Glaukos® Corporation iStent infinite® Trabecular Micro-Bypass System

Instructions for Use

DIRECTIONS FOR USE TABLE OF CONTENTS

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1. DEVICE DESCRIPTION

The iStent infinite® Trabecular Micro-Bypass System, Model i53 contains three preloaded intraocular stents (Model G2-W) that are manufactured from implant grade titanium (Ti6Al4V ELI) and are coated with stearalkonium heparin (note: the heparin is from a porcine source). The stent has a single piece design, is 360 µm in diameter, 360 µm in height, and the central inlet and outlet lumen has a diameter of 80 µm (**Figure 1**). The head of the stent has four side outlets that each have a diameter of 50 µm.

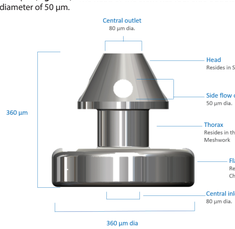


Figure 1. iStent infinite Stent Dimensions

The iStent infinite stent has a rear flange which resides in the anterior chamber, and head that resides in Schlemm's canal. The thorax of the stent is retained by the trabecular meshwork. The stent is symmetrical and is designed to be implanted in either the left or right eye (**Figure 2**). Three preloaded intraocular stents are provided in the injector (**Figures 3a & 3b**).

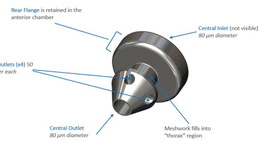


Figure 2. iStent infinite Stent (Model G2-W Stent)

Figure 3a. iStent infinite Injector Design

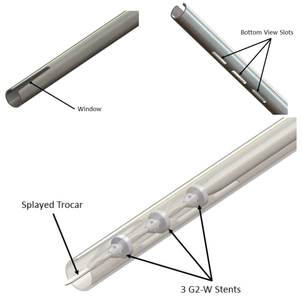


Figure 3b. iStent infinite Injector Distal End

When properly implanted, the iStent infinite stent is intended to create a bypass through the trabecular meshwork into Schlemm's canal to improve aqueous outflow through the natural physiologic pathway. The implant is provided in a pre-loaded configuration allowing for precise implantation into Schlemm's canal. The injector has been designed by Glaukos® Corporation to hold three stents to be implanted one at a time into Schlemm's canal.

2. INDICATIONS FOR USE

The iStent infinite Trabecular Micro-Bypass System Model i53 is an implantable device intended to reduce the intraocular pressure (IOP) of the eye. It is indicated for use in adult patients with primary open-angle glaucoma in whom previous medical and surgical treatment has failed.

3. CONTRAINDICATIONS

The iStent infinite Trabecular Micro-Bypass System is contraindicated under the following circumstances or conditions:

- In eyes with angle closure glaucoma where angle has not been surgically opened
- In eyes with acute traumatic, malignant, active uveitic, or active neovascular glaucoma or discernible congenital anomalies of the anterior chamber (AC) angle
- 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 the gonioscopic view in the intended implant location.
2. The surgeon should perform a slit lamp gonioscopy examination 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. Non-clinical testing has demonstrated that the iStent infinite stents are MR Conditional. Please see the "MRI SAFETY INFORMATION" section at the end of this document on conditions for safe scanning.

5. PRECAUTIONS

1. The surgeon should inform the patient that the stents are 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 iStent infinite stents implanted in their eye.
2. After the surgery, the surgeon should give the patient the Patient ID card (enclosed in the iStent infinite 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 infinite 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 additional therapy to reduce intraocular pressure.
4. The stent is comprised of implant grade titanium (Ti6-Al-4V ELI) with a stearalkonium heparin coating. The total amount of heparin is estimated to be less than 0.9 microgram per stent, or approximately 0.01 to 0.02 units.
5. The surgeon should be careful to avoid contact with the cornea and iris during stent implantation in order to minimize sequelae associated with device-cornea touch, stent obstruction and/or iritis.
6. Please note that three out of 61 participants (4.9%) in the pivotal clinical trial were phakic. Therefore, there is insufficient evidence to determine whether the clinical performance of the device may be different in those who are phakic versus in those who are pseudophakic.

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 possibly be associated with the use of the device include but are not limited to the following: allergic reaction, aqueous misdirection, atrophy/phthisis, choroidal effusion, choroidal hemorrhage, chronic pain, corneal decompensation, corneal injury, corneal opacification, cyclodialysis cleft, damage to crystalline lens, damage to iris, damage to trabecular meshwork, device malfunction identified after entry of the injector system into the eye but prior to contact with the target tissue, failure to implant 3 stents, flat or shallow anterior chamber, hypopyon, hypotony maculopathy, inadvertent perforation of the sclera, infection, IOL damage/dislocation, iridodialysis, loss of eye, loss of stent in eye, loss of vitreous, perforation of sclera, posterior capsular bag rupture or tear, proliferative vitreoretinopathy, ptosis, pupillary block, pupillary membrane formation, retinal detachment, retinal dialysis, retinal flap tears, secondary surgical intervention, including but not limited to glaucoma surgery, premature stent release, stent dislocation, stent explant, stent migration, stent-cornea touch, stent not retrievable, stent not visible, over implanted stents that are not visible with gonioscopy, Toxic Anterior Segment Syndrome (TASS), and vitreous hemorrhage.

7. INSTRUCTIONS FOR USE

The iStent infinite injector is intended for placement through a clear corneal incision after the implantation site has been confirmed through adequate visualization of the anterior chamber angle. The stent implantations are designed for nasal placement; therefore, it is suggested that surgery is performed from the temporal side of the head. An intracameral miotic can be injected to deepen the angle prior to placement of the iStent infinite stent. To mitigate difficulty with patient movement or non-compliance, consider using a peri-bulbar or retro-bulbar block.

1) Prepare the eye and implant site for proper visualization of the trabecular meshwork (TM) using the operating microscope and gonioprism as follows:
   a. Instill a miotic, as needed in order to achieve good visualization, up to two hours prior to the procedure.
   b. Tilt the patient's head away from the surgeon (about 15-25°).
   c. Tilt the surgical microscope back toward the surgeon (about 35°). Total angle should be approximately 50-60° for both the patient and microscope tilts to achieve the ideal view.
   d. Place a small amount of viscoelastic on the cornea. Position the gonioprism on the cornea using light touch gonioscopy.
   e. Adjust the microscope to focus at focus on the TM.
   f. Inspect AC angle structures with a gonioprism to ensure that a good view is available at the nasal implant location. Identify the 3 targets approximately 2 clock hours apart for best implantation of the stents, See **Figure 4**.

Figure 4. iStent infinite Implant Location

   g. After visualization of the trabecular meshwork, the Tyvek® tray lid containing the iStent infinite system should be opened and presented to the user. The device should be handled in the sterile field. Caution: Do not use the device if the Tyvek lid has been opened or if the packaging appears damaged. In such cases, the sterility of the device may be compromised.
   h. Remove the Stent Delivery Button Lock from the injector. Hold the injector as shown in **Figure 5a** with your index finger comfortably on the Stent Delivery Button and within reach of the Singulator. Hold the injector as shown in **Figure 5b** with your index finger comfortably on the Stent Delivery Button and within reach of the Singulator

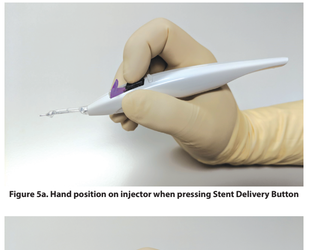


Figure 5a. Hand position on injector when pressing Stent Delivery Button

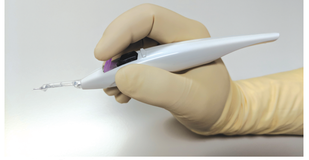


Figure 5b. Hand position on injector when pressing Singulator

2) Prepare for and perform surgery
   a. Standard ophthalmic surgery techniques should be used to prepare the patient and the eye.
   b. Make a clear corneal incision of adequate length to allow entry of the introducer tip of the injector into the anterior chamber. Recommended incision location is the temporal peripheral cornea for either eye.
   c. Ophthalmic viscoelastic (cohesive) should be used to form the anterior chamber, as necessary. Deepen the anterior chamber by injecting with viscoelastic as needed, being careful not to overinflate.
3) The iStent infinite injector insertion steps are as follows:
   a. With the gonioprism removed from the cornea, insert the injector introducer tip through the clear corneal incision into the anterior chamber, and advance it to the pupillary margin toward the targeted trabecular meshwork tissue (i.e., the *ab interno* approach). Take care to avoid contact with the lens, iris, or cornea.
   b. Place the gonioprism on the cornea and position the patient and 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 (**Figures 6a & 6b**). 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.

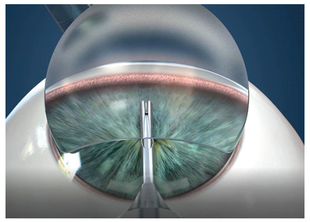


Figure 6a. iStent infinite Implant Site

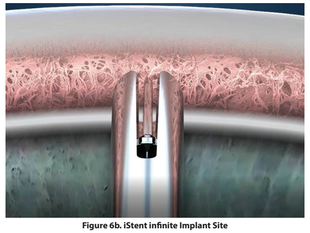
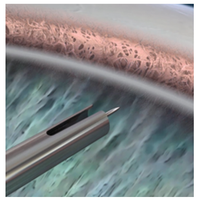
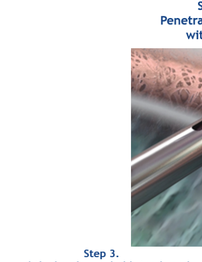


Figure 6b. iStent infinite Implant Site

   c. Advance the injector tip towards the TM; the introducer will auto-retract and expose the insertion tube and tips. Prior to targeting the implantation site, confirm through the window that the stent is in position. Advance the insertion tube containing the trocar towards the TM (just above the scleral spur) and penetrate the trocar tip through the center of the TM. The trocar is used to not only penetrate the TM, but will remain in the tissue to act as an axial guide for the stent as the stent traverses over the trocar through to Schlemm's canal.
   d. Gently hold the insertion tube against the TM and apply appropriate pressure to slightly indent or "dimple" the tissue (tissue should stretch just enough to form a "V" when pressing on the TM); see **Figure 7.**





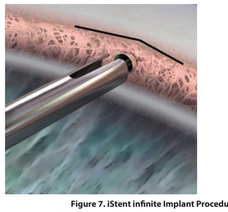


Figure 7. iStent infinite Implant Procedure
(left: approach the TM; center: trocar pierces TM;
right: dimple tissue and deploy stent)

   e. Looking through the window in the insertion tube, ensure the trocar remains centered in the insertion tube.
   f. Slowly squeeze and hold down the implantation button to automatically inject the stent head through the TM and into Schlemm's canal.
   g. Look through the window in the insertion tube to verify the stent has been implanted properly. When the stent is implanted properly, the head of the conical portion of the stent should reside fully within Schlemm's canal while the stent's wide flange remains visible on the surface of the TM in the anterior chamber.
   h. Withdraw the injector straight back from the stent.
   i. Verify that the stent is well-positioned and secured in the TM.
   j. Actuate the Singulator to prepare the next stent for implantation. Listen for the two audible clicks, and verify that the next stent is visible in the window of the insertion tube.
   k. Carefully relocate the tip of the injector approximately 2 clock hours away from the first stent for implantation of the second stent. Implant the next stent using the same procedure as the previous stent.
   l. Repeat the previous step for the third stent, placing the third stent approximately 2 clock hours away from either of the first two stents. Note: it may be desirable to exit the eye after the first or second stent implant. Ensure comfortable surgeon positioning and angle of approach to target stent implant site prior to subsequent stent implantations.
4) Intraoperative confirmation of proper stent positioning is as follows:
   a. After completion of stent implantations and withdrawing the injector from the anterior chamber, irrigate the anterior chamber of any refluxed blood to visualize the implanted stents.
   b. Confirm proper placement of the three implanted stents, ensuring that each stent flange is visible in the anterior chamber (shown below in **Figure 8**). The stent's wide flange should be visible and flush with the surface of the TM, and the stent's inlet should be unobstructed. Note: minimal blood reflux is a normal physiological response to placement of the stents, although this does not occur in all cases.

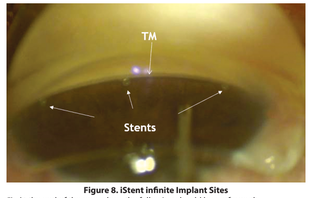


Figure 8. iStent infinite Implant Sites

5) 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. Repeat as needed until all viscoelastic has been removed.
   b. Inflate the anterior chamber with saline solution as needed to achieve physiologic pressure.
   c. Hydrate the wound and ensure that the corneal incision is sealed, and place 10-0 nylon suture if needed.
   d. Dispose of the injector in a sharps container.

Important Notes:

- If a stent is under implanted and remains on the trocar, do not actuate the singulator; re-attempt stent implantation in the nearest available trabecular meshwork tissue (within 1/2 clock hour away); see **Figure 9**
- If a stent is under implanted and remains on the trocar **and** the singulator was then actuated (i.e., two stents visible on the trocar), use an alternative "flush technique" procedure to re-attempt stent implantation in the nearest available trabecular meshwork tissue (within 1/2 clock hour away); see **Figure 9**.
- If a stent is under implanted **and does not** remain on trocar, the stent can be "rethreaded" by placing the trocar through the central inlet (**Figure 9**). Use the appropriate tissue pressure technique, "dimple technique" if one stent is on the trocar or the "flush technique" if two stents are visible on the trocar.

Figure 9. iStent infinite rethreading of stent (left)
and flush technique (right)

- Rethreading can be considered if the surgeon prematurely releases a stent prior to engaging the trocar with the trabecular meshwork.
- In the event that the first injector does not deliver three stents successfully, confirm that the number of stents implanted is less than three (3) before utilizing a second injector. Perform the following steps:
  - o Inspect the micro-insertion tube under the surgical microscope and verify that at least one stent remains within the injector, or verify that at least one stent has been retrieved from the eye.
  - o After successful delivery of 3 stents, do not attempt delivery of any additional stents remaining in the second injector.

Postoperative Instructions

1. Patients should be managed postoperatively for IOP increases that may occur in the early postoperative period as a possible sequela in patients with glaucoma. Additionally, monitor the patient postoperatively and consider an appropriate treatment regimen to reduce intraocular pressure if need be.
2. Gonioscopy should be performed to assess the iStent infinite stent position postoperatively.
3. Ultrasound biomicroscopy (UBM) is a useful adjunctive diagnostic aid in case of poor visualization of stents via gonioscopy.
4. Variations in gonioscopic visualization and limitations of UBM may prevent localization of a stent. However, in the absence of clinical sequelae, device adjustment or removal is not recommended.
5. It is highly recommended that Glaukos be contacted prior to postoperative device removal.

Postoperative Retrieval of a Stent

If the surgeon determines that an instrument is required to recapture a stent after the procedure, micro forceps of the surgeon's choice can be used by the surgeon as follows:

1. Prep the patient as one would for stent implantation surgery.
2. Re-open the eye at the preferred location to reach the stent. A clear corneal incision measuring approximately 1.5 mm in length is recommended.
3. Use cohesive viscoelastic to inflate the anterior chamber to create access to the stent's location, move the stent away from a delicate structure if loose, and/or protect intraocular tissues.
4. Use a gonioscope if needed to visualize the location of the stent in the anterior chamber.
5. Insert a micro forceps device through the corneal incision and grasp the stent in a convenient and secure manner before removing the stent from the anterior chamber.
6. Irrigate the anterior chamber with balanced salt solution (BSS) through the corneal wound to remove all viscoelastic. Press down on the posterior edge of the incision as needed to facilitate complete removal of viscoelastic. Repeat as needed until all viscoelastic has been removed.
7. Inflate the anterior chamber with saline solution as needed to achieve normal physiologic pressure.
8. Ensure that the corneal incision is sealed.

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

The iStent infinite System is for single use only and is supplied as follows: Three stents are preloaded within the single-use injector system, and the system is provided sterile and non-pyrogenic in a Tyvek tray. Each stent system is individually serialized, and the serial number is provided on the tray lid and unit carton. The system 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 (Tyvek 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 before the expiration date. This device should not be used past the indicated sterility expiration date. Do not resterilize.

12. RETURN GOODS POLICY

Please contact Glaukos Corporation.

13. iSTENT INFINITE SYSTEM – PIVOTAL CLINICAL TRIAL RESULTS

A prospective, multi-center, single arm, open-label, clinical trial was conducted at 15 sites in the U.S. (14) and the Philippines (1) to evaluate the safety and effectiveness of the iStent infinite in glaucoma subjects where previous filtering or cilioablative procedures failed. Sixty-one subjects were implanted with the iStent infinite and 12-month data were collected. In this clinical investigation a medication washout was not performed.

Subject Accountability

Sixty subjects (60/61 or 98.4%) completed the 12-month visit. One subject died due to respiratory failure unrelated to treatment prior to the Month 12 visit.

Demographics and Preoperative Characteristics

The mean age of subjects was 71.7 years and there were 28 males (28/61 or 45.9%) and 33 females (33/61 or 54.1%). Thirty-seven (37/61 or 60.7%) subjects were White, 15 (15/61 or 24.6%) were Black, 6 (6/61 or 9.8%) were Asian; race was not reported for 3 (3/61 or 4.9%) subjects. Eleven subjects (11/61 or 18.0%) had ethnicity reported as Hispanic or Latino. Fifty-five subjects were diagnosed with primary open angle glaucoma (POAG), 3 subjects had pseudoexfoliative glaucoma, and 3 subjects had pigmentary glaucoma. All 61 subjects had undergone prior filtering or cilioablative glaucoma procedures. Preoperatively, the mean visual field mean deviation (MD) score was -15.1 (SD 8.56) dB. Twenty-two subjects at screening had severe mean VF scores of worse than -20 dB. The other subjects' visual fields ranged from -20 dB to > -12 dB (n = 15) and -12 dB to 0 dB (n=24).

The mean medicated IOP at baseline was 23.5 (SD 2.8) mmHg. At baseline, subjects were using a mean of 3.0 (± 0.9) ocular hypotensive medications, with 19 (19/61 or 31.1%) on 2 or fewer medications and 42 (42/61 or 68.9%) on 3 or more medications.

Operative Parameters and Intraoperative Ocular Adverse Events

Operative parameters are summarized in **Table 1**. All 61 eyes (61/61 or 100%) were implanted with 3 stents. Overall, in the vast majority (56/61 or 91.8%) of surgeries, only one injector was used to implant iStent infinite. The vast majority of subjects (91.8%; n = 56/61) reported no issues with implantation. In the 5 eyes with implantation issues, a second injector was required (for four participants, the second stent did not advance in the first injector, and in another participant, the third stent did not advance in the first injector, and there was also head movement noted). There were no untoward safety findings attributed to the use of second injectors.

Table 1
Operative Parameters
ITT Population

	N = 61 Subjects	
	Number	Percent
# of Stents Implanted		
1 Stent	0	0.0%
2 Stents	0	0.0%
3 Stents	61	100.0%
# of Injectors Used		
1	56	91.8%
2	5	8.2%
Implantation Issues		
Yes	5	8.2%
No	56	91.8%

% = 100 × (n ÷ N)

No intraoperative adverse events were reported as shown in **Table 2.** There were no cases in which stent implantation was attempted and 0 stents were implanted (i.e., failure to implant 3 stents).

Table 2
Intraoperative Ocular Adverse Events in the Study Eye
Safety Population

Intraoperative Adverse Event	N = 61 Number of Reports	N = 61 Number (Percent) of Subjects with Event
Choroidal effusion	0	0 (0.0%)
Choroidal hemorrhage	0	0 (0.0%)
Cyclodialysis cleft	0	0 (0.0%)
Device malfunction identified after entry of the injector system into the eye but prior to contact with the target tissue	0	0 (0.0%)
Failure to implant three stents	0	0 (0.0%)
Flat anterior chamber requiring anterior chamber reformation	0	0 (0.0%)
Inadvertent perforation of the sclera	0	0 (0.0%)
Lens trauma/IOL scratched	0	0 (0.0%)
Lens/IOL dislocation	0	0 (0.0%)
Loss of stent in eye	0	0 (0.0%)
Significant capsular bag tear/rupture resulting in vitreous loss or prolapse	0	0 (0.0%)
Significant corneal injury	0	0 (0.0%)
Significant hyphema (i.e., >= 10% of anterior chamber)	0	0 (0.0%)
Significant iris damage	0	0 (0.0%)
Total	**0**	**0 (0.0%)**

Postoperative Ocular Adverse Events

There were no unanticipated adverse device effects. There were no serious ocular adverse events. There were no reports of corneal decompensation, choroidal effusion, choroidal hemorrhage, hypotony maculopathy, deep stents ("buried" in the trabecular meshwork) that were not visible at the last three scheduled visits of the study, stent explantation, stent dislocation, or stent repositioning. Approximately half of the study eyes (30/61 or 49.2%) had no reports of AEs.

A list of AEs reported and the associated rates are provided in **Table 3**

Table 3
Postoperative Ocular Adverse Events in the Study Eye
(Sorted Alphabetically) Safety Population

Postoperative Adverse Event	N = 61 Number of Reports	N = 61 Number (Percent) of Subjects with Event
A significant increase in crystalline lens opacity from baseline defined as a change of ARLNS grade of three half-step increments of 0.5 per increment or greater for nuclear opalescence, cortical or posterior subcapsular opacities (as applicable to phakic eyes)	0	0 (0.0%)
Age-related macular degeneration	0	0 (0.0%)
Allergic reaction	0	0 (0.0%)
An increase of three half-step increments of 0.5 per increment or greater in anterior subcapsular opacities or a clinically significant cataract eligible for phacoemulsification with BCVA loss (ETDRS) of greater than 10 letters from baseline (as applicable to phakic eyes)	0	0 (0.0%)
Aqueous misdirection	0	0 (0.0%)
Atrophy/phthisis	0	0 (0.0%)
Blepharitis	3	3 (4.9%)
Choroidal effusion	0	0 (0.0%)
Choroidal hemorrhage	0	0 (0.0%)
Chronic pain in the study eye present greater than 3 months postoperative	0	0 (0.0%)
Clinically significant cystoid macular edema	0	0 (0.0%)
Conjunctival erosion due to tube shunt	1	1 (1.6%)
Conjunctivitis	1	1 (1.6%)
Corneal abrasion	0	0 (0.0%)
Deep stents ("buried" in the trabecular meshwork) that are not visible at the last three scheduled visits of the study	0	0 (0.0%)
Disc hemorrhage	1	1 (1.6%)
Elevated IOP[1]	1	1 (1.6%)
Endophthalmitis	0	0 (0.0%)
Flat or shallow anterior chamber (e.g., shallowing of the anterior chamber that causes any amount of iris-cornea touch)	0	0 (0.0%)
Hyperemia	2	2 (3.3%)
Hypotony (IOP < 6 mmHg) associated with clinically significant findings	1	1 (1.6%)
IOP increase >= 10 mmHg vs. baseline IOP[1]	6	5 (8.2%)
at Day 0 to Day 1	3	3 (4.9%)
at > Week 1 to < Month 1	1	1 (1.6%)
at >= Month 1	2	2 (3.3%)
IOP increase requiring oral medication[1]	2	2 (3.3%)
at > Day 1 to <= Week 1	1	1 (1.6%)
at >= Month 1	1	1 (1.6%)
IOP increase requiring surgical intervention;[1,3]	3	3 (4.9%)
at > Week 1 to < Month 1	1	1 (1.6%)
at >= Month 1	2	2 (3.3%)
Increase in C/D ratio of > 0.3 units on ophthalmoscopic examination	0	0 (0.0%)
Intraocular inflammation arising after the protocol's specified medication regimen is complete	1	1 (1.6%)
Intraocular inflammation following tube shunt surgery	2	2 (3.3%)
Iridodialysis	0	0 (0.0%)
Lens/IOL dislocation	0	0 (0.0%)
Loss of best spectacle corrected visual acuity (BSCVA) of 2 lines or more[2]	7	7 (11.5%)
<= 30 days	1	1 (1.6%)
> 30 days	6	6 (9.8%)
Loss of eye	0	0 (0.0%)
Macular edema	2	2 (3.3%)
Ocular hypotensive medication intolerance	3	3 (4.9%)
Ocular pain	1	1 (1.6%)
Ocular surface disease	7	7 (11.5%)
Perioperative inflammation	4	4 (6.6%)
Posterior vitreous detachment	1	1 (1.6%)
Proliferative vitreoretinopathy	0	0 (0.0%)
Ptosis	0	0 (0.0%)
Pupillary block	0	0 (0.0%)
Retinal detachment	0	0 (0.0%)
Retinal dialysis	0	0 (0.0%)
Retinal flap tears	0	0 (0.0%)
Significant corneal complications including opacification and decompensation	0	0 (0.0%)
Significant corneal edema	0	0 (0.0%)
Significant corneal injury	0	0 (0.0%)
Significant damage to trabecular meshwork	0	0 (0.0%)
Significant hyphema (i.e, >= 10% of anterior chamber)	2	2 (3.3%)
Significant iris damage	0	0 (0.0%)
Stent dislocation	0	0 (0.0%)
Stent explant	0	0 (0.0%)
Stent migration[2]	2	1 (1.6%)
Stent obstruction[4]	2	2 (3.3%)
Stent-cornea touch	0	0 (0.0%)
Stye	1	1 (1.6%)
Subconjunctival hemorrhage	1	1 (1.6%)
Toxic Anterior Segment Syndrome (TASS)	0	0 (0.0%)
Transient hypotony	1	1 (1.6%)
Visual field loss < 2.5 dB	1	1 (1.6%)
Visual field loss >= 2.5 dB	5	4 (6.6%)
Vitreous hemorrhage	0	0 (0.0%)
Total	**64**	**31 (50.8%)**

[1] A total of 8 eyes (8/61 or 13.1%) experienced 12 AEs of increased IOP (consisting of elevated IOP, IOP increase >= 10 mmHg vs. baseline IOP, IOP increase requiring oral medication and IOP increase requiring surgical intervention). The 4 eyes with more than one AE of increased IOP are as follows:

- One eye had an AE of IOP increase >= 10 mmHg vs. baseline IOP and an AE of IOP increase requiring secondary surgical intervention
- One eye had an AE of IOP increase requiring oral medication and an AE of IOP increase requiring secondary surgical intervention
- One eye had an AE of elevated IOP and an AE of IOP increase requiring secondary surgical intervention
- One eye had 2 AEs of IOP increase >= 10 mmHg vs. baseline IOP

1. The 3 events of IOP increase requiring surgical intervention are included below in **Table 4.**
2. Five AEs of BSCVA loss of 2 lines or more were ongoing at Month 12
3. One subject was reported with 2 events of stent migration. The PI acknowledged that the visualization was impaired during implantation of the 1:00 and 4:30 stents due to corneal arcus, striae and external location-marking dye. The stent reported as implanted at 1:00 was identified in the 1:00 position via UBM ("embedded deep beyond iris insertion"), and the stent reported as implanted at 4:30 was identified in the 7:30 position via both gonioscopy and UBM.
4. The 2 AEs of stent obstruction involved complete obstruction of 2 stents each. The investigators reported associated findings of significant hyphema in 1 case and pre-existing and postoperative focal goniosynechiae in both cases. One case of stent obstruction resolved following treatment with pilocarpine, and 1 case was not treated and was ongoing at Month 12. Both subjects experienced Month 12 MDIOP reduction on the same medication regimen as preoperative.

The proportion of all AEs considered definitely related to study treatment by the study investigators was 22.2%, and consisted of AEs of elevated IOP, IOP increase ≥ 10 mmHg at Day 0 to Day 1, IOP increase requiring oral medication within 1 week, loss of BSCVA of 2 lines or more occurring within 30 days, perioperative inflammation, significant hyphema, stent migration, stent obstruction, subconjunctival hemorrhage and transient hypotony. Please note that the one device-related AE of early, transient BSCVA loss of 2 lines was reported for a subject in whom the BSCVA loss occurred following an AE of significant hyphema; this BSCVA loss was transient and fully resolved after the AE of hyphema had resolved.

Secondary Surgical Interventions

Secondary surgeries over the course of the 12-month follow-up are shown in **Table 4.** Tube shunt surgery was reported for 3 eyes (3/61 or 4.9%). None of the AEs requiring SSIs were device-related.

Table 4
Secondary Surgical Interventions in the Study Eye
Safety Population

Secondary Surgical Intervention	N = 61 n (%)
Overall	**3 Reports from 3 Subjects**
Tube shunt	3[1] (4.9%)

The counts (n) are the number of subjects reported with the corresponding events. % = 100 × (n ÷ N).
All SSIs, regardless of reason, were included.

1. One subject reported with Month 12 MDIOP higher than baseline MDIOP and underwent tube shunt surgery 1 week after the Month 12 exam.

Effectiveness Results

The iStent infinite is effective in reducing intraocular pressure in this glaucoma study population. **Tables 5 and 6** provide an overview of the primary effectiveness analyses based on 12-month diurnal IOP data.

Table 5
Analyses of Responder Effectiveness Endpoint
Proportion of Responders at Month 12

Analysis Population/Imputation Method for Missing Data	n/N (%) (95% CI) N= 61
ITT Population/Worst Postoperative IOP & Last Available Medication Classes[1]	44/61 (72.1%) (59.2%, 82.9%)[2]
ITT Population/Failure Assumption[3]	44/61 (72.1%) (59.2%, 82.9%)[2]
PP Population	43/59 (72.9%) (59.7%, 83.6%)[2]
ITT PopulationExclusion from Cohort[4]	44/60 (73.3%) (60.3%, 83.9%)[2]
ITT PopulationMultiple Imputation[5]	73.4%[6] (62.2%, 84.6%)[6]

Subjects with ≥ 20% reduction in MDIOP at Month 12 vs. Baseline on the same or fewer ocular hypotensive medication classes as Baseline were responders.

Subjects with (i.) hypotony (IOP < 6 mmHg) associated with clinically significant findings, (ii.) loss of light perception, (iii.) IOP-related SSIs, (iv.) cyclodialysis cleft, and/or (v.) no stents visible were treated as non-responders.

1. Responder status for the 1 subject with missing data at Month 12 was determined using the worst postoperative IOP and the last available number of medication classes.
2. Exact confidence limits using the Clopper-Pearson method.
3. The 1 subject who missed the 12-month evaluation was considered a non-responder.
4. The 1 subject who missed the 12-month evaluation was excluded from the total cohort.
5. Multiple imputation was used for the 1 subject with missing data at Month 12.
6. Based on the normal approximation to the binomial distribution.

Table 6
Analyses of IOP Change from Baseline Effectiveness Endpoint
12-Month Diurnal IOP Change from Baseline

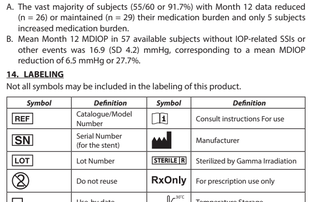
Analysis Population/Imputation Method for Missing Data	N Mean ± SD (95% CI)[1]
ITT Population/Worst Postoperative IOP[2]	61 -5.5 ± 5.24 (-6.9, -4.2)
PP Population	59 -5.5 ± 5.29 (-6.9, -4.1)
ITT Population/Exclusion from Cohort[3]	60 -5.6 ± 5.27 (-6.9, -4.2)
ITT Population/Multiple Imputation[4]	61 -5.5 ± 0.67[5] (-6.9, -4.2)

The following imputation methods were used for the 12-month MDIOP:
i. For subjects with hypotony associated with clinically significant findings, cyclodialysis cleft, and/or no stents visible, the worst postoperative IOP on the same or greater number of OHT medication classes as Baseline was used. Note: if a subject was on fewer OHT medication classes than Baseline, then the Baseline IOP was used.
ii. For subjects with loss of light perception, the observed 12-month MDIOP was used.
iii. For subjects with IOP-related SSIs, the worst postoperative IOP prior to SSI on the same or greater number of OHT medication classes as Baseline was used. Note: if a subject was on fewer OHT medication classes than Baseline, then the Baseline IOP was used.
iv. For subjects on more OHT medication classes than at Baseline, the worst postoperative IOP on the same or greater number of OHT medication classes as Baseline was used.

1. Based on the t-distribution.
2. The worst postoperative IOP was used as the 12-month MDIOP for the 1 subject who missed the 12-month evaluation.
3. The 1 subject who missed the 12-month evaluation was excluded from the total cohort.
4. Multiple imputation was used for the 1 subject with missing data at Month 12.
5. Mean ± SE for this value.

Effectiveness stratified by age, sex, race, and ethnicity, as well as baseline IOP and glaucoma type is provided in **Figure 10.**

Figure 10
Forest Plot of Responder Effectiveness Endpoint
Proportion of Subjects with MDIOP Reduction ≥ 20% from Baseline at 12 Months on the Same or Fewer Medication Classes by Demographic/ Preoperative Characteristics
ITT Population


Subgroup
N
Percent (95% CI)
Overall N = 61 72.1 (59.2, 82