

DIRECTIONS FOR USE/PACKAGE INSERT

Glaukos® Corporation iStent® Trabecular Micro-Bypass Stent System

DIRECTIONS FOR USE TABLE OF CONTENTS

1. DEVICE DESCRIPTION
2. INDICATIONS FOR USE
3. CONTRAINDICATIONS
4. WARNINGS
5. PRECAUTIONS/REACTI
6. ADVERSE REACTIONS
7. INSTRUCTIONS FOR USE
8. ADVERSE EVENT REPORTING
9. HOW SUPPLIED
10. STORAGE REQUIREMENTS
11. EXPIRATION DATE
12. RETURN GOODS POLICY
13. CLINICAL TRIAL RESULTS
14. POST-APPROVAL STUDY RESULTS
15. LABELING
16. MRI SAFETY INFORMATION
17. CAUTION

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 wide, with a snorkel length of 0.25 mm, and a snorkel bore diameter of 120µm (**Figure 1**).

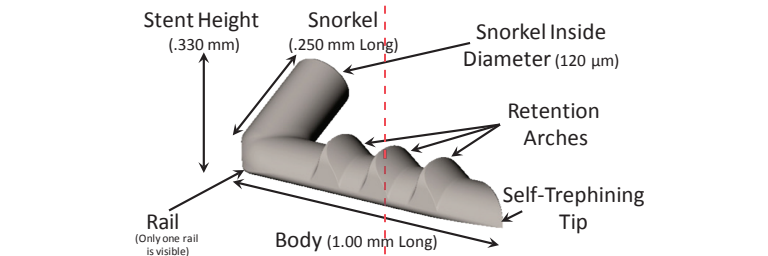


Figure 1. iStent; front view of right stent GTS100R

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.

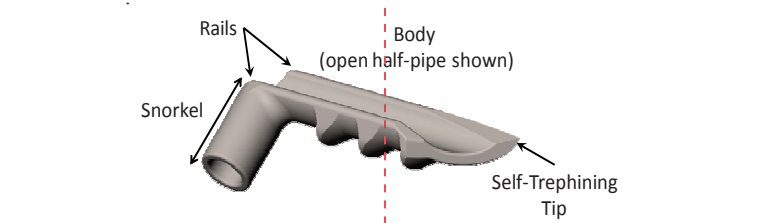


Figure 2. iStent; view of open stent body (right stent GTS100R)

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 permit 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 retrolental 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 implantation 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, cycloidal 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.

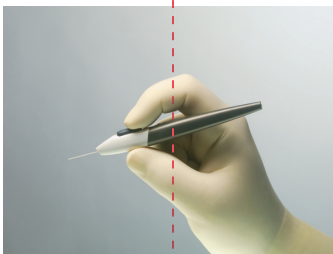


Figure 3. Hand position on inserter

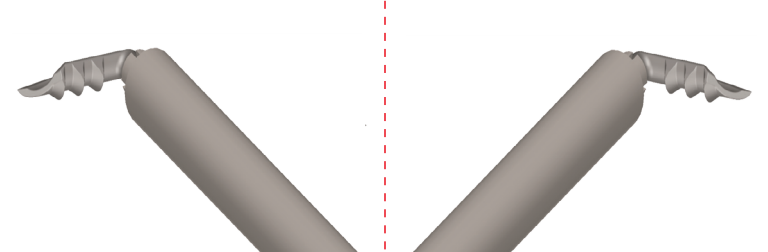


Figure 4a. Model GTS100L (top view)

Stent tip is inferior and points left

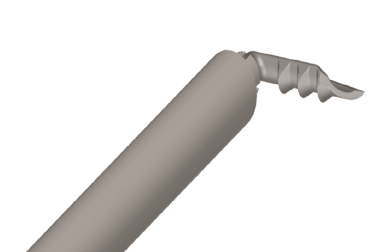


Figure 4b. Model GTS100R (top view)

Stent tip is inferior and points right

4. Inspect angle with a gonioscope 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 gonioscope, 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.

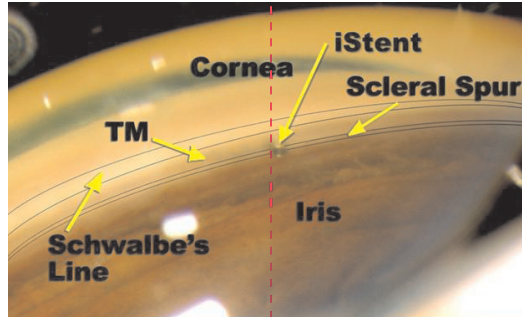


Figure 5. iStent Implant Site

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 gonioscope into the desired position (see **Figure 6** for Model GTS100R).

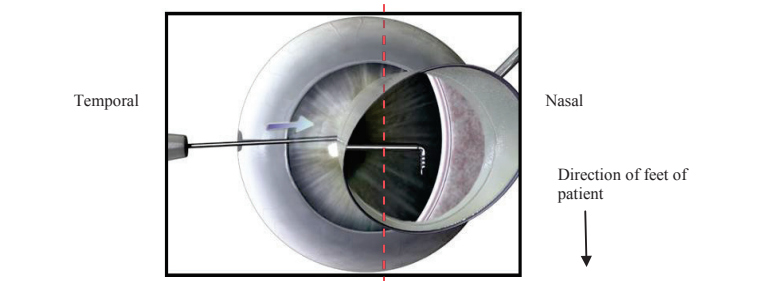


Figure 6.

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 o'clock position for the right eye; 8 to 9 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 15° 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.

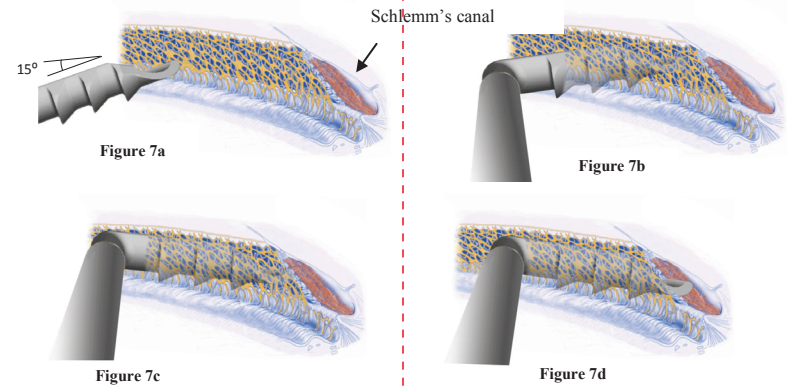


Figure 7. Insertion of Stent through Trabecular Meshwork

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.

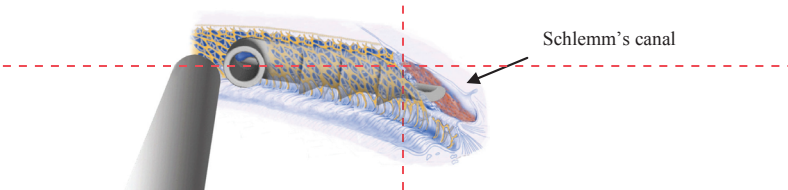


Figure 8.

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**.

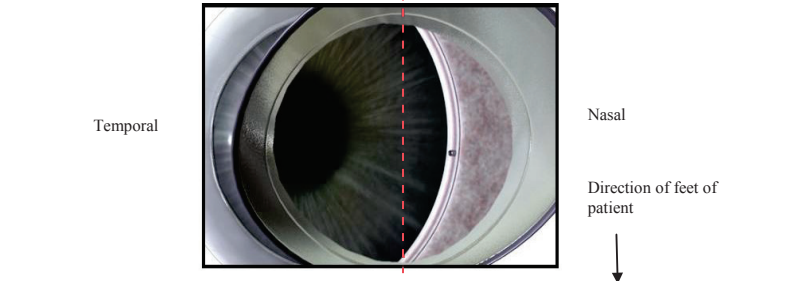


Figure 9.

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 gonioscope.
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.

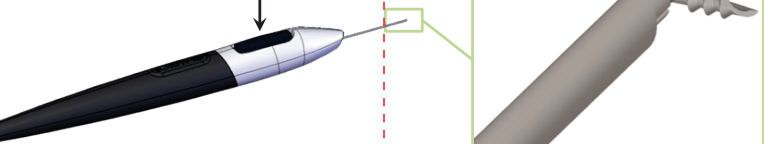
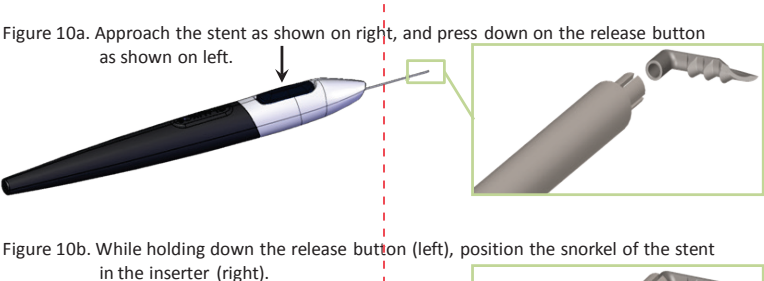


Figure 10a, 10b and 10c: Steps To Reacquire an Implanted Stent

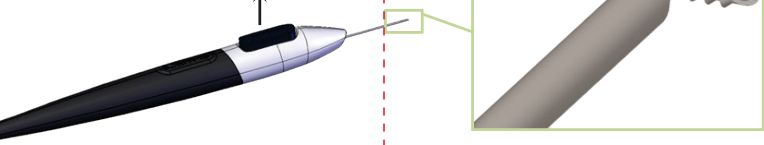


Figure 10a, 10b and 10c: Steps To Reacquire an Implanted Stent

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 15-30° 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 $\geq 20\%$ 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* 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.

*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 n (%) | 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 $\geq 20\%$ 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 $\geq 20\%$ 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 | | |
|---|---------|---------|
| Adverse Events | 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%) |

| 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 ¹ (1%) | 2 ¹ | 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 ² | 36 (23%) | 56 | 28 (23%) | 41 |

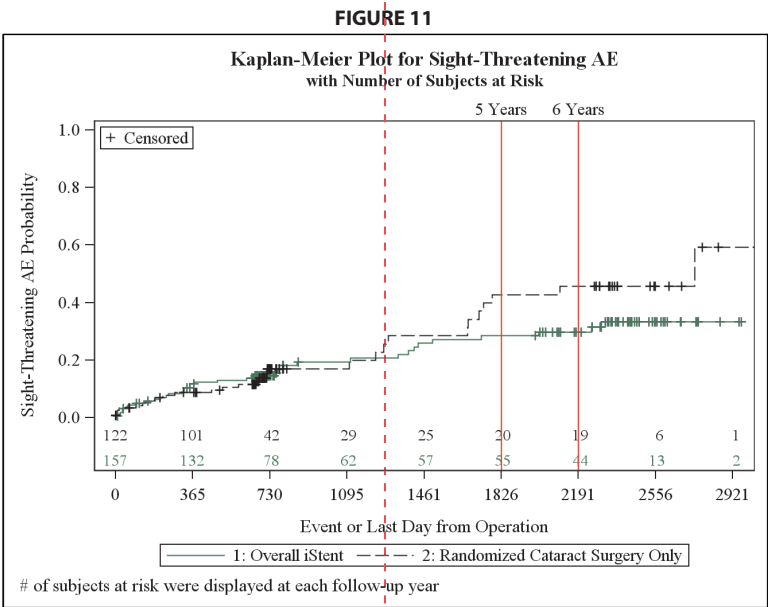
1. Advanced open angle glaucoma and advanced optic atrophy were reported for 1 subject in the iStent group. Choroidal neovascularization was reported for 1 subject in the iStent group and 1 subject in the control group.

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 states 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, add 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.



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 |

| TABLE 12 (Continued) 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 |
| 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 postoperatively) | 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 |
| Druisen | 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 |
| Epitretinal membrane | 3 (4%) | 3 | 1 (3%) | 2 |
| Epiptericis | 0 (0%) | 0 | 1 (3%) | 1 |
| Floppy eyelid syndrome | 1 (1%) | 1 | 0 (0%) | 0 |
| Foreign body sensation | 3 (4%) | 3 | 2 (6%) | 2 |
| Fuchs' 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; >0 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%) | 0 |
| 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 | 1 (1%) | 1 | 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 ¹ (3%) | 2 ¹ | 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 ² | 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 18). 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 states 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 Fuchs' 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 |
| Dicrocystorhinostomy/ 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 | 2 (3%) | 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 states 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. | | | | |
| GTS100-Post Approval Study 2 (GTS100-PAS2) | | | | |
| Study Objective | | | | |
| In accordance with the PMA conditions of approval, a post-approval study was conducted. The GTS100-PAS2 protocol was approved by the FDA on March 8, 2013, and the updated protocol was approved by the FDA on May 13, 2016. The goal of this study was to demonstrate that use of the iStent Trabecular Micro-Bypass Stent Model GTS100 in conjunction with cataract surgery did not result in a rate of sight-threatening adverse events, within 3 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 | | | | |
| In this prospective, multicenter, post-approval study, 183 subjects with mild to moderate open-angle glaucoma currently treated with ocular hypotensive medication and scheduled to undergo cataract surgery underwent iStent implantation during cataract surgery and 276 subjects underwent cataract surgery only. | | | | |
| Study Population/Data Source | | | | |
| In the GTS100-PAS2 initial study design, subjects with mild to moderate open-angle glaucoma currently treated with ocular hypotensive medication and scheduled to undergo cataract surgery were randomized/assigned to iStent + cataract surgery or cataract surgery only. The revised study design allowed 1 enrollment of iStent + cataract surgery subjects and 2 use of data from other trials to comprise a control group of subjects who underwent cataract surgery. | | | | |
| 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, 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, Follow-up Rates | | | | |
| In the GTS100-PAS2 study, a total of 357 subjects were enrolled with 207 subjects at 23 sites assigned to either iStent + cataract surgery (n=183) or cataract surgery only (n=24). The final subject was enrolled on April 23, 2018. A total of 252 cataract surgery only subjects were enrolled at 46 sites in other trials. Subjects were followed through 3 years postoperatively. | | | | |
| In the iStent + cataract surgery group of 183 subjects, follow-up rates were 97.8% at Month 12, 87.8% at Month 24, and 86.5% at Month 36. | | | | |
| In the cataract surgery only group of 276 subjects, follow-up rates were 97.4% at Month 12, 92.9% at Month 24, and 86.0% at Month 36. | | | | |
| Final Safety Findings - Sight Threatening Adverse Events | | | | |
| Table 14 presents all sight-threatening adverse events reported for the iStent + cataract surgery group and cataract surgery only group. | | | | |
| TABLE 14 ALL SIGHT-THREATENING ADVERSE EVENTS (SORTED ALPHABETICALLY) GTS100-PAS2 | | | | |
| Adverse Event | Cataract Surgery with iStent N = 183 | | Cataract Surgery Only N = 276 | |
| | Number of Reports | Number (%) of Subjects with Event | Number of Reports | Number (%) of Subjects with Event |
| Age related macular degeneration or worsening of age related macular degeneration | 2 | 2 (1.1%) | 4 | 4 (1.4%) |
| Anterior scleritis | 0 | 0 (0.0%) | 1 | 1 (0.4%) |
| Any intraocular inflammation (non pre-existing) remaining or arising after the protocol's specified medication regimen is complete | 11 | 11 (6.0%) | 13 | 11 (4.0%) |
| Blot macular hemorrhage | 1 | 1 (0.5%) | 0 | 0 (0.0%) |
| Central retinal artery occlusion | 0 | 0 (0.0%) | 1 | 1 (0.4%) |
| Corneal opacity | 0 | 0 (0.0%) | 3 | 3 (1.1%) |
| Corneal ulcer | 0 | 0 (0.0%) | 1 | 1 (0.4%) |
| Cotton wool spots | 1 | 1 (0.5%) | 0 | 0 (0.0%) |
| Diabetic retinopathy | 0 | 0 (0.0%) | 3 | 3 (1.1%) |
| Disc hemorrhage | 1 | 1 (0.5%) | 8 | 7 (2.5%) |
| Epitretinal membrane | 5 | 5 (2.7%) | 4 | 4 (1.4%) |
| Glaucoma progression requiring secondary surgical intervention | 3 | 3 (1.6%) | 3 | 3 (1.1%) |
| Hypertensive retinopathy | 1 | 1 (0.5%) | 0 | 0 (0.0%) |

| TABLE 14 (Continued) ALL SIGHT-THREATENING ADVERSE EVENTS (SORTED ALPHABETICALLY) GTS100-PAS2 | | | | |
|---|---|-----------------------------------|----------------------------------|-----------------------------------|
| Adverse Event | Cataract Surgery with iStent N = 183 | | Cataract Surgery Only N = 276 | |
| | Number of Reports | Number (%) of Subjects with Event | Number of Reports | Number (%) of Subjects with Event |
| Hypotony (IOP < 6 mmHg) at one month postoperative or later | 0 | 0 (0.0%) | 4 | 2 (0.7%) |
| IOL dislocation | 0 | 0 (0.0%) | 1 | 1 (0.4%) |
| IOP increase >= 10 mmHg vs. baseline IOP occurring >= Month 1 | 2 | 2 (1.1%) | 4 | 3 (1.1%) |
| IOP increase requiring oral medication | 2 | 2 (1.1%) | 13 | 10 (3.6%) |
| IOP increase requiring secondary surgical intervention | 3 | 3 (1.6%) | 7 | 6 (2.2%) |
| Iris atrophy | 0 | 0 (0.0%) | 1 | 1 (0.4%) |
| Iris neovascularization | 0 | 0 (0.0%) | 1 | 1 (0.4%) |
| Juxtafoveal telangiectasia | 0 | 0 (0.0%) | 1 | 1 (0.4%) |
| Loss of BSCVA of 3 lines or more compared to baseline or best recorded visual acuity at any time postoperatively persisting at time of study exit | 1 | 1 (0.5%) | 4 | 4 (1.4%) |
| Macular edema | 5 | 4 (2.2%) | 3 | 3 (1.1%) |
| Nerve fiber layer loss | 0 | 0 (0.0%) | 2 | 2 (0.7%) |
| Optic nerve thinning/cupping | 0 | 0 (0.0%) | 1 | 1 (0.4%) |
| Peripapillary atrophy | 1 | 1 (0.5%) | 0 | 0 (0.0%) |
| Retained crystalline lens fragments | 1 | 1 (0.5%) | 0 | 0 (0.0%) |
| Retinal detachment | 2 | 1 (0.5%) | 1 | 1 (0.4%) |
| Retinal flap tears | 1 | 1 (0.5%) | 1 | 1 (0.4%) |
| Retinal hemorrhage | 1 | 1 (0.5%) | 0 | 0 (0.0%) |
| Retinal pigment epithelial changes | 4 | 4 (2.2%) | 0 | 0 (0.0%) |
| Segmental loss of neuroretinal ring (notching) | 0 | 0 (0.0%) | 2 | 2 (0.7%) |
| Significant corneal complications including edema, opacification, decompensation | 0 | 0 (0.0%) | 1 | 1 (0.4%) |
| Significant hyphema (i.e., >= 10% of anterior chamber) | 1 | 1 (0.5%) | 0 | 0 (0.0%) |
| Visual field loss >=2.5 dB | 2 | 2 (1.1%) | 4 | 3 (1.1%) |
| Vitreous hemorrhage | 0 | 0 (0.0%) | 2 | 2 (0.7%) |
| Wound dehiscence | 0 | 0 (0.0%) | 1 | 1 (0.4%) |
| Any ^a | 51 | 39 (21.3%) | 95 | 59 (21.4%) |

^a Number of subjects reported with any adverse events. Subjects could report with more than one adverse event.



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