

## INSTRUCTIONS FOR USE

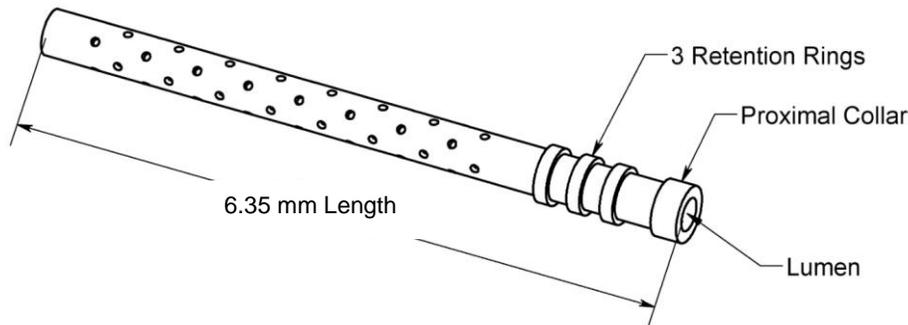


**CyPass® System**  
**REF # CYP-241-S**

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

### **A. DEVICE DESCRIPTION**

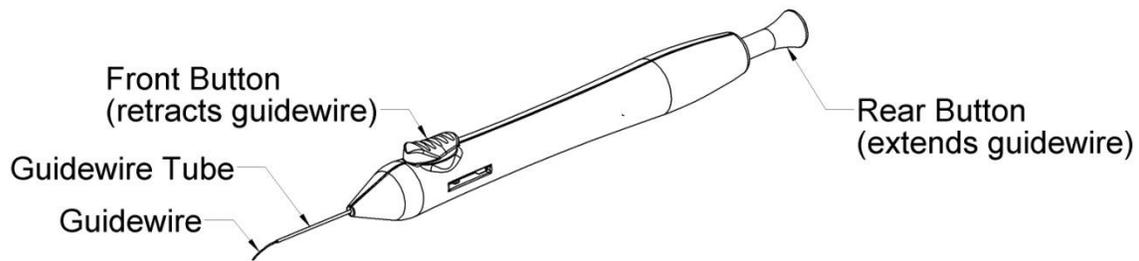
The CyPass® system consists of the CyPass Micro-Stent, which is contained in a loading device (loader), and the CyPass applicator. The CyPass Micro-Stent (Figure 1) is a polyimide tube with a fenestrated lumen. The stent has a single piece design and is 0.25" (6.35 mm) long. The inner diameter of the stent is 0.012" (0.30 mm) and the outer diameter is 0.017" (0.43 mm). The CyPass Micro-Stent is designed for placement in the angle of the eye, with the proximal end extending from the angle into the anterior chamber (AC) and the distal end residing in the supraciliary space.



**Figure 1: CyPass Micro-Stent**

When properly implanted, the CyPass Micro-Stent is intended to allow outflow of aqueous fluid from the AC, where the device proximal end resides, through and around the fenestrated lumen and distal end of the tube into the supraciliary and suprachoroidal space via the uveoscleral pathway.

The CyPass applicator (Figure 2) is the hand-held surgical instrument used to implant the CyPass Micro-Stent. The applicator consists of a medical-grade polymer handpiece with a guidewire assembly. The guidewire assembly includes a nitinol implant delivery guidewire extending from inside the handpiece through and beyond the distal end of a stainless steel tube (guidewire tube) that supports the guidewire. The guidewire is 0.011" (0.28 mm) in diameter and formed with a 0.48" (12 mm) radius of distal curvature and a blunt distal tip to facilitate location and blunt dissection of the plane between the ciliary body and sclera. The CyPass applicator delivers the CyPass Micro-Stent to the desired location within the eye.



**Figure 2: CyPass applicator with guidewire extended**

The CyPass Micro-Stent is loaded onto the guidewire before insertion into the eye. Once the guidewire has positioned the CyPass Micro-Stent at the desired location within the eye, the implant is released from the guidewire using the front button on the CyPass applicator. This action withdraws the guidewire back into the guidewire tube, leaving the CyPass Micro-Stent in position in the eye.

## **B. INDICATIONS FOR USE**

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

## **C. CONTRAINDICATIONS**

Use of the CyPass system is contraindicated under the following circumstances or conditions:

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

## **D. WARNINGS**

1. Clear media for adequate visualization is required. The following conditions may prohibit sufficient visualization of the angle required for safe and successful implantation of the CyPass Micro-Stent: corneal haze, corneal opacity, or any other conditions that may inhibit gonioscopic view in the intended implant location.
2. The surgeon should perform gonioscopy prior to surgery to exclude congenital anomalies of the angle, peripheral anterior synechiae (PAS), angle closure, rubeosis and any other angle abnormalities that could lead to improper placement of the stent and pose a hazard.
3. The surgeon should monitor the patient postoperatively for proper maintenance of IOP. If IOP is not adequately maintained after surgery, the surgeon should consider appropriate additional therapy to maintain target IOP.

4. The CyPass Micro-Stent is intended for implantation in conjunction with cataract surgery, which may impact corneal health. Therefore, caution is indicated in eyes with evidence of corneal compromise (e.g., corneal guttae or low endothelial cell density) or with risk factors for corneal compromise following cataract surgery (e.g., advanced age, severe nuclear sclerosis).

#### **E. PRECAUTIONS**

1. The safety and effectiveness of the CyPass Micro-Stent has not been established in patients with the following circumstances or conditions:
  - Age 21 years or younger
  - Eyes with significant prior trauma
  - Eyes with abnormal anterior segment
  - Eyes with chronic inflammation
  - Eyes with glaucoma associated with vascular disorders
  - Pseudophakic eyes with glaucoma
  - Eyes with uveitic glaucoma
  - Eyes with pseudoexfoliative or pigmentary glaucoma
  - Eyes with other secondary open angle glaucomas
  - Eyes that have undergone prior incisional glaucoma surgery or cilioablative procedures
  - Eyes with laser trabeculoplasty performed  $\leq$  3 months prior to the surgical screening visit
  - Eyes with unmedicated IOP  $<$  21 mmHg or  $>$  33 mmHg
  - Eyes with medicated IOP  $>$  25 mmHg
  - In the setting of complicated cataract surgery with iatrogenic injury to the anterior or posterior segment.
  - When implantation is without concomitant cataract surgery with IOL implantation for visually significant cataract
2. The safety and effectiveness of use of more than a single CyPass Micro-Stent has not been established.
3. The CyPass Micro-Stent has not been established as an alternative to the primary treatment of glaucoma with medications.
4. The Patient Identification Card included in the package is to be completed and given to the patient, together with instructions to keep the card as a permanent record to be shown to any health care practitioner that the patient consults in the future.

#### **F. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH**

Below is a list of potential adverse effects that may be associated with the use of the CyPass system in conjunction with cataract surgery. Adverse effects that occurred in the pivotal clinical trial are indicated with an asterisk and additional information regarding these adverse effects is summarized in Section N - Pivotal Clinical Trial Results.

Potential intraoperative adverse effects may include, but are not limited to: choroidal detachment, choroidal hemorrhage or effusion, difficulty with CyPass Micro-Stent implantation\*, hyphema obscuring the surgeon's view\*, inability to implant the CyPass Micro-Stent\*, inadvertent perforation of sclera, loss of vitreous not associated with the cataract procedure, posterior capsular rupture with or without vitreous

## CyPass® System

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loss resulting from cataract surgery\*, significant corneal damage, significant iris injury or trauma\*, and zonular dialysis.

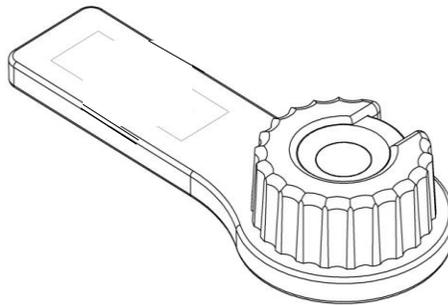
Potential postoperative adverse effects may include, but are not limited to: AC cell and flare requiring either extension of the standard postoperative steroid regimen or re-initiation of steroids after steroid regimen completion\*; AC flattening with lens/cornea touch; AC shallowing with iridocorneal apposition; atrophy/phthisis; choroidal hemorrhage or effusion; chronic pain in the implanted eye; corneal edema\*; corneal opacification; corneal decompensation\*; CyPass Micro-Stent malposition, dislodgement or movement\*; CyPass Micro-Stent explantation\*; CyPass Micro-Stent obstruction\*; elevated IOP requiring treatment with oral or intravenous medications or with surgical intervention\*; endophthalmitis; hypotonic maculopathy\*; increase in C:D ratio; loss of best-corrected visual acuity (BCVA)\*; persistent significant foreign body sensation\*; persistent hyphema\*; persistent hypotony\*; maculopathy\*; retinal complications (dialysis, flap tears, retinal detachment or proliferative vitreoretinopathy)\*; significant ptosis; worsening in visual field loss\*; unplanned secondary ocular surgical intervention\*; and wound dehiscence (persistent aqueous leak or fistula formation).

## G. DIRECTIONS FOR USE

### Surgical Procedure

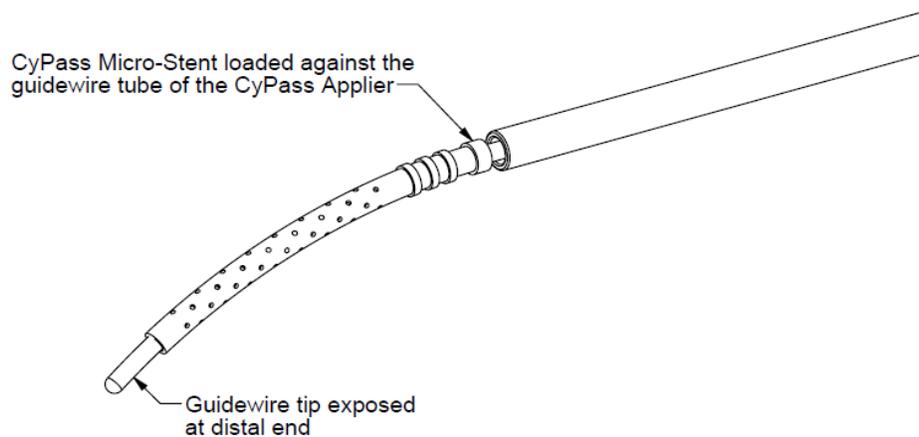
The implantation procedure is performed as follows, after completion of cataract extraction and intraocular lens implantation.

1. Instill a miotic agent to constrict the pupil.
2. Tilt the microscope approximately 35 - 45° towards the surgeon and rotate the patient's head approximately 10° away from the surgeon to facilitate direct visualization of the anterior angle.
3. Confirm the AC angle is open.
4. Open the tray containing the CyPass system onto a sterile field. Do not use either the CyPass Micro-Stent or the CyPass applicator if the packaging has been opened or damaged.
5. Remove the CyPass applicator from the sterile tray and examine its condition. First, press the rear button on the handle to verify the guidewire extends from the guidewire tube. Then, press the front button on the handle to confirm the guidewire fully retracts into the guidewire tube.
6. Remove the loader containing the CyPass Micro-Stent (Figure 3) from the sterile tray.



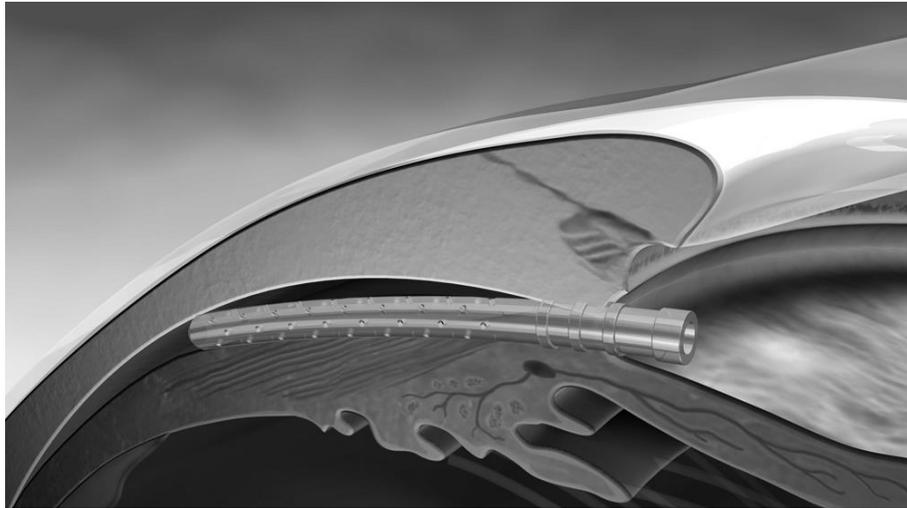
**Figure 3: CyPass Micro-Stent packaged in the loader**

7. Rotate the cap of the loader clockwise until the opening is aligned with the CyPass Micro-Stent.
8. Confirm the CyPass applicator guidewire is fully retracted into the guidewire tube.
9. Push the distal tip of the guidewire tube into the loader until it contacts the CyPass Micro-Stent and stops. Push the rear button of the applicator to extend the guidewire into the Micro-Stent. Remove the CyPass applicator with loaded CyPass Micro-Stent.
10. Examine the assembly. Confirm the condition of the CyPass Micro-Stent and that the guidewire is fully exposed at the distal end (Figure 4). If either the CyPass Micro-Stent or the CyPass applicator guidewire is damaged, do not use and contact Alcon.



**Figure 4: CyPass Micro-Stent loaded onto CyPass applicator guidewire**

11. Examine the AC angle with the gonio lens under the microscope. Take note of angle anatomy to identify the best implantation site. Avoiding the area of the anterior ciliary arteries at 3, 6, 9 and 12 o'clock may help reduce the possibility of significant bleeding.
12. Fill the AC with ophthalmic viscoelastic (OVD) and use additional OVD as necessary to maintain a deep, stable AC during the CyPass Micro-Stent implantation process.
13. Introduce the loaded CyPass applicator guidewire tube through the cataract incision and advance towards the intended site of implantation until the guidewire tube and sleeve have cleared the incision. When crossing the AC, rotate the CyPass applicator guidewire such that its curvature is parallel to the iris plane.
14. Position the CyPass applicator guidewire radially toward the scleral spur/ciliary body interface. Care should be taken to align the curvature of the CyPass on the guidewire with the curvature of the sclera bordering the supraciliary space to reduce the possibility of encountering resistance during insertion. To gain access, place the distal end of the guidewire at the scleral spur/ciliary body interface and smoothly advance the guidewire through the tissue plane between the ciliary body and adjacent sclera to separate the ciliary body from the scleral spur at the point of implantation.
15. Continue to advance the guidewire until only the most proximal retention ring and the collar of the CyPass Micro-Stent are located in the AC (Figure 5). An additional confirmatory placement landmark is when the top of the CyPass Micro-Stent collar is even with Schwalbe's line. In this position, the distal tip of the CyPass Micro-Stent should be resting against the sclera in the supraciliary space anterior to both retinal and choroidal tissues.



**Figure 5: CyPass Micro-Stent at implant site**

16. Hold the CyPass applicator stationary and carefully press the front button on the CyPass applicator to retract the guidewire into the guidewire tube, leaving the Micro-Stent anchored between the sclera and ciliary body.
17. Remove the CyPass applicator from the eye.
18. If resistance is encountered or adequate implantation is not achieved at the initial implant site, implantation at a location at least 2 clock hours away from any area of ciliary body disinsertion can be considered if there is no significant iris trauma or hemostasis and if the CyPass Micro-Stent remains properly positioned on the guidewire and adequate visualization can be maintained. Make sure that the position of the patient's head and the tilt of the microscope allow adequate gonioscopic visualization of the angle structures. Increase magnification and fine focus the microscope as needed. Additional viscoelastic tamponade may be needed to assure hemostasis and maintain visibility during CyPass Micro-Stent implantation. Align the curvature of the CyPass on the guidewire with the curvature of the sclera bordering the supraciliary space to reduce the possibility of encountering resistance during insertion.
19. Termination of the procedure should be considered after 2 failed attempts at device placement or if adequate visibility cannot be maintained during implantation.
20. Use gonioscopy to confirm CyPass Micro-Stent position. Optimal position of the CyPass Micro-Stent is when only the collar and the first retention ring are visible in the AC. Anterior positioning with more than 2 retention rings visible in the AC can be associated with corneal endothelial cell loss. Posterior positioning such that the collar is not visible can be associated with reduced device effectiveness.
  - a. If the CyPass Micro-Stent appears to be too anterior, use the guidewire tube of the CyPass applicator to gently push the device deeper into the supraciliary space until it is optimally positioned. If the proximal end of the CyPass Micro-Stent appears to be too posterior, use a micro-forceps to grasp the CyPass Micro-Stent collar and gently pull it into the AC until the implant is optimally positioned. Do not use the irrigation/aspiration (I/A) tip for CyPass Micro-Stent positioning.
  - b. If proper placement cannot be achieved, implant removal should be considered. Use direct gonioscopy visualization and supplementary viscoelastic for safe removal.

21. Since retained viscoelastic can lead to elevated IOP in the early postoperative period, irrigate and aspirate viscoelastic from the AC, taking care to avoid irrigation/aspiration (I/A) tip proximity to the CyPass Micro-Stent. *Note: The flow of irrigation fluid near the Micro-Stent may cause implant movement.*
22. After completion of I/A, verify CyPass Micro-Stent location and confirm the absence of CyPass Micro-Stent lumen obstruction.
23. Confirm that the surgical incision is sealed by either pressure challenge testing or Seidel testing. Use a suture or ocular sealant for closure, if needed.

### **Postoperative Instructions**

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

Gonioscopy should be performed to assess CyPass Micro-Stent position postoperatively. Anterior positioning of the CyPass Micro-Stent such that more than 2 retention rings are visible in the AC may result in reduced endothelial cell density and a need for secondary surgical intervention (e.g., device repositioning, device trimming, or device removal). If the CyPass Micro-Stent is close to the corneal endothelium, early repositioning or removal of the CyPass Micro-Stent and/or periodic follow-up assessments of endothelial cell density using specular microscopy should be considered.

If ciliary body edema is suspected due to forward movement of the ciliary body-lens diaphragm, ultrasound biomicroscopy (UBM) may be a useful adjunctive diagnostic aid in the evaluation of the ciliary body and suprachoroidal space.

### **Postoperative CyPass Micro-Stent Adjustment or Removal**

Situations that may merit consideration of CyPass Micro-Stent position adjustment or removal include, but are not limited to: intermittent or persistent contact between the CyPass Micro-Stent and the corneal endothelium; significant decrease in endothelial cell density that appears related to CyPass Micro-Stent positioning or stability; iris-cornea touch; persistent hypotony; persistent uncontrolled uveitis; recurrent or persistent hyphema with IOP elevation above target pressure; or any anatomic or functional clinical sequelae of the anterior or posterior segment that may cause a threat to vision. Variations in gonioscopic visualization or other alterations in angle anatomy may be interpreted as micro-movement of the CyPass Micro-Stent; however, in the absence of clinical sequelae, device adjustment or removal is not recommended.

Healing response and progressive engagement of implant retention features must be factored into the decision to remove the CyPass Micro-Stent after the immediate postoperative period (e.g., after 1 month postoperative). It is advised to consider less invasive intervention, such as positional adjustment or trimming of the CyPass Micro-Stent proximal end (if the device is considered too anteriorly positioned) as a first alternative to device removal. It is also highly recommended that Alcon be contacted prior to device removal.

• **Procedure for CyPass Micro-Stent Repositioning or Removal**

Surgical access for CyPass Micro-Stent repositioning or removal is primarily *ab-interno* through a minimum 1.5 mm clear cornea incision under direct gonioscopy and AC viscoelastic stabilization. Use of retinal micro-forceps and retinal instrumentation is encouraged for optimal surgical control and access.

The steps for this procedure are as follows:

1. Construct the clear corneal incision and instill OVD into the AC.
2. Utilizing a gonioscope for visualization, grasp the CyPass Micro-Stent with toothed micro forceps around the anterior rim and gently either reposition until optimal positioning is achieved, or remove the device from its position. Carefully observe any tension or traction on surrounding tissues.
3. Remove remaining OVD from the AC and adjust the tension in the eye by injecting and/or allowing egress of BSS; then close the incision.

• **Procedure for CyPass Micro-Stent Proximal End Trimming**

After the immediate postoperative period, trimming of the proximal end of the CyPass Micro-Stent may be considered when anterior positioning of the CyPass is likely to compromise corneal endothelial health. The steps for this procedure are as follows:

1. Construct 2 clear corneal incisions under OVD, utilizing either direct observation or a gonioscope for visualization.
2. Hold the proximal portion of the CyPass Micro-Stent with micro-forceps, and incise distally with micro-scissors.
3. Remove the separated proximal portion through the corneal incision.
4. Inspect the remaining distal portion of the CyPass Micro-Stent with a gonioscope to confirm optimal positioning.
5. Remove remaining OVD from the AC utilizing irrigation alone or automated irrigation/aspiration, then adjust the tension in the eye by allowing egress of aqueous and seal the incision.

After surgery, patients should be monitored for IOP changes that may occur as possible sequelae following intraocular surgery in patients with glaucoma. Patients should also be periodically evaluated using specular microscopy to assess changes in endothelial cell density.

**H. ADVERSE EVENT REPORTING**

Adverse events and/or potentially sight-threatening complications that may reasonably be regarded as related to the CyPass system must be reported to Alcon Medical Safety.

Alcon Laboratories, Inc.,  
Medical Safety (AB 2-6),  
6201 South Freeway, Fort Worth, TX 76134-2099  
Call Toll free: 1-800-757-9780

**I. HOW SUPPLIED**

The CyPass system is supplied sterile and non-pyrogenic in a sealed tray. The sealed tray is placed in a unit box containing product labeling and product information. The CyPass system has been sterilized using radiation.

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

The CyPass system and manufacturing processes do not contain latex.

Used CyPass applicators should be discarded only in a suitable, biohazardous sharps container.

**J. STORAGE REQUIREMENTS**

The CyPass system should be stored at room temperature in the range of 68-75°F.

**K. EXPIRATION DATE**

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

**L. MRI INFORMATION**

The CyPass Micro-Stent is magnetic resonance (MR) Safe: the implant is constructed of polyimide material, a non-conducting, non-metallic, non-magnetic polymer that poses no known hazards in all magnetic resonance imaging environments.

**M. RETURNED GOODS POLICY**

In the United States, returned product will only be accepted in exchange for other products, not credit. All returns must be accompanied by an Alcon Laboratories, Inc. Returned Goods Number and be shipped via traceable means. A Returned Goods Number is obtained by contacting Alcon's Customer Service Department. Issuance of this number does not constitute final acceptance of the returned products. For detailed policy guidelines including exchange, please contact your Sales or Customer Service Representative. Outside the United States, contact local Alcon offices or distributors regarding returned goods policy.

## **N. PIVOTAL CLINICAL TRIAL RESULTS**

The pivotal study for the CyPass Micro-Stent, known as the COMPASS Trial (Protocol TMI-09-01), was a prospective, randomized, comparative, multicenter investigation conducted in the United States, in which a total of 505 subjects from 24 sites were randomized in a 3:1 fashion to undergo either implantation of the CyPass Micro-Stent after uncomplicated cataract surgery (CyPass group) or to undergo cataract surgery without implantation of the CyPass Micro-Stent (Control group). A total of 374 subjects were randomized to the CyPass group and 131 subjects were randomized to the Control group. In each subject, only one eye was considered to be the study eye. Enrollment in the study began in September of 2009 and the last study subject was randomized in March of 2013. Randomized subjects were followed for 2 years postoperatively.

To participate in the study, subjects were required to have a diagnosis of POAG in the study eye. Additional study eye key inclusion criteria were:

- At the Screening Visit, a mean (or median) medicated IOP  $\leq 25.0$  mmHg or an unmedicated IOP  $\geq 21.0$  mmHg and  $\leq 33.0$  mmHg.
- At the Baseline Visit, an unmedicated mean diurnal IOP  $\geq 21.0$  mmHg and  $\leq 33.0$  mmHg, which was  $\geq 3.0$  mmHg higher than the Screening Visit medicated IOP.
- Gonioscopy confirming normal angle anatomy at the anticipated site of CyPass implantation and Shaffer grade  $\geq$  III in all 4 quadrants of the eye.

Subjects could not participate in the study if they had a diagnosis of acute angle closure, traumatic, congenital, malignant, uveitic, pseudoexfoliative, and pigmentary or neovascular glaucoma in the designated study eye. Subjects who had undergone previous incisional or cilioablative glaucoma procedures were also excluded from the study. Also, subjects who experienced cataract surgery complications were exited from the study prior to randomization. Subjects were not required to be using ocular hypotensive medications for inclusion in the study; however use of oral ocular hypotensive medication or more than 3 ocular hypotensive medications was an exclusion criterion.

The mean age of the study population was 70.3 years, with the majority (76.0%) between 60 and 79 years of age at the time of enrollment. Slightly more females ( $n = 269$ ) than males ( $n = 236$ ) were randomized. The majority of subjects were White (83.6%), with Black/African American subjects being the second most frequently enrolled race (9.3%). Screening and baseline characteristics were balanced between the 2 study groups.

The primary effectiveness endpoint was defined as the proportion of subject eyes with  $\geq 20\%$  decrease in the 24-month unmedicated mean diurnal IOP (DIOP) compared to the baseline DIOP. Subjects were defined as IOP non-responders if:

- they did not achieve the primary effectiveness endpoint,
- they missed the 24-month IOP assessment,
- ocular hypotensive medication use was not terminated prior to the 24-month DIOP assessment,
- they underwent an IOP-affecting secondary surgical procedure (i.e., iridotomy, iridectomy, trabeculectomy, glaucoma shunt implantation, argon laser trabeculoplasty, selective laser trabeculoplasty), or other surgery that would affect IOP, or

- they underwent CyPass explantation or repositioning. Subjects in which CyPass implantation was not successful were also considered to be IOP non-responders.

The first secondary effectiveness endpoint was the mean change in 24-month DIOP from baseline, and the second secondary effectiveness endpoint was defined as the proportion of subject eyes with 24-month unmedicated mean DIOP  $\geq 6$  mmHg and  $\leq 18$  mmHg.

Each endpoint required a comparison between the CyPass and Control groups. The primary and secondary effectiveness analyses were performed using the Intent to Treat (ITT) population, comprised of all randomized subjects grouped according to their randomization assignment.

During the COMPASS Trial, the CyPass Micro-Stent was implanted using a CyPass applier slightly different from the commercially available applier. The applier used in the COMPASS Trial used a different mechanism to hold the CyPass on the delivery guidewire prior to implantation, and guidewire retraction was performed by sliding the retraction button toward the back of the applier hand piece. The commercially available CyPass applier was clinically tested in a multi-surgeon case series of 91 subjects evaluating the intraoperative safety and performance in a similar patient population to that of the COMPASS Trial. In this study, the CyPass Micro-Stent was successfully implanted in all cases. Device implantation was successful on the initial placement attempt in 87 cases (95.6%); 1 case required 2 implantation attempts, while the number of attempts was undocumented for the remaining 3 cases. Postoperative gonioscopy revealed the CyPass to be visible, adequately positioned and without obstruction in the vast majority of cases reviewed. Adverse events (AE) related to device placement and stability were similar in nature to AEs observed in the CyPass arm of the COMPASS Trial.

### **Effectiveness Results**

Results from the primary and secondary endpoints are shown in Table 1. The primary effectiveness endpoint was met, with 72.5% in the CyPass group and 58.0% in the Control group achieving a clinically significant ( $\geq 20\%$ ) decrease in unmedicated mean DIOP from baseline to the hypotensive medication-free 24-month postoperative examination. This difference between groups was statistically significant ( $p=0.0030$ ).

The first secondary endpoint, a clinically significant mean change in IOP between baseline and hypotensive medication-free 24-month postoperative examination, was met. The mean reduction in unmedicated mean DIOP from baseline to 24 months was 7.0 mmHg (SD 4.5) in the CyPass group compared to 5.3 mmHg (SD 4.0) in the Control group ( $p < 0.0001$ ).

The second secondary effectiveness endpoint was also met, with 61.2% in the CyPass group and 43.5% in the Control group achieving unmedicated mean DIOP  $\geq 6$  mmHg and  $\leq 18$  mmHg at the hypotensive medication-free 24-month postoperative examination. The difference between groups was statistically significant ( $p=0.0005$ ).

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

Effectiveness Endpoint (Evaluated at 24 Months Postoperatively)	CyPass N=374	Control N=131	Difference (CyPass - Control)	p-value
<b>Primary Effectiveness Endpoint</b>				
Proportion of subject eyes with unmedicated mean DIOP reduction $\geq$ 20% from baseline	72.5%	58.0%	14.4%	0.003
<b>1<sup>st</sup> Secondary Effectiveness Endpoint</b>				
Difference in unmedicated mean DIOP (mmHg) reduction from baseline	-7.0	-5.3	-1.7	<0.0001
<b>2<sup>nd</sup> Secondary Effectiveness Endpoint</b>				
Proportion of subject eyes with unmedicated mean DIOP $\geq$ 6 mmHg and $\leq$ 18 mmHg	61.2%	43.5%	17.7%	0.0005

Additional detail regarding the reasons patients did not achieve the primary endpoint (IOP non-responders) is shown in Table 2.

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

	Cataract Surgery with CyPass N = 374 n (%)	Cataract Surgery Only N = 131 n (%)
Total Non-Responders	103 (27.5%)	55 (42.0%)
Non-Responders: 24-month unmedicated mean DIOP reduction < 20% vs. baseline	74 (19.8%)	44 (33.6%)
Non-Responders for reasons other than IOP reduction <sup>1</sup>	29 (7.8%)	11 (8.4%)
- Did not undergo glaucoma medication washout	0 (0.0%)	1 (0.8%)
- Secondary glaucoma surgery <sup>2</sup>	3 (0.8%)	4 (3.1%)
- Other IOP-affecting secondary surgery <sup>3</sup>	6 (1.6%)	0 (0.0%)
- CyPass implantation discontinued	2 (0.5%)	NAP
- Missed 24-month visit	19 (5.1%)	6 (4.6%)

n = number of eyes meeting corresponding criteria.

<sup>1</sup> One subject is included in more than 1 category of "Non-Responders for reasons other than IOP reduction"

<sup>2</sup> Secondary glaucoma surgeries include iridotomy, iridectomy, trabeculectomy, glaucoma shunt implantation and laser trabeculoplasty.

<sup>3</sup> Other IOP-affecting secondary surgeries include CyPass reposition, CyPass explant, vitrectomy, and laser lysis of presumed CyPass device obstruction.

**Safety Results**

Because final study eligibility and randomization to treatment were determined post-cataract surgery, no subjects experiencing an intraoperative cataract surgery-related AE were randomized to the study. Accordingly, intraoperative AEs occurred only in the CyPass group, and are shown in Table 3. A total of 25 intraoperative AEs were reported in 20 out of 374 CyPass subjects (5.3%).

Implantation of the CyPass Micro-Stent was successful in almost all cases, with non-implantation reported in only 2 subjects (0.5%)

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

Adverse Event	Cataract Surgery with CyPass (N = 374) n (%)
Subjects with Any Adverse Event	20 (5.3%)
Secondary ocular surgical intervention – AC lavage	1 (0.3%)
Choroidal detachment	0 (0.0%)
Choroidal hemorrhage or effusion	0 (0.0%)
Corneal abrasion	1 (0.3%)
Corneal damage, significant	0 (0.0%)
Cyclodialysis cleft, oversized	7 (1.9%)
CyPass non-implantation	2 (0.5%)
Descemet’s membrane break	1 (0.3%)
Hyphema obscuring surgeon’s view	10 (2.7%)
Iris injury or trauma, significant – iridodialysis	1 (0.3%)
Scleral perforation	0 (0.0%)
Subconjunctival hemorrhage	2 (0.5%)
Vitreous loss (not associated with cataract surgery)	0 (0.0%)
Zonular dialysis	0 (0.0%)

**Postoperative Adverse Events**

Postoperative ocular AEs are reported in Table 4. There were no reports of flat AC with lens cornea touch, shallow AC with iridocorneal apposition, shallow AC with peripheral iridocorneal apposition, wound dehiscence, endophthalmitis, corneal opacification or decompensation, choroidal hemorrhage or effusion, ptosis, atrophy/phthisis or cup-to-disc (C:D) increase of  $\geq 0.3$ . A similar number of subjects in each group experienced postoperative ocular AEs (39.3% of subjects [n = 147] in the CyPass group and 35.9% of subjects [n = 47] in the Control group). A similar proportion of randomized subjects in both groups underwent secondary ocular surgical intervention during the study. In the CyPass group, 5.3% of

subjects (n = 20) underwent secondary ocular surgeries, while in the Control group, 5.3% of subjects (n = 7) had secondary ocular surgeries.

Corneal edema associated with the surgical procedure resolved within the first postoperative month in 98% of CyPass group subjects. Only a single case of persistent corneal edema occurred, an incidence of 0.27% in the CyPass group. Anterior segment inflammation, which was generally mild, resolved in 95% of CyPass subjects by 3 months. Of note, subjects in the CyPass group underwent two interventions (cataract surgery and CyPass implantation) but had the same standard course of prophylactic steroids and NSAIDs that was used for cataract surgery alone. No cases of retinal detachment, pupillary block, endophthalmitis, or hypopyon occurred during the study. Based on available data at the 24-month visit, BCVA was 20/40 or better for 98.6% of subjects (n = 350) in the CyPass group and 98.4% of subjects (n = 126) in the Control group.

Only 2 ocular serious adverse events (SAE) were reported during the course of the study. One of these SAEs, peripheral anterior choroidal effusion, was considered to be related to the CyPass Micro-Stent. This event was not reported as “choroidal hemorrhage or effusion” because it did not meet the pre-specified criteria for that adverse event, i.e., there was no hemorrhagic component obstructing vision or causing pain; in addition, the effusion was restricted to the anterior supraciliary space and was only detectable with ultrasound imaging. This SAE was associated with IOL subluxation, which was successfully addressed with IOL repositioning and other complications, all of which resolved without sequelae by the 24-month visit. The other SAE was pseudophakic bullous keratopathy (PBK). Descemet stripping endothelial keratoplasty (DSEK) was performed approximately 1 year postoperatively.

TABLE 4: POSTOPERATIVE ADVERSE EVENTS\*

Adverse Event	Cataract Surgery with CyPass (N = 374) n (%)	Cataract Surgery Only (N = 131) n (%)
<b>Subjects with Any Adverse Event</b>	<b>147 (39.3%)</b>	<b>47 (35.9%)</b>
Corneal edema at/after 30 days postoperative, or severe in nature	13 (3.5%)	2 (1.5%)
Subconjunctival hemorrhage	6 (1.6%)	1 (0.8%)
CyPass malposition <sup>1</sup>	7 (1.9%)	Not applicable
CyPass movement/dislodgement without sequelae <sup>2</sup>	10 (2.7%)	Not applicable
CyPass obstruction by iris, vitreous, lens, fibrous overgrowth, fibrin or blood	8 (2.1%)	Not applicable
Hypotony (IOP < 6 mmHg) at/after 30 days postoperative	11 (2.9%)	0 (0.0%)
IOP => 10 mmHg over baseline at/after 30 days postoperative <sup>^</sup>	16 (4.3%)	3 (2.3%)
Maculopathy, cystoid edema	5 (1.3%)	1 (0.8%)
Maculopathy, hypotonic	3 (0.8%)	0 (0.0%)
Worsening in visual field MD by => 2.5 dB as compared with preoperative	25 (6.7%)	13 (9.9%)
AC cell and flare requiring steroid treatment at/after 30 days postoperative <sup>3</sup>	32 (8.6%)	5 (3.8%)
Conjunctivitis	4 (1.1%)	3 (2.3%)
Keratitis	1 (0.3%)	1 (0.8%)
BCVA loss => 10 letters read at/after 3 month postoperative visit	33 (8.8%)	20 (15.3%)
Worsening in any ocular symptom by ≥ 2 points to severe/very severe at/after 3 months postoperative:	21 (5.6%)	4 (3.1%)
- Blurred vision	7 (1.9%)	2 (1.5%)
- Dry eye	2 (0.5%)	1 (0.8%)
- Foreign body sensation	4 (1.1%)	1 (0.8%)
- Glare	10 (2.7%)	3 (2.3%)
- Halos	10 (2.7%)**	2 (1.5%)
- Inability to read without glasses	1 (0.3%)	0 (0.0%)
- Ocular pain	5 (1.3%)	1 (0.8%)
- Pulsing lines of light	1 (0.3%)	0 (0.0%)
- Redness	1 (0.3%)	0 (0.0%)
- Scratchiness & itchiness	0 (0.0%)	1 (0.8%)
- Starbursts	1 (0.3%)	0 (0.0%)

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

\*\* Two subjects in the CyPass group who reported worsening of symptoms of halos had received multifocal IOLs.

<sup>1</sup> CyPass malposition is defined as CyPass positioning after deployment with resulting clinical sequela, including secondary surgical intervention to modify device position (e.g., repositioning, proximal end trimming or explantation), corneal endothelial touch by device, or progressive endothelial cell loss > 30%. All cases of CyPass malposition were reported within the first postoperative week. Secondary surgical intervention to modify device position was performed in 5 cases: surgeries were performed within the first postoperative week in 3 cases (CyPass explant and repositioning) and at postoperative months 32 and 48 months (CyPass proximal end trimming) for the remaining 2 cases. Endothelial cell loss > 30% at 24 months postoperatively was reported in 3 cases; 2 cases were those in which device trimming surgery was performed at postoperative 32 and 48 months respectively.

<sup>2</sup> One case of CyPass movement without sequelae was reported within the first postoperative week, while the remaining 9 cases were reported between 3 and 24 months postoperatively. No secondary surgeries to modify device positioning were performed in these cases and none of the cases had endothelial cell loss > 30% at 24 months postoperatively.

<sup>3</sup> One case of chronic anterior uveitis was reported in a subject in whom CyPass implantation was complicated by an oversized cyclodialysis cleft.

<sup>^</sup> While not reported as an AE, IOP  $\geq$  10 mmHg over baseline *within* the initial 30 days postoperatively occurred in 6.4% (n = 24) of CyPass subjects and 20.6% (n = 27) of Control subjects. Short-term use of oral ocular hypotensive medication for pressure control was employed for 3 subjects in the CyPass group and 3 subjects in the Control group; paracentesis on postoperative day 1 was performed in 1 additional subject in the Control group.

In addition to the AEs reported in Table 4, AEs that occurred at < 2% in both groups included ocular medication allergy, corneal abrasion, non-proliferative diabetic retinopathy, proliferative diabetic retinopathy, diabetic macular edema, eyelid dermatitis and significant foreign body sensation at or after 3 months postoperative. Adverse events that occurred at <2% in the CyPass group included environmental allergy, map-dot fingerprint dystrophy, dry eye syndrome, hordeolum, trichiasis, foreign body with mucus filament, peripheral anterior choroidal effusion, ciliary body edema, hyphema > 2mm after 1 day postoperative, IOL complication (Crystalens Z syndrome, anterior malposition, and subluxation), worsening in slit lamp findings at or after 3 months postoperative (corneal staining and pigment deposition), choroidal folds without hypotony, wet age-related maculopathy, posterior vitreous detachment, vitreal-macular traction, blepharitis, episcleritis, ocular migraine, and vertical binocular diplopia. Adverse events that occurred at < 2% in the control group included chalazion, metallic foreign body, ectropion, and chronic ocular pain after 3 months postoperative.

### **Secondary Ocular Surgical Interventions**

Secondary ocular surgeries during the course of the study occurred in 5.3% of CyPass group subjects (n = 20) and 5.3% (n = 7) of subjects in the Control group. Three additional subjects had CyPass-related surgical procedures after completion of study participation. Secondary surgeries reported in both groups are shown in Table 5.

**TABLE 5: SECONDARY OCULAR SURGICAL INTERVENTION ADVERSE EVENTS  
AVAILABLE DATA FROM SAFETY POPULATION**

<b>Adverse Event</b>	<b>Cataract Surgery with CyPass (N = 374) n (%)</b>	<b>Cataract Surgery Only (N = 131) n (%)</b>
<i>Subjects with any event in category</i>	20 (5.3%)	7 (5.3%)
AC reformation for choroidal folds treatment <sup>1</sup>	1 (0.3%)	0 (0.0%)
CyPass explantation	1 (0.3%)	Not applicable
CyPass obstruction lysis <sup>2</sup>	1 (0.3%)	Not applicable
CyPass reposition	3 (0.8%)	Not applicable
DSEK	1 (0.3%)	0 (0.0%)
IOL reposition	3 (0.8%)	0 (0.0%)
Combined procedure - CyPass lumen occlusion/trabeculectomy/vitreotomy	1 (0.3%)	Not applicable
Laser trabeculoplasty	0 (0.0%)	3 (2.3%)
Paracentesis at/after 1 week postoperative	5 (1.3%)	0 (0.0%)
Pigment lysis <sup>3</sup>	1 (0.3%)	0 (0.0%)
Trabeculectomy	0 (0.0%)	2 (1.5%)
Tube-shunt implant	2 (0.5%)	0 (0.0%)
Secondary surgeries related to trabeculectomy or tube-shunt implant	2 (0.5%)	1 (0.8%)
<b>Secondary Surgeries unrelated to CyPass</b>		
Aspiration of lens material	2 (0.5%)	0 (0.0%)
Combined procedure - blepharoplasty/browpexy	0 (0.0%)	1 (0.8%)
Combined procedure – pars plana vitrectomy/membrane peeling/capsulotomy	1 (0.3%)	0 (0.0%)
Lid cyst excision	1 (0.3%)	0 (0.0%)
Limbal relaxing incisions	1 (0.3%)	2 (1.5%)
Macular photocoagulation	0 (0.0%)	1 (0.8%)
Panretinal photocoagulation	2 (0.5%)	1 (0.8%)

<sup>1</sup> Sodium hyaluronate AC reformation was performed 5 times for treatment of low IOP and persistent choroidal folds.

<sup>2</sup> Nd:YAG laser photolysis was performed a single time for removal of iris tissue obstructing CyPass.

<sup>3</sup> Laser photolysis was performed 4 times for removal of pigment deposition on the anterior IOL optic secondary to iris trauma caused by a failed CyPass implant attempt.

### **Other Postoperative Observations**

Reporting of other ocular observations was at the study investigator's discretion. Similar data may not be reported for every subject, or consistently within the course of a given subject's study participation. Consequently, no conclusions regarding the overall frequency of these findings can be drawn from the incidence rates noted. The other ocular observations that were reported postoperatively and which could impact safety in CyPass subjects included, but were not limited to: microhyphema (16%; n = 59); focal peripheral anterior synechiae (13%; n = 48); early hypotony, defined as IOP < 6 mmHg with the first 30 days postoperatively (9%; n = 35); partial obstruction of the CyPass lumen (5%; n = 31); AC shallowing

(6%; n = 21); and pigment dispersion (4%; n = 16). Other ocular observations reported at a rate < 2% include: chemosis (n = 9), CyPass intraluminal blood (n = 7), Schlemm’s intracanalicular blood (n = 6), pseudophacodonesis (n = 2), posterior synechiae (n = 2), pupillary miosis (n = 1), and transient forward IOL movement related to AC shallowing (n = 1).

Presented in Table 6 are incidence rates of ocular symptoms reported by patients in the CyPass and Control groups to be “severe” or “very severe” at various time points during the study. The questionnaire used to collect these data has not been validated, and therefore the true rates of these symptoms may differ from those presented in Table 6.

**TABLE 6: OCULAR SYMPTOMS CONSIDERED BY PATIENTS TO BE SEVERE OR VERY SEVERE  
AVAILABLE DATA FROM SAFETY POPULATION**

Symptom	Severity	Screening n (%)	Month 3 n (%)	Month 12 n (%)	Month 24 n (%)
<b>Cataract Surgery with CyPass (N = 374)</b>					
Blurred Vision	Severe	44 (11.8)	5 (1.4)	4 (1.1)	3 (0.8)
	Very Severe	7 (1.9)	1 (0.3)	2 (0.6)	
Glare	Severe	62 (16.6)	11 (3.1)	9 (2.6)	9 (2.5)
	Very Severe	13 (3.5)	1 (0.3)	1 (0.3)	1 (0.3)
Foreign Body Sensation	Severe	11 (2.9)	1 (0.3)	2 (0.6)	3 (0.8)
	Very Severe	5 (1.3)	1 (0.3)	2 (0.6)	
Pain in Eye	Severe	4 (1.1)	2 (0.6)	2 (0.6)	2 (0.6)
	Very Severe			1 (0.3)	
Halos	Severe	22 (5.9)	7 (1.9)	3 (0.9)	3 (0.8)
	Very Severe	6 (1.6)	1 (0.3)	1 (0.3)	
<b>Cataract Surgery Only (N = 131)</b>					
Blurred Vision	Severe	12 (9.2)	3 (2.4)	2 (1.6)	1 (0.8)
	Very Severe	4 (3.1)			1 (0.8)
Glare	Severe	21 (16.0)	4 (3.3)	3 (2.5)	5 (3.9)
	Very Severe	7 (5.3)		1 (0.8)	2 (1.6)
Foreign Body Sensation	Severe	2 (1.5)	2 (1.6)	2 (1.6)	1 (0.8)
	Very Severe				
Pain in Eye	Severe	1 (0.8)		2 (1.6)	1 (0.8)
	Very Severe	1 (0.8)			
Halos	Severe	12 (9.2)			1 (0.8)
	Very Severe	5 (3.8)		1 (0.8)	1 (0.8)

### **Corneal Endothelial Cell Density**

There was little difference in endothelial cell loss (ECL) between the CyPass and Control groups and results were consistent with the peer-review literature benchmarks of cataract-related ECL<sup>1,2</sup>. In the 24-month consistent cohort of subjects in the safety population (n = 322 CyPass subjects and 114 Control subjects), mean endothelial cell density (ECD) was 2107 cells/mm<sup>2</sup> (± 482) at 24 months in comparison with 2422 cells/mm<sup>2</sup> (± 409) at baseline in the CyPass group. Mean ECD was 2181 cells/mm<sup>2</sup> (± 441) at 24 months in comparison with 2427 cells/mm<sup>2</sup> (± 359) at baseline in the Control group. Mean ECD change at 24 months in the CyPass group was -13% (± 14). Mean ECD change at 24 months in the Control group was -10% (± 14). A similar proportion of subjects in each group (11% [95% CI: 7.2, 13.9] in the CyPass group and 9% [95% CI: 3.6, 14.0] in the Control group) experienced significant ECL (e.g., ECL > 30%) at 24 months postoperatively.

Study data collection methodology was a confounding factor in the determination of a relationship between CyPass positioning and ECL. The primary landmark used for determination of CyPass positioning was the number of CyPass retention rings visible; however, these data were not reported for every subject, nor were they reported consistently within the course of a given subject's study participation.

Endothelial cell loss > 30% was noted in 9.6% (16/166) of subjects for whom 1 CyPass retention ring was reported visible at 2 or more postoperative examinations and there were no reports of 2 or more rings visible at any examination for these subjects. In the group of subjects for whom 2 CyPass rings were visible at 2 or more postoperative examinations, ECL > 30% was noted in 9.8% (4/41) of subjects.

### **Additional Safety Data Gathered after Study Exit**

Post-study exit, the following CyPass-related secondary ocular surgeries have been reported, which are not included in Table 5:

- One subject underwent planned surgical occlusion of the CyPass lumen with Prolene suture for IOP control approximately 28 months post-CyPass implantation.
- Another subject underwent secondary surgery for CyPass proximal end trimming due to anterior device positioning associated with significant endothelial cell loss approximately 32 months post-CyPass implantation. Anterior device positioning was reported within the first postoperative week.
- One subject underwent secondary surgery for CyPass proximal end trimming due to anterior device positioning associated with significant endothelial cell loss approximately 48 months post-CyPass implantation. Anterior device positioning was reported within the first postoperative week.

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<sup>1</sup> Reuschel, A., *et al.*, Comparison of endothelial changes and power settings between torsional and longitudinal phacoemulsification. *J Cataract Refract Surg*, 2010. 36(11): p. 1855-61.

<sup>2</sup> Buys, Y.M., *et al.*, Prospective randomized comparison of one- versus two-site Phacotrabeculectomy two-year results. *Ophthalmology*, 2008. 115(7): p. 1130-1133 e1.

**Medication Usage**

Of subjects who were responders (e.g., 24-month unmedicated mean DIOP was reduced by  $\geq 20\%$  as compared with baseline in the absence of IOP-affecting surgery during the study), 96.5% of subjects in the CyPass group (251/271) and 72.4% of subjects in the Control group (55/74) were not using ocular hypotensive medication at 24 months.

**O. PHYSICIAN TRAINING**

Physician training by certified Alcon personnel is required prior to use of this device. Training consists of three main parts:

- Didactic session
- Simulated implantation of CyPass Micro-Stent
- Supervised CyPass Micro-Stent implantation clinical cases until implantation proficiency is demonstrated.

**P. MANUFACTURER**

Alcon Laboratories, Inc.,  
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CyPass® System

SYMBOLS	ENGLISH
	Caution, consult accompanying documents
	Consult instructions for use
	Catalog number
	Batch code
	Serial Number
	Quantity
	Date of manufacture (YYYY-MM-DD: Year-Month-Day)
	Manufacturer
	Use by last day of (YYYY-MM-DD: Year-Month-Day)
	Sterilized using radiation
	Do not reuse
	Do not resterilize
	Do not use if package is crushed or damaged
	Caution: Federal law restricts this device to sale by or on the order of a physician
	Store at room temperature (68° to 75° F [22± 2°C])
	Keep dry
	MR Safe. The CyPass Micro-Stent poses no known hazards in all magnetic resonance imaging environments



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