EXPIRATION DATE

The expiration date on the device package (tray lid) is the sterility expiration date. In addition, there is a sterility expiration date that is clearly indicated on the outside of the unit carton. Sterility is assured if the tray seal is not punctured or damaged until the expiration date. This device should not be used past the indicated sterility expiration date.

12. RETURN GOODS POLICY

Please contact Glaukos Corporation.

13. PIVOTAL CLINICAL TRIAL RESULTS

Description of the Randomized Clinical Trial

The study was a prospective, randomized, controlled, open-label, multicenter trial. A total of 27 sites throughout the U.S. enrolled subjects in the randomized phase of the study. A total of 240 eyes of 239 patients meeting the study eligibility criteria were randomized in a 1:1 fashion to undergo either implantation of the iStent® in conjunction with cataract surgery (treatment group) or cataract surgery without implantation of the iStent® (control group). Subjects in this randomized population were treated from April 13, 2005 through June 28, 2007. All subjects were followed for a period of 2 years. A total of 117 eyes of 116 subjects were enrolled in the treatment group, and 123 subjects were enrolled in the control group. To obtain additional safety information, the study also included a separate non-randomized arm of patients to undergo iStent® implantation in conjunction with cataract surgery. A total of 50 subjects were enrolled in this arm of the study (also see additional detail below in the section entitled "Non-Randomized Cohort"). Study subjects were diagnosed with mild to moderate open-angle glaucoma (OAG). Pseudoexfoliative and pigmentary glaucoma were acceptable diagnoses.

Mild to moderate open-angle glaucoma was defined in the study protocol as:

1. Enlarged C:D ratio consistent with glaucoma, but still ≤ 0.8, given the requirement for early stage glaucomatous disease
2. Either visual field defect or nerve abnormalities consistent with glaucoma.

In the case of visual field defect, the following criteria were to be met:

- no severe nasal steps worse than 4 continuous clustered points
- no more than 3 clustered points with sensitivity less than 15dB within 15 degrees from the fixation point
- no other evidence at clinical examination of moderate to advanced nerve fiber bundle defects (i.e. Bjerrum scotoma)

In the case of nerve abnormalities consistent with glaucoma, one or more of the following was acceptable for diagnosis:

- segmental loss of neuroretinal rim (notching)
- Drance disc hemorrhage (splinter hemorrhage)
- nerve fiber layer loss (as observed with an ophthalmoscope)
- pseudo pit of the disc
- visible laminar dots
- optic nerve abnormalities determined by Heidelberg retina tomograph (HRT) confocal scanning imaging
- findings on polarimetry consistent with early glaucoma such as a wedge shaped-defect connecting to the optic nerve head with values at or below the 5th percentile as evidenced on the deviation map, any parameter below the 5th percentile, or the nerve fiber indicator (NFI) >35 using GDx
- findings on optical coherence tomography (OCT) of retinal nerve fiber layer (RNFL) thickness outside of the normal range consistent with clinical evaluation of the optic nerve and RNFL

Subjects with secondary OAG were excluded, except for 4 eyes in the randomized treatment group and 3 in the randomized control group with pigmentary glaucoma and 7 eyes in each of the randomized groups with pseudoexfoliative glaucoma in the study eye based upon the protocol inclusion and exclusion criteria. Subjects were required to have best corrected visual acuity of 20/40 or worse with medium Brightness Acuity Tester, and clinically significant cataract eligible for phacoemulsification, to qualify for the study. Subjects were required to be on one to three ocular hypotensive medications, with a medicated IOP of ≤ 24 mmHg at screening evaluation, and with an unmedicated IOP ≥ 22 mmHg and ≤ 36 mmHg at baseline visit, after washout.

Of the 116 subjects in the treatment group, 68% were 70 years of age or older at the time of surgery, with a mean age of 74 years. Most subjects (60%) were female, and the majority of subjects (71%) were Caucasian. There were equal proportions of right eyes and left eyes. Similar demographic characteristics were seen in the 123 control subjects, where 65% were 70 years of age or older with a mean age of 73 years. Fifty-eight percent were female. The majority of subjects (72%) were Caucasian, and there were equal proportions of right eyes and left eyes.

The primary effectiveness outcome was defined as IOP ≤ 21 mmHg without use of ocular hypotensive medication at 12 months (Intent to Treat (ITT) using Last Observation Carried Forward (LOCF)). The proportion of subjects with this outcome was compared between the two study groups. The secondary effectiveness outcome was defined as IOP reduction from baseline of ≥ 20% without use of ocular hypotensive medication at 12 months (ITT using LOCF). The proportion of subjects with this outcome was compared between the two study groups.

Efficacy Results – Randomized Trial

Primary and Secondary Efficacy Endpoints

Sixty-eight percent of subjects in the treatment group (combined cataract and iStent® implantation) met the primary endpoint of IOP ≤ 21 mm Hg with no medications at 12 months (mITT[1] using non-responder analysis) (**Table 2**). In comparison, only 50% of subjects in the control group (cataract surgery only) met the primary endpoint. This treatment difference of 18% in favor of the iStent® group on the primary endpoint at 12 months was statistically (p = .004) and clinically significant.

[1]The ITT population included 117 eyes of 116 subjects randomized to undergo iStent® implantation. The modified ITT population (mITT) included 116 eyes of 116 subjects (excluded 1 eye from same subject).

TABLE 2
IOP ≤ 21 MMHG WITHOUT OCULAR HYPOTENSIVE MEDICATIONS AT 12 MONTHS

Analysis Population and Imputation Method	Cataract Surgery with iStent N=116 (%)	Cataract Surgery Only N=123 (%)	P-value[1]
mITT Using Non-Responder Analysis	68%	50%	.004

1. Two-sided Z-test.

The secondary endpoint in the GC-003 pivotal trial was the proportion of patients with IOP reduced ≥ 20% from baseline without medications at 12 months (mITT using non-responder analysis). In the iStent® treatment group, 64% of subjects implanted met this endpoint compared to 47% in the cataract control group (**Table 3**). This treatment difference of 17% was also statistically (p = .010) and clinically significant.

TABLE 3
IOP REDUCTION ≥ 20% WITHOUT OCULAR HYPOTENSIVE MEDICATIONS AT 12 MONTHS

Analysis Population and Imputation Method	Cataract Surgery with iStent N=116 (%)	Cataract Surgery Only N=123 (%)	P-value[1]
mITT Using Non-Responder Analysis	64%	47%	.010

1. Two-sided Z-test.

Safety Results – Adverse Events

Intraoperative Complications

Intraoperative complications specifically related to implantation of the iStent® are summarized in **Table 4** for the 112 subjects in whom stent implantation was attempted. These events included iris touch (n=8), endothelium touch (n=1), intraoperative stent removal and replacement (n=1), failure to implant stent (n=1) and stent malposition (n=1).

These data show that stent implantation was successful in the majority of cases, with only one report of stent implantation not completed due to poor visualization of the angle, and a low incidence of operative complications and adverse events.

TABLE 4
OPERATIVE COMPLICATIONS AND ADVERSE EVENTS FROM STENT IMPLANTATION

N = 112	n (%)
Iris touched by the device	8 (7.1%)
Endothelium touched	1 (0.9%)
Intraoperative stent removal and replacement	1 (0.9%)
Failure to implant stent	1 (0.9%)
Stent malposition	1 (0.9%)

Postoperative Ocular Adverse Events

A summary of postoperative ocular adverse events reported in the safety population during the randomized clinical trial is presented below. Anticipated, early postoperative events included transient events such as corneal edema, trace folds, trace striae, transient hypotony at 5-7 hours, inflammation, epithelial defect and discomfort as expected following cataract surgery. Iritis, anterior chamber cells and uveitis were considered separate and unique adverse event categories of intraocular anterior segment inflammation. The combined incidence of these events was 2% in the treatment group (1 iritis, 1 uveitis) vs. 6% in the control group (6 iritis, 1 anterior chamber +1 cells requiring treatment).

One adverse event in each group was deemed by investigators to be severe. One subject in the treatment group experienced BCVA loss ("count fingers") after suffering a stroke. One subject in the control group had macular traction, macular hole and macular edema treated with vitrectomy; this subject also had BCVA loss of ≥ 1 line at ≥ 3 months postoperative.

With the exception of adverse events specifically related to stent malposition or obstruction, adverse events occurred at a low incidence in both groups and were representative for the elderly, post-cataract surgery population evaluated in this study. Thus, there were no serious or unanticipated safety concerns related to implantation of the iStent® in conjunction with cataract surgery.

TABLE 5
POSTOPERATIVE OCULAR ADVERSE EVENTS*
SAFETY POPULATION

Adverse Events	Cataract Surgery with iStent N = 116 n (%)	Cataract Surgery Only N = 117 n (%)
Anticipated early postoperative event		
Early postop corneal edema	9 (8%)	11 (9%)
Early postop anterior chamber cells	4 (3%)	2 (2%)
Early postop corneal abrasion	3 (3%)	2 (2%)
Early postop corneal striae	2 (2%)	1 (1%)
Early postop discomfort	1 (1%)	2 (2%)
Early postop subconjunctival hemorrhage	1 (1%)	0 (0%)
Early postop superficial punctate keratitis	0 (0%)	2 (2%)
Early postop blurry vision	0 (0%)	1 (1%)
Early postop floaters	0 (0%)	1 (1%)
Any BCVA loss of at least 1 line at or after the three month visit	8 (7%)	12 (10%)
Posterior capsular opacification	7 (6%)	12 (10%)
Stent obstruction by iris, vitreous, fibrous overgrowth,fibrin, blood, etc.	5 (4%)	0 (0%)
Blurry vision or visual disturbance	4 (3%)	8 (7%)
Elevated IOP – other	4 (3%)	5 (4%)
Stent malposition	3 (3%)	0 (0%)
Subconjunctival hemorrhage	2 (2%)	2 (2%)
Epiretinal membrane	2 (2%)	1 (1%)
Drusen	2 (2%)	0 (0%)
Iris atrophy	2 (2%)	0 (0%)
Iritis	1 (1%)	6 (5%)
Conjunctival irritation due to hypotensive medication	1 (1%)	3 (3%)
Disc hemorrhage	1 (1%)	3 (3%)
Elevated IOP requiring treatment with oral or intravenous medications or with surgical intervention	1 (1%)	3 (3%)
Allergic conjunctivitis	1 (1%)	2 (2%)
Dry eye	1 (1%)	2 (2%)
Macular edema	1 (1%)	2 (2%)
Cystoid macular edema	1 (1%)	1 (1%)
Bleeding (vitreous hemorrhage or persistent & non-preexisting hyphema)	1 (1%)	0 (0%)
Corneal edema	1 (1%)	0 (0%)
Transient hypotony	1 (1%)	0 (0%)
Mild pain	0 (0%)	5 (4%)
Foreign body sensation	0 (0%)	4 (3%)
Posterior vitreous detachment	0 (0%)	4 (3%)
Rebound inflammation from tapering steroids	0 (0%)	2 (2%)
Choroidal detachment	0 (0%)	1 (1%)
Endophthalmitis	0 (0%)	1 (1%)

*occurring at ≥ 2% in either group, or other adverse events known to be associated with glaucoma procedures or potential risk with stent implantation.

In addition to the adverse events reported in **Table 5** (i.e., adverse events that occurred at an incidence of ≥ 2% in either group), adverse events that occurred at < 2% in both

groups included worsening of glaucoma and allergy to cosmetics. Adverse events that occurred at < 2% in the treatment group included age-related macular degeneration, uveitis, blepharospasm, dysesthesia and/or photophobia, endo pigment, eye splash injury, eyelid bruise due to fall, metallic particle on iris, mild throbbing pain, periorbital hematoma due to fall, possible bacterial conjunctivitis, seasonal allergies, and subjconjunctival hemorrhage secondary to aspirin. Adverse events that occurred at < 2% in the control group included blepharoconjunctivitis, worsening of age-related macular degeneration, anterior chamber (1+) cells at one month requiring treatment, burning due to dry eye, carotid artery disease, choroidal tubercle, and conjunctivitis.

Secondary Surgical Interventions

One subject in the treatment group underwent trabeculoplasty (**Table 6**). Another subject underwent focal argon laser coagulation for diabetic macular edema. Stent-specific secondary surgical interventions (**Table 6**) were reported in 5 randomized iStent® subjects (3 stent repositionings, 1 stent removal and replacement, 1 Nd:YAG laser iridoplasty) to resolve stent malposition or obstruction observed by investigators in the early postoperative period.

In the cataract surgery only group, two subjects underwent laser trabeculoplasty, one subject underwent deep sclerectomy followed by revision and laser sclerostomy five weeks later, one subject underwent vitrectomy for macular traction, macular hole and macular edema, and one subject underwent three separate procedures of wound resuture because of wound leak, pupilloplasty, and IOL removal and replacement.

Table 6
Secondary Surgical Interventions – Postoperative Ocular Adverse Events
Safety Population

Secondary Surgical Intervention Adverse Events	Randomized Group	
	Cataract Surgery with iStent N = 116 n (%)	Cataract Surgery Only N = 117 n (%)
Paracentesis[1]	31 (27%)	34 (29%)
Nd:YAG laser capsulotomy	7 (6%)	11 (9%)
Stent repositioning	3 (3%)	0 (0%)
Punctal cautery/punctal plugs	1 (1%)	3 (3%)
Trabeculoplasty	1 (1%)	2 (2%)
Nd:YAG laser iridoplasty for stent obstruction	1 (1%)	0 (0%)
Focal argon laser photocoagulation	1 (1%)	0 (0%)
Stent removal and replacement	1 (1%)	0 (0%)
Deep sclerectomy/sclerostomy	0 (0%)	1 (1%)
IOL removal and replacement	0 (0%)	1 (1%)
LASIK	0 (0%)	1 (1%)
Pupilloplasty	0 (0%)	1 (1%)
Vitrectomy	0 (0%)	1 (1%)
Wound resuture due to wound leak	0 (0%)	1 (1%)

1. included paracentesis at the 5-7 hr exam

Non-Randomized Cohort

As described earlier, a non-randomized arm of the study was performed. A total of 50 subjects were enrolled at 10 sites in the non-randomized phase of the study subsequent to the completion of enrollment of the randomized population. Subjects enrolled in this non-randomized phase underwent iStent® implantation in conjunction with cataract surgery. The purpose of this non-randomized phase of the study was to collect safety data on additional subjects. The randomized and non-randomized phases of the study used identical inclusion and exclusion criteria. Both phases used the same standardized procedures, applied the same surgical techniques, and placed the stent in the same anatomical location. Of the 50 subjects enrolled, 46 were implanted with the iStent®, 2 subjects withdrew before surgery and 2 subjects were exited after surgery following unsuccessful iStent® implantation. Preoperative parameters in the non-randomized population were similar to those in the randomized population.

Results of the 46 subjects successfully implanted with the iStent® (the Non-Randomized Population) are presented in **Tables 7- 10**. Forty-four subjects completed follow-up through Month 24, and 2 subjects terminated from the study prior to Month 24. There were no stents removed or replaced during the 24-month follow-up period.

Table 7
IOP ≤ 21 mmHg without Ocular Hypotensive Medications
IOP Reduction ≥ 20% without Ocular Hypotensive Medications
Non-Randomized Population At 12 Months

Non-Randomized Cataract Surgery with iStent (N = 46)	IOP ≤ 21 mmHg without Ocular Hypotensive Medications (%)	IOP Reduction ≥ 20% without Ocular Hypotensive Medications (%)
ITT using Non-Responder Analysis	78%	72%

Table 8
Operative Complications from Stent Implantation
Subjects with iStent Implant

Non-Randomized Cataract Surgery with iStent (N = 46)	n (%)
Iris damage*	1 (2.2%)
Stent malposition*	1 (2.2%)
Ocular pain during insertion	1 (2.2%)
Iris touched by the device	3 (6.5%)
Endothelial touch	1 (2.2%)
Anterior chamber collapse	1 (2.2%)

* same eye
Note: Two subjects were discontinued before surgery, and two did not have successful stent implantation. These four subjects are not in the populations of subjects with an iStent implant and were excluded from calculations in the table.

Table 9
Postoperative Ocular Adverse Events
Non-Randomized Population

Adverse Events	Cataract Surgery with iStent N = 46 n (%)
Anticipated early postoperative event	
Early postop anterior chamber cells	2 (4%)
Early postop corneal edema	2 (4%)
Early postop anterior chamber inflammation	1 (2%)
Early postop corneal abrasion	1 (2%)
Early postop corneal erosion	1 (2%)
Early postop corneal striae	1 (2%)
Early postop pain	1 (2%)
Epiretinal membrane	4 (9%)
Posterior capsular opacification	4 (9%)
Any BCVA loss of at least 1 line at or after the three month visit	3 (7%)
Blepharitis	2 (4%)
Blurry vision or visual disturbance	2 (4%)
Posterior vitreous detachment	2 (4%)
Stent malposition	2 (4%)
Stent obstruction by iris, vitreous, fibrous overgrowth,fibrin, blood, etc.	2 (4%)
Vitreous floaters	2 (4%)
Age related macular degeneration	1 (2%)
Allergic conjunctivitis	1 (2%)
Blepharoconjunctivitis	1 (2%)
Cystoid macular edema	1 (2%)
Elevated IOP – other	1 (2%)
Iris incarceration	1 (2%)
Keratitis	1 (2%)
Periorbital swelling	1 (2%)
Unwanted eyelid sensation	1 (2%)
Uveitis	1 (2%)
Vitreous condensations	1 (2%)
Worsening of age related macular degeneration	1 (2%)
Worsening of glaucoma	1 (2%)
Bleeding (vitreous hemorrhage or persistent & non-preexisting hyphema)	0 (0%)
Corneal edema	0 (0%)
Transient hypotony	0 (0%)
Choroidal detachment	0 (0%)
Endophthalmitis	0 (0%)

Table 10
Secondary Surgical Interventions – Postoperative Ocular Adverse Events
Non-Randomized Population

Secondary Surgical Intervention Adverse Events	Non-Randomized Cataract Surgery with iStent N = 46 n (%)
Paracentesis[1]	12 (26%)
Nd:YAG laser capsulotomy	7 (15%)
Nd:YAG laser for stent obstruction	1 (2%)
Iris reposition	1 (2%)

1.included paracentesis at the 5-7 hr. exam

14. POST-APPROVAL STUDY RESULTS

Study Objective

In accordance with the PMA conditions of approval, a post-approval study was conducted. Following approval by FDA on March 5, 2013 of the study protocol entitled "GTS100-Post Approval Study (PAS)", the study was initiated. The goal of this study was to demonstrate that use of this device in conjunction with cataract surgery did not result in a rate of sight-threatening adverse events, after 5 years of implantation, that was higher than the rate of sight-threatening adverse events that occurs after cataract surgery alone, by more than a non-inferiority margin of 5%.

Study Design

This was an extended follow-up study involving subjects previously enrolled in Glaukos Study GC-003. Extended follow-up was planned in subjects eligible to participate in this follow-up study. Subjects were to be followed for five years postoperatively (one final visit was conducted on those subjects who were past the five year post-operative time-point). Please note that no postoperative specular microscopy was performed, because preoperative specular microscopy was not performed in the pivotal trial.

Study Population

The study included subjects previously enrolled in Glaukos Study GC-003 who would be able and willing to participate in this extended follow-up study. The study excluded subjects previously enrolled in Glaukos Study GC-003 who would not be able or willing to participate in this extended follow-up study, as well as patients not previously enrolled in Glaukos Study GC-003.

Study Endpoint

The primary endpoint was the occurrence of sight-threatening adverse events. Sight-threatening adverse events included events such as BCVA loss ≥ 3 lines vs. baseline, endophthalmitis, corneal decompensation, retinal detachment, severe choroidal hemorrhage, severe choroidal detachment and aqueous misdirection.

Total Number of Enrolled Study Sites and Subjects; Length of Follow-Up

The first subject had enrolled in Pivotal Trial GC-003 in 2005, and the final subject had enrolled in February, 2008. The final subject exited Study GC-003 on March 18, 2010. At the time the study protocol was approved by FDA in March of 2013, all eligible subjects had passed the Month 60 visit window. Overall, the time from surgery to the final GTS100-PAS visit was 6.6 years in the overall iStent® + cataract surgery group (pooled randomized phase and non-randomized cohort subjects) and 6.8 years in the randomized cataract surgery group.

Of the 27 original study sites participating in Pivotal Trial GC-003, 25 sites participated in this post-approval study. Of the 279 subjects (162 overall iStent® + cataract surgery subjects plus 117 cataract surgery only subjects), a total of 255 subjects (148 overall iStent® + cataract surgery subjects plus 107 cataract surgery only subjects) had completed follow-up through 2 years in Study GC-003 and were eligible for enrollment. Of these, 108 subjects (73 iStent® + cataract surgery subjects and 35 cataract surgery only subjects) were enrolled in the post-approval study. The reasons for 108 of 255 subjects enrolled were due to the extended length of time between final subject exit from Study GC-003 (March 18, 2010) and approval by FDA of the post-approval extended follow-up study 3 years later, by which time many of the exited subjects in this elderly population had either expired or were no longer available or willing to participate in a clinical study. To this point, the average age at time of enrollment was 78 (SD 8.0) years in the overall iStent® + cataract surgery group and 75 (SD 8.4 years) in the cataract surgery only group.

Final Safety Findings – All Sight-Threatening Adverse Events from Pivotal Trial and Post-Approval Study

Table 11 presents all sight-threatening adverse events reported from both Pivotal Trial

GC-003 and Study GTS100-PAS for the overall iStent® + cataract surgery group and the randomized cataract surgery only group.

Table 11
All Sight-Threatening Adverse Events
(Data from GC-003 and GTS100-PAS)

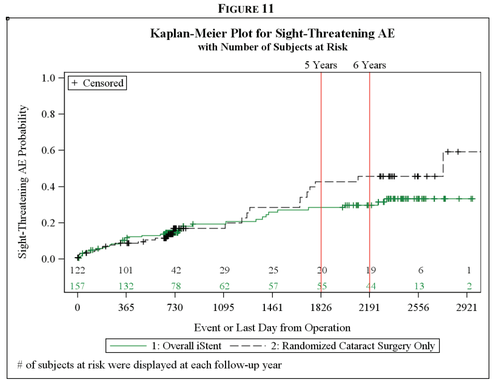
Adverse Event	Overall Cataract Surgery with iStent® N = 157		Randomized Cataract Surgery Only N = 122	
	n of Subjects with Event (%)	n of Events	n of Subjects with Event (%)	n of Events
Epiretinal membrane	9 (6%)	9	2 (2%)	4
Loss of BCVA of 3 lines or more vs. baseline at any time postoperatively	2 (1%)	2	7 (6%)	7
Age related macular degeneration or worsening of age related macular degeneration	9 (6%)	10	7 (6%)	7
Worsening of glaucoma	4 (3%)	4	2 (2%)	2
IOP increase requiring management with oral or intravenous medications or surgical intervention (IOP treated with oral medication at 6 hour visit is not an Adverse Event)	4 (3%)	5	3 (2%)	3
Cystoid macular edema	4 (3%)	4	1 (<1%)	1
Increased cup to disc ratio	4 (3%)	4	0 (0%)	0
Disc hemorrhage	1 (<1%)	1	3 (2%)	3
Elevated IOP requiring treatment with oral or intravenous medications or surgical intervention	1 (<1%)	1	3 (2%)	6
Macular edema	1 (<1%)	1	2 (2%)	2
Any other event that could lead to significant vision loss, if not appropriately treated[1]	2 (1%)	2	1 (<1%)	1
Iris atrophy	2 (1%)	2	0 (0%)	0
Retinal detachment	2 (1%)	2	0 (0%)	0
Significant corneal complications including edema, opacification, decompensation	2[2] (1%)	2[2]	0 (0%)	0
Uveitis	2 (1%)	3	0 (0%)	0
Corneal edema	1 (<1%)	1	0 (0%)	0
Eye splash injury	1 (<1%)	1	0 (0%)	0
Metallic particle on iris	1 (<1%)	1	0 (0%)	0
Retinal flap tears	1 (<1%)	1	0 (0%)	0
Choroidal detachment	0 (0%)	0	1 (<1%)	1
Endophthalmitis	0 (0%)	0	1 (<1%)	1
Macular hole	0 (0%)	0	1 (<1%)	1
Proliferative diabetic retinopathy	0 (0%)	0	1 (<1%)	1
Segmental loss of neuroretinal rim	0 (0%)	0	1 (<1%)	1
Any choroidal hemorrhage	0 (0%)	0	0 (0%)	0
Aqueous misdirection	0 (0%)	0	0 (0%)	0
Any[3]	**36 (23%)**	**56**	**28 (23%)**	**41**

1. Advanced open angle glaucoma and advanced optic atrophy were reported for 1 subject in the iStent group. Choroidal neovascularization was reported for 1 subject in the iStent group and 1 subject in the control group.
2. Two subjects with pre-existing Fuchs' dystrophy prior to iStent + cataract surgery reported with corneal decompensation. (A third iStent subject with pre-existing Fuchs' dystrophy did not report with corneal decompensation.) The two subjects underwent Descemet's stripping endothelial keratoplasty 4 and 5 years, respectively, after their iStent surgery (also refer to Table 13). Both subjects experienced worsening of the disease in their fellow eyes as well, and one subject underwent penetrating keratoplasty in their fellow eye. The investigators considered these events "definitely unrelated" to iStent. One of the investigators stated the adverse event was "typical chronic evolution of Fuchs' corneal dystrophy".
3. Number of subjects reported with any adverse events. Subjects could report with more than one adverse event.

Rate of Sight-Threatening Adverse Events from Pivotal Trial and Post-Approval Study

Figure 11 presents the KM curves involving sight-threatening adverse events for the overall iStent® + cataract surgery group and the cataract surgery only group. Due to the small denominators beyond 6 years, the KM analyses comparisons were performed at 6 years. At 5 years, the rate of sight-threatening AEs was 28.5% for the overall iStent® + cataract surgery group and 42.8% in the cataract surgery only group. At 6 years, the rate of sight-threatening AEs was 29.9% for the overall iStent® + cataract surgery group and 45.7% in the cataract surgery only group, and the p-value for the comparison between the overall iStent® + cataract surgery group and cataract surgery only group, and against a non-inferiority margin of 5%, was 0.011, indicating that the overall iStent® + cataract surgery group was not inferior to the cataract surgery only group. In addition, the p-value of the log rank test was 0.317, confirming that the sight-threatening rate over 6 years was not statistically different between the overall iStent® + cataract surgery group and cataract surgery only group.

Figure 11



Postoperative Ocular Adverse Events

Table 12 presents all postoperative ocular adverse events reported from Study GTS100-PAS for the overall iStent + cataract surgery group and the randomized cataract surgery only group. Table 13 summarizes ocular surgeries from Study GTS100-PAS.

Table 12
Postoperative Ocular Adverse Events for Study Eyes
GTS100-PAS

Adverse Event	Overall Cataract Surgery with iStent® N = 73		Randomized Cataract Surgery Only N = 35	
	n of Subjects with Event (%)	n of Events	n of Subjects with Event (%)	n of Events
Age related macular degeneration or worsening of age related macular degeneration	6 (8%)	7	6 (17%)	6
Amaurosis fugax	0 (0%)	0	1 (3%)	1
Anterior ischemic optic neuropathy	0 (0%)	0	1 (3%)	1
Any intraocular inflammation (non pre-existing) remaining or arising after the protocol's specified medication regimen is complete (1+ cells or flare will not be considered an AE unless persisting >=1 month postoperative)	1 (1%)	1	0 (0%)	0
Any other event that could lead to significant vision loss, if not appropriately treated[1]	2 (3%)	2	1 (3%)	1
Bleeding (vitreous hemorrhage or persistent & non-preexisting hyphema)	1 (1%)	1	0 (0%)	0
Blepharitis	6 (8%)	6	4 (11%)	6
Blurry vision or visual disturbance	4 (5%)	5	0 (0%)	0
Branch retinal vein occlusion	1 (1%)	1	0 (0%)	0
Brow ache	1 (1%)	1	0 (0%)	0
Chalazion	0 (0%)	0	1 (3%)	1
Conjunctival hyperemia	1 (1%)	1	0 (0%)	0
Conjunctival irritation due to hypotensive medication	1 (1%)	1	1 (3%)	1
Conjunctivitis	2 (3%)	3	1 (3%)	1
Corneal abrasion	0 (0%)	0	1 (3%)	1
Corneal graft edema	1 (1%)	1	0 (0%)	0
Cotton wool spot	0 (0%)	0	1 (3%)	1
Cystoid macular edema	2 (3%)	2	0 (0%)	0
Deep stents ("buried" in the trabecular meshwork) that are not visible	2 (3%)	2	0 (0%)	0
Dermatochalasis	4 (5%)	4	2 (6%)	2
Dot hemorrhage	0 (0%)	0	1 (3%)	1
Drusen	1 (1%)	1	1 (3%)	1
Dry eye	18 (25%)	18	7 (20%)	8
Ectropion	1 (1%)	1	0 (0%)	0
Elevated IOP	1 (1%)	1	2 (6%)	2
Epiphora	2 (3%)	2	0 (0%)	0
Epiretinal membrane	3 (4%)	3	1 (3%)	2
Episcleritis	0 (0%)	0	1 (3%)	1
Floppy eyelid syndrome	1 (1%)	1	0 (0%)	0
Foreign body sensation	3 (4%)	3	2 (6%)	2
Fuch's dystrophy	1 (1%)	1	0 (0%)	0
Glaucoma progression	2 (3%)	2	1 (3%)	1
Goniosynechiae	2 (3%)	2	0 (0%)	0
Hollenhurst plaque	1 (1%)	1	0 (0%)	0
Hyperemia	1 (1%)	1	0 (0%)	0
IOP increase >= 10 mmHg vs. baseline IOP occurring at any visit	2 (3%)	2	0 (0%)	0
IOP increase requiring management with oral or intravenous medications or with surgical intervention (Note: IOP treated with oral medication at the 6 hour visit is not an Adverse Event)	4 (5%)	5	3 (9%)	3
Implicated meibomian glands	1 (1%)	1	0 (0%)	0
Increased cup to disc ratio	4 (5%)	4	0 (0%)	0
Lacrimal stenosis	1 (1%)	1	0 (0%)	0
Lid edema	0 (0%)	0	1 (3%)	1
Loss of best corrected visual acuity (BCVA) of 3 lines or more vs. baseline at any time postoperatively	1 (1%)	1	2 (6%)	2
Loss of best spectacle corrected visual acuity (BSCVA) of 2 lines or more (logMAR scale; 10 letters or more on ETDRS chart) postoperative as compared to baseline or best recorded visual acuity measured at any visit postoperative (NOTE: a loss of BSCVA in conjunction with posterior capsular opacification, followed by Nd:YAG capsulotomy and improvement of BSCVA, is NOT considered an adverse event)	17 (23%)	17	7 (20%)	7
Macular hemorrhage	1 (1%)	1	0 (0%)	0
Macular scar	0 (0%)	0	1 (3%)	1
Meibomian cyst	1 (1%)	1	0 (0%)	0
Meibomitis	1 (1%)	1	0 (0%)	0
Nerve fiber layer loss	0 (0%)	0	1 (3%)	1
Nonproliferative diabetic retinopathy	4 (5%)	4	0 (0%)	0
Notched lids	1 (1%)	1	0 (0%)	0
Ocular irritation/itching	4 (5%)	5	0 (0%)	0
Ocular migraine	1 (1%)	1	0 (0%)	0
Ocular pain	1 (1%)	1	1 (3%)	1
Optic TIA	1 (1%)	1	0 (0%)	0
Pain	2 (3%)	2	0 (0%)	0
Papilloma	3 (4%)	3	0 (0%)	0
Periorbital redness	1 (1%)	1	0 (0%)	0
Periorbital swelling	1 (1%)	1	0 (0%)	0
Peripapillary scarring	1 (1%)	1	0 (0%)	0
Photophobia	2 (3%)	2	0 (0%)	0
Pigmentary macular fibrosis	1 (1%)	1	0 (0%)	0
Posterior capsular opacification	18 (25%)	18	9 (26%)	10
Posterior vitreous detachment	8 (11%)	8	3 (9%)	3
Postoperative discomfort (NOTE: postoperative discomfort up to and including the Week 1 postoperative exam is NOT considered an adverse event)	1 (1%)	1	0 (0%)	0
Ptosis	4 (5%)	4	2 (6%)	2
Punctal eversion	2 (3%)	2	0 (0%)	0
Retinal detachment	2 (3%)	2	0 (0%)	0
Retinal flap tears	1 (1%)	1	0 (0%)	0
Retinal pigment epithelial changes	1 (1%)	1	1 (3%)	1
Scotoma	2 (3%)	2	3 (9%)	3
Secondary surgical intervention	1 (1%)	1	0 (0%)	0
Significant corneal complications including edema, opacification, decompensation (NOTE: a classification of mild or moderate corneal edema up to and including Week 1 postoperative is NOT considered an adverse event)	2[2] (3%)	2[2]	0 (0%)	0
Stent malposition	1 (1%)	1	0 (0%)	0
Stent obstruction (i.e., positive visualization of lumen obstruction), partial or complete, regardless of how long the obstruction is present	1 (1%)	1	0 (0%)	0
Stye	0 (0%)	0	1 (3%)	1
Subconjunctival hemorrhage	2 (3%)	2	0 (0%)	0
Telangiectasia	1 (1%)	1	0 (0%)	0
Trichiasis	3 (4%)	3	0 (0%)	0
Visual field defect	8 (11%)	8	1 (3%)	1
Vitreous floaters	8 (11%)	9	3 (9%)	4
Vitreous in anterior chamber	0 (0%)	0	1 (3%)	1
Vitreous syneresis	1 (1%)	1	1 (3%)	1
Watery eyes	1 (1%)	1	1 (3%)	1
Any[3]	**60 (82%)**	**202**	**28 (80%)**	**84**

1. Advanced open angle glaucoma and advanced optic atrophy were reported for 1 subject in the iStent group. Choroidal neovascularization was reported for 1 subject in the iStent group and 1 subject in the control group.
2. Two subjects with pre-existing Fuchs' dystrophy prior to iStent + cataract surgery reported with corneal decompensation. (A third iStent subject with pre-existing Fuchs' dystrophy did not report with corneal decompensation.) The two subjects underwent Descemet's stripping endothelial keratoplasty 4 and 5 years, respectively, after their iStent surgery (also refer to Table 13). Both subjects experienced worsening of the disease in their fellow eyes as well, and one subject underwent penetrating keratoplasty in their fellow eye. The investigators considered these events "definitely unrelated" to iStent. One of the investigators stated the adverse event was "typical chronic evolution of Fuchs' corneal dystrophy".
3. Number of subjects reported with any adverse events. Subjects could report with more than one adverse event.

Table 13
Ocular Surgeries After GC-003 Study
GTS-100 PAS

Adverse Event	Overall Cataract Surgery with iStent® N = 73		Randomized Cataract Surgery Only N = 35	
	n of Subjects with Event (%)	n of Events	n of Subjects with Event (%)	n of Events
Nd:YAG laser capsulotomy	13 (18%)	13	11 (31%)	11
Selective laser trabeculoplasty	1 (1%)	1	3 (9%)	3
Blepharoplasty	2 (3%)	2	0 (0%)	0
Descemet's stripping endothelial keratoplasty (treat pre-existing Fuch's dystrophy prior to stent + cataract surgery)	2[1] (3%)	2[1]	0 (0%)	0
Basal cell carcinoma excision/lid reconstruction	1 (1%)	2	0 (0%)	0
Dacryocystorhinostomy/lacrimal irrigation	1 (1%)	2	0 (0%)	0
Retinal tear repair (laser photocoagulation, retinal buckle)	1 (1%)	2	0 (0%)	0
Laser iridoplasty	1 (1%)	1	0 (0%)	0
Trabeculectomy	1 (1%)	1	0 (0%)	0
Any choroidal hemorrhage	0 (0%)	0	0 (0%)	0
Aqueous misdirection	0 (0%)	0	0 (0%)	0

1. Two subjects with pre-existing Fuchs' dystrophy prior to iStent + cataract surgery reported with corneal decompensation. (A third iStent subject with pre-existing Fuchs' dystrophy did not report with corneal decompensation.) The two subjects underwent Descemet's stripping endothelial keratoplasty 4 and 5 years, respectively, after their iStent surgery. Both subjects experienced worsening of the disease in their fellow eyes as well, and one subject underwent penetrating keratoplasty in their fellow eye. The investigators considered these events "definitely unrelated" to iStent. One of the investigators stated the adverse event was "typical chronic evolution of Fuchs' corneal dystrophy".

Study Strength and Weaknesses

The main reason for the large number of potentially available subjects who did not enroll or complete the study is the 5+ year gap between subjects exiting Study GC-003 and the date of final approval by FDA of the protocol for this extended follow-up study. Many of the surviving patients in this elderly population had increased health issues or age-related reasons for not enrolling in the follow-up study. There were more subjects in the overall iStent® + cataract surgery group than the cataract surgery only group, because the non-randomized cohort of iStent® + cataract surgery subjects had been added to the randomized iStent® + cataract surgery group.

Importantly, there were no unanticipated adverse device effects (UADE) identified during the study, which extended to greater than 6 years after iStent® implantation + cataract surgery.

15. LABELING

The following symbols are used on the device packaging.

Symbol	Description
REF	Catalogue/Model Number
SN	Serial Number (for the stent)
LOT	Lot Number
2	Do not re-use
YYYY-MM-DD	Use By (year-month-day)
	Do not use if package is damaged
STERILE R	Sterilized by Gamma Irradiation
15°C 25°C	Temperature Storage Requirements
CE 0086	CE Marking
MR	MR Conditional
Rx Only	For prescription use only
	Consult Instructions For Use.
	Manufacturer
EC REP	Authorized European Representative

16. MRI SAFETY INFORMATION

MR

Non-clinical testing has demonstrated that the iStent® Trabecular Micro-Bypass Stent (Models GTS100R and GTS100L) is MR Conditional. A patient with this device can be safely scanned in an MR system meeting the following conditions:

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

Under the scan conditions defined above, the iStent® Trabecular Micro-Bypass Stent (Models GTS100R and GTS100L) is not expected to produce a clinically significant temperature rise after 15 minutes of continuous scanning.

In non-clinical testing, the image artifact caused by the device extends less than 15 mm from the device when imaged with a gradient echo pulse sequence and a 3.0 T MRI system.

17. CAUTION

Federal law restricts this device to sale by, or on the order of, a physician.

Physician training is required prior to use of the device, and consists of three main parts:

- Webinar
- Didactic session with Glaukos surgical representative
- Observation of surgical cases by Glaukos representative until implantation proficiency is demonstrated

Manufacturer:
Glaukos Corporation
229 Avenida Fabricante
San Clemente, CA 92672 U.S.A.
Tel: 949.367.9600, Fax: 949.367.9984
www.glaukos.com
Toll-Free: 1-800-GLAUKOS (452-8567)

