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Long Term Efficacy of a Supraciliary Micro-stent Combined with Cataract Surgery in the Treatment of Glaucoma

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Long Term Efficacy of a Supraciliary Micro-Stent Combined with Cataract Surgery in the Treatment of Glaucoma

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Table of Contents:

Abstract:

Long Term Efficacy of a Supraciliary Micro-Stent Combined with Cataract Surgery in the Treatment of Glaucoma

Purpose: The purpose of this study is to evaluate the long-term efficacy of supraciliary micro-stent implantation in combination with phacoemulsification in the treatment of mild-moderate primary open angle glaucoma (POAG).

Methods: Retrospective data of patients previously enrolled in the "Study of an Implantable Device for Lowering Intraocular Pressure in Glaucoma Patients Undergoing Cataract Surgery" (COMPASS trial), in which patients with mild-moderate POAG had undergone either cataract surgery alone or cataract surgery combined with implantation of a supraciliary micro-stent, were collected. Eligible patients had since exited the trial and had 5-8 years of postoperative data available. The primary outcome measure was the proportion of eyes with a "complete success" defined as an IOP ≤ 18 mmHg on no glaucoma medications and not having undergone any secondary surgical procedures for IOP control. Thirty-three eyes were in the treatment group and 12 eyes were in the control group. Device safety was also reviewed.

Results: Significantly more eyes in the treatment group achieved a "complete success" (61%) versus those eyes in the control group (17%) ($p<0.05$). When controlling for patient age, sex, preoperative visual field, preoperative IOP, and preoperative anti-glaucoma medication usage, eyes in the treatment groups were 9 times more likely to meet the primary outcome measure versus control group ($p=0.004$). Mean postoperative IOP was 17.7 ± 4.8 in the control group versus 15.0 ± 4.4 in the treatment group ($p=0.08$), while mean medication usage was 0.9 ± 0.7 in the control group versus 0.4 ± 0.7 in the treatment group ($p=0.01$). Average follow up was 6.38 years. No device related adverse events, such as corneal decompensation occurred.

Conclusion: Implantation of a supraciliary micro-stent combined with cataract surgery in eyes with mild-moderate POAG demonstrates better long term IOP control than those eyes undergoing cataract surgery alone.

Introduction:

Glaucoma is a chronic and progressive optic neuropathy that remains the second leading cause of blindness in the world.[1] It is estimated that nearly 3% of all individuals aged 40-80 years old have primary open angle glaucoma (POAG).[2] Currently the only method of treatment is lowering intraocular pressure (IOP) to reduce ganglion cell damage, and thus prevent vision loss. Topical hypotensive medications are the first line of treatment and have been shown to delay progression of optic nerve damage.[3] Despite the availability of multiple drug options, IOP control can still be challenging. Compliance with medication is poor,[4] and may create ocular surface disease and tolerability issues.[5] Laser trabeculoplasty has proven to be both a good first line and adjunctive treatment in the management of glaucoma.[6] While considered a safe option, it's effect may not persist over time and further IOP lowering may be required.[6] Traditional incisional surgical options such as trabeculectomy (gold standard) and tube shunt devices have excellent IOP lowering capability, but are associated with significant ocular morbidity and high failure rates.[7] This has limited their use to those patients with more advanced disease in which other methods have failed.[8] Over the last decade there has been a push toward less invasive glaucoma surgical techniques that cause as little trauma as possible to the target tissue involved.[9] Reproducible techniques that are not only efficacious, but also effectively lowering IOP and the medication burden are of interest to not only glaucoma specialists, but to all practitioners who manage glaucoma. Micro-invasive glaucoma surgery (MIGS) is an attractive option as it provides a safer and less invasive method for IOP lowering while enhancing patient comfort and recovery time.[10] Current MIGS devices and procedures increase aqueous outflow in one of three ways; bypassing the trabecular meshwork, i.e. iStent (Glaukos, San Clemente, California), increasing uveoscleral outflow via the suprachoroidal space, i.e. CyPass Micro-Stent (Alcon Laboratories, Inc., Fort Worth, Texas), or creating a subconjunctival conduit, i.e. XEN45 gel stent (Allergan PLC, Irvine, California). [11] These MIGS procedures may represent a suitable option to fill the therapeutic gap between drug therapy and traditional incisional glaucoma surgeries.

The CyPass Micro-Stent is implanted in the supraciliary space and provides a

permanent channel through which aqueous can exit the anterior chamber through the suprachoroidal space thus increasing non-trabecular flow.[12] It is a fenestrated 6.35 mm long stent made of polyimide, and has an inner lumen of 300 microns. Using a specialized guidewire, it is inserted ab interno underneath the scleral spur and into the supraciliary space where it is secured in place by a series of retention rings. Once stabilized in the iridocorneal angle, aqueous may flow through the stent and into the suprachoroidal space (Figures 1 and 2).[8,13] Approved by the FDA in August 2016, it is indicated for the treatment of mild to moderate primary open angle glaucoma in patients undergoing concurrent cataract surgery.

The suprachoroidal space represents an interesting and attractive pathway for new glaucoma surgical procedures as it has the ability to lower IOP below that of episcleral venous pressure without the formation of a subconjunctival bleb.[14] Under normal physiologic conditions, the aqueous humor exits the anterior chamber by flowing between the ciliary muscle bundle fibers and into the suprachoroidal space.[15] Once in this space, it may flow through the scleral connective tissue and into the lymphatic system.[14] This may best be described as non-trabecular flow. It has been shown that a negative pressure gradient between the anterior chamber and the suprachoroidal space drives this flow.[16] The ciliary muscle represents the greatest resistance to aqueous in this pathway, thus bypassing it may effectively lower IOP.[14] Relaxation of the ciliary muscle with atropine increases uveoscleral outflow while contraction with pilocarpine reduces it.[17] Intuitively this pathway may be seen as a good target for MIGS devices as prostaglandin analogues exploit this same route to some degree, but rather than bypassing the ciliary body entirely, they exhibit their effect by reducing extracellular matrix components within the ciliary muscle so aqueous may pass more easily.[18] Cyclodialysis clefts, whether iatrogenic or traumatic, have also been shown to lower IOP, sometimes to very low levels with resulting posterior pole changes.[19] When the CyPass Micro-Stent is secured in the supraciliary space, it essentially functions as a permanent and controlled cyclodialysis cleft, allowing aqueous to bypass the ciliary body.

The purpose of this study is to determine if the CyPass Micro-Stent is a safe and effective long-term solution in the treatment of glaucoma. Traditional surgical glaucoma therapies i.e., trabeculectomy and shunt devices have failure rates of approximately 47%

and 30% respectively after five years, along with a high risk of complications including blindness.[7,20] A better long-term solution is needed without sacrificing patient safety. To our knowledge, this will represent the largest group of patients maintaining this length of follow up (5-8 years) per our search of the PubMed database. Additionally, all patients in this study will have been previously enrolled in the COMPASS trial, meaning that we have true unmedicated IOP data. Long-term, effective solutions are needed for the treatment of glaucoma, and long-term follow up is lacking concerning suprachoroidal MIGS devices.

Methods:

Study Design:

Design: Retrospective case control

Treatment Group: Patients with mild to moderate POAG implanted with the CyPass Micro-Stent in conjunction with cataract surgery

Control Group: Patients with mild to moderate POAG that underwent cataract surgery alone

Follow up Period: Approximately 5-8 years (1794-3131 days)

Number of Subjects Planned/Analyzed:

-33 eyes of 33 patients in treatment group

-12 eyes of 12 patients in control group

Primary Outcome Measure:

Complete success is defined as an IOP ≤ 18 mmHg without a need for postoperative medication and/or any secondary procedure needed to control IOP.

Qualified success is defined as an IOP ≤ 18 mmHg with no more than 1 postoperative medication and/or laser trabeculoplasty to control IOP

Failure defined as an IOP > 18 mmHg, more than 1 medication needed to control IOP, or incisional surgery needed to control IOP

Secondary Outcome Measures:

Change in mean anti-glaucoma medications between groups
Change in mean IOP between groups
Change in visual field mean deviation scores between groups

Safety data collected in the form of loss of best-corrected visual acuity (BCVA), IOP changes, slit lamp and fundus abnormalities, and adverse events.

Study Subjects:

The study protocol was approved by the NOVA Southeastern University institutional review board and conformed to both the Declaration of Helsinki tenets and the Health Insurance Portability and Accountability Act regulations.

All patients included in analysis were part of the COMPASS FDA approved clinical trial and had since exited the study. Data concerning 33 eyes of 33 patients in the treatment arm (CyPass combined with phacoemulsification) and 12 eyes of 12 patients in the control arm (Phacoemulsification alone) were reviewed by research coordinators and investigators for study inclusion. Below are subject inclusion/exclusion criteria as worded from the COMPASS trial.

Subject Inclusion Criteria (COMPASS Trial)

Individuals will be assessed for study eligibility based on the criteria presented below. Ocular criteria relates to the study eye only.

1. Individuals 45 years of age or older, male or female.
2. A diagnosis of primary open angle glaucoma (POAG).
3. At the Screening Visit, a mean (or median) **medicated** IOP of ≤ 25 mmHg or an **unmedicated** IOP of ≥ 21 mmHg and ≤ 33 mmHg.
4. At the Baseline Visit, a mean **unmedicated** IOP of ≥ 21mmHg and ≤33 mmHg. The mean will be derived from the diurnal IOP reading taken over the course of the Baseline Visit day. **Additionally, the baseline mean unmedicated diurnal IOP must be ≥ 3 mmHg higher than the mediated IOP measured in the Screening Visit.**
5. Diagnosis of glaucoma within 90 days prior to the Screening Visit substantiated using the ophthalmoscopy and visual field testing with the Humphrey automated perimeter using the SITA Standard 24-2 testing algorithm. Mean deviation score must be ≥-12.0 dB and < 0 dB.

a. For subjects without a previously document history of glaucoma, Humphrey 24-2 SITA Standard visual field testing confirming diagnosis of glaucoma must be performed at least twice by the time of the Baseline Visit.
b. For subjects who have utilized ocular hypotensive medications for ≥ 3 months prior to the Screening Visit but who have visual field mean deviation scores ≥ 0 dB, nerve findings characteristic of glaucoma must be documented. Any of the following optic disc and nerve fiber layer findings are considered characteristic of glaucoma:
    i. Cupping with increased vertical cup-to-disc ratio
    ii. Nerve fiber layer loss consistent with glaucoma
    iii. Segmental loss of neuroretinal rim (notching of the rim)
    iv. Presence of a splinter disc hemorrhage

Optical scanning lasers may be used to document and support the presence of glaucomatous optic nerve changes, but may not be considered as a substitute for ophthalmoscopy for the purpose of establishing glaucoma diagnosis. Acceptable optical scanning laser diagnostics include:

- **Heidelberg Retina Tomography (HRT)**: abnormal nerve fiber layer (NFL) findings indicated by a yellow exclamation mark and/or a red x.
- **Zeiss/Humphrey Glaucoma Diagnostic Unit (GDx)**: abnormal NFL findings with a Nerve Fiber Index (NFI) reading of > 31 and/or < 5% p-value indicator for NFL.
- **Optical Coherency Testing (OCT):** abnormal NFL findings in the red or yellow areas, below the area of normal on the Analysis of Thickness.

6. Gonioscopy confirming normal angle anatomy at the site of implantation.
7. Shaffer grade of ≥ III in all four quadrants.
8. An operable age-related cataract with BCVA of 20/40 or worse, eligible for phacoemulsification. (If the BCVA is better than 20/40, testing with a Brightness Acuity Meter (BAT) on a medium setting must result in a BCVA of 20/40 or worse.)

Subject Exclusion Criteria (COMPASS Trial)

Excluded from the study will be individuals with the following characteristics. Unless specified otherwise, all ocular criteria refer to the study eye only.

1. Inability to complete a reliable 24-2 SITA Standard Humphrey visual field on the study eye at screening (fixation losses, false positive errors and false negative errors should not be greater than 30%).
2. Use of more than 3 ocular hypotensive medications. (Combination medications count as 2 medications.)
3. Use of oral hypotensive medication treatment for glaucoma in the fellow eye.
4. Significant risk by a washout of medication including those subjects with advanced glaucoma evidenced by an afferent pupillary defect, a C: D ratio ≥ 0.9 or encroachment of field loss within the central 5 degrees as indicated by ≥ 2 depressed points of 0.5% probability on the 24-2 SITA Standard Humphrey visual field.
5. Previous glaucoma procedure with or without an implantable glaucoma device (with exception of laser treatments to the trabecular meshwork such as a Laser Trabeculoplasty performed more than three months prior to study enrollment.)
6. History of elevated intraocular pressure due to steroid response.
7. Proliferative diabetic retinopathy.
8. Previous surgery for retinal detachment.
9. Central corneal thickness > 620 microns.
10. Clinically significant corneal dystrophy.
11. Previous corneal surgery.
12. Wet age-related macular degeneration.
13. Clinically significant ocular pathology, other than cataract and glaucoma.
14. Diagnosis of acute angle closure, traumatic, congenital, malignant, uveitic, pseudoexfoliative, pigmentary or neovascular glaucoma.
15. Best corrected visual acuity worse than 20/80 in the fellow eye.

16. Clinically significant ocular inflammation or infection within thirty days prior to screening.
17. Uncontrolled systemic disease that in the opinion of the Investigator would put the subject's health at risk and/or prevent the subject from completing all study visits.
18. Pregnant or nursing females.

Subject Inclusion Criteria (Current Study)

1. Both male and female subjects with no preference given to either gender.
2. Must have been previously enrolled in COMPASS trial and returned to general clinic.

Subject Exclusion Criteria (Current Study)

1. History of corneal refractive surgery since exiting COMPASS trial, i.e. LASIK
2. Wet-Age macular degeneration requiring Anti-VEGF injections
3. Pregnant or nursing females
4. Other surgical intervention not for the purpose of IOP control that may have long term impact on IOP, i.e. retinal detachment repair
5. Development of secondary type glaucoma, i.e. neovascular glaucoma

Surgical Technique

Using a clear corneal temporal approach, a paracentesis site was made and the anterior chamber filled with viscoelastic. A 2.4 mm incision was made using a keratome. Following phacoemulsification and removal of the lens, a posterior chamber IOL was placed into the capsular bag. Following successful cataract surgery, the microstent was loaded onto the guidewire of the applier (Figure 3). Under direct gonioscopy, the microstent was implanted through blunt dissection between the plane of the ciliary body and sclera using the guidewire tip. Once secured in place, the applier was withdrawn from the eye and viscoelastic evacuated.[13]

Statistical Methods:

Statistical analysis performed with support of,
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Descriptive statistics were calculated for all study variables. This included the mean and standard deviation for continuous measures, counts and frequencies for categorical measures. R 3.2.2 was used for all statistical analysis and statistical significance was found at $p < 0.05$. For the primary outcome measure, a bivariate analysis using a Fisher's exact test was first conducted to investigate group differences in the proportion of patients with "complete success" defined as an IOP ≤ 18 mmHg without need for postoperative medication, laser trabeculoplasty, or incisional surgery, "qualified success" defined as an IOP ≤ 18 mmHg with no more than 1 postoperative medication and/or laser trabeculoplasty needed to control IOP, and "failures" defined as individuals with IOP >18 mmHg and/or individuals with more than 1 postoperative medication, and/or individuals who subsequently underwent a secondary incisional ocular procedure to control IOP. We then dichotomized the dependent variable into two measures: Success vs. Other (Qualified or Failure) and created a logistic regression model containing group (CyPass vs. Other), age, gender, preoperative visual field mean deviation, preoperative washout IOP, and preoperative anti-glaucoma medication usage. For continuous measures we first conducted bivariate analyses across the following measures to see if we had comparable groups: Age, preoperative visual field mean deviation, postoperative visual field mean deviation, preoperative IOP, preoperative washout IOP, postoperative IOP, preoperative anti-glaucoma medications, postoperative anti-glaucoma medications, and follow up period since surgery. For this analysis we used a Wilcoxon-Mann-Whitney test. We then created difference scores for the variables visual field, intraocular pressure and medication use and compared group differences using a Wilcoxon-Mann-Whitney test. Lastly, we created linear models to look for changes in visual field, intraocular

pressure and medication use. The dependent variable in all models was the change measure, and the independent variables were treatment group (CyPass vs. Other), age and gender. As medication use was a count variable we used a negative binomial distribution to analyze this change. Patients undergoing secondary incisional ocular procedures to control IOP were treated as non-responders. For these patients mean diurnal washout IOP at baseline was imputed as the mean postoperative IOP. The same method was used for medications, with the baseline preoperative medication use imputed for postoperative medication usage. Please refer to Table 1 for patient baseline, preoperative, and postoperative data.

Results:

Twenty eyes in the CyPass group were categorized as complete success versus 2 eyes in the control group. Nine patients were classified as qualified success in the microstent group based on the following; 5 for medication usage, 2 for laser trabeculoplasty, and 2 requiring both modalities. Five patients were classified as qualified success in the control group based on the following; 4 for medication usage and 1 for laser trabeculoplasty. Four patients were classified as "failures" in the microstent group based on the following: 1 for medication usage, 1 for IOP, 1 for both IOP and medication usage, and 1 for IOP and secondary incisional surgery. Five patients were classified as "failures" in the control group based on the following: 1 for medication usage, 1 for IOP, and 3 for secondary incisional surgery. Summarized data may be found in Table 3. Results from the bivariate Fisher's Exact test indicate that significantly more subjects in the CyPass group (61%) experienced complete success than the control group (17%) ($p < 0.05$) (Table 2). Results of the binary logistic regression model indicate that there was a significant difference between the CyPass and control groups when controlling for preoperative baseline parameters ($\chi 2(6) = 19.045$, $p = 0.004$). The odds ratio for the group coefficient is 9.02 with a 95% confidence interval of [1.69,75.78]. This suggests that controlling for the effects of age, sex, preoperative visual fields, preoperative IOP, and preoperative anti-glaucoma medication usage, individuals in the control group are 9 times more likely to have a failed surgery than those in the CyPass group. Mean postoperative IOP was 17.7±4.8 in the control group versus 15.0±4.4 in the treatment group (p=0.08), while mean medication usage was 0.9±0.7 in the control group versus 0.4±0.7 in the treatment group (p=0.01). Figures 5 and 6 show pre and postoperative medication usage and IOP respectively. Average follow up was 2298±433 days for the treatment group, and 2419.3±469 for the control group (p=0.43).

Discussion:

The COMPASS trial was the pivotal FDA clinical trial that endorsed the approval of the CyPass in the United States.[13] It was a 2-year randomized trial with over 500 patients involved, and represented the largest interventional MIGS trial to date. Three hundred seventy-four patients received the CyPass device. The study compared the efficacy and safety of patients with POAG undergoing CyPass implantation in conjunction with cataract surgery versus those undergoing cataract surgery alone. Our center enrolled 88 patients in the trial, 64 in the treatment group and 24 in the control group (Figure 4, Site 05). The 45 patients in the current trial represent a long-term follow up subgroup that had exited the study and returned to general clinic. Our findings demonstrate that the CyPass Micro-Stent has good long-term effectiveness in the treatment of mild-moderate POAG when combined with cataract surgery. A significantly higher percentage of eyes in the CyPass group (61%) versus control (17%) maintained an IOP of ≤ 18 mmHg without the need for medical therapy, laser trabeculoplasty, or incisional surgical intervention ($p < 0.05$) (Table 2). No patient had an IOP of lower than 6, and there were no incidences of hypotony maculopathy or corneal decompensation. By comparison, the COMPASS trial demonstrated 65% of all microstented subjects maintaining washout IOP of between 6 and 18 mmHg inclusive at 24 months in per-protocol (PP) analysis vs. 44% in control group.[13] In intention-to-treat (ITT) analysis the 24-month proportion of COMPASS patients achieving an IOP level of 6 to 18 mmHg were 61% in microstented subjects vs. 44 % in control group ($P<0.001$).[13] The results of the current study are nearly equivalent to that of microstented subjects in COMPASS, and demonstrate that patients continued to maintain a good level of IOP control after a 24-month period with significantly longer follow up in the current study, compared with control patients having poorer IOP control, more medication usage, and incisional surgical intervention over the same time period of time. Patients in the current study also required less ocular hypotensive medications than control, 0.4 ± 0.7 vs. 0.9 ± 0.7 respectively (p=0.01) (Figure 5). Comparatively microstented patients in COMPASS required 0.2 ± 0.6 medications vs. 0.6 ± 0.8 in control group.[13] Although not statistically significant, there was a clear trend when comparing IOP reduction at medicated baseline vs. last follow up in the current study, with the microstent group obtaining a reduction of 17.7 ± 3.3 to 15.0 ± 4.4 (15% reduction) vs. 18.6 ± 4.4 to 17.7 ± 4.8 in control group (5% reduction) (p=0.08) (Figure 6). When evaluating the subset of patients that were classified as “complete

success" in the CyPass group (20 of 33 eyes), and comparing washout IOP at baseline to postoperative IOP, patients had a reduction in IOP from a mean of 23.75 ± 1.75 mmHg to 14.30 ± 2.89 (40% reduction) ($p<0.001$) at an average follow up of 6.27 years. Preoperatively this group went from 1.35 ± 0.93 medications to zero at follow up.

One of 33 (3%) eyes underwent secondary incisional surgical intervention (trabecular outflow procedure) in the CyPass group versus 3 of 12 eyes (25%) in the control group, with 2 eyes undergoing a trabecular outflow type procedure and 1 eye requiring a trabeculectomy. There was no progression in visual fields in either group ($p=0.93$). This finding is somewhat surprising given that patients in the control group had a trend toward higher IOP levels, however the control group still maintained a mean IOP of under 18 mmHg (17.7 ± 4.8), albeit at the expense of higher medication usage and more surgical intervention needed to achieve this goal. It is possible that changes in visual field loss between groups would manifest over a longer follow up period. Furthermore, there is often a discrepancy between functional and structural changes in glaucoma, and many patients may show progressive structural changes in the absence of changes on automated visual field testing[21]. As long-term nerve fiber layer data was not collected, we are unable to be certain if there were changes in this parameter.

The CyPass Microstent compares favorably to other MIGS procedures/devices, however caution must be exercised when comparing trial results secondary to different methodologies used as well as different inclusion/exclusion criteria. The iStent trabecular micro-bypass device is implanted through the trabecular meshwork to target Schlemm's canal and enhance trabecular outflow.[22] At the 24-month time point 61% of patients in the stent group achieved an unmedicated IOP of ≤ 21 mmHg, compared with 61% in the current trial meeting the more stringent criterion of ≤ 18 mmHg.[23] Furthermore, the difference in the anti-glaucoma medication usage between the stent group and control group had dissipated by the 24 month mark, while it remained clinically significant in the current trial at a mean of over 6 years. The HORIZON trial was a randomized clinical trial comparing another trabecular device, the Hydrus Microstent, (Ivantis Inc, Irvine, CA), in combination with phacoemulsification. At 24 months the microstent group demonstrated a 7.6 reduction in mean IOP versus baseline versus 9.5 mmHg at over 5 years in the current trial when considering unmedicated patients, demonstrating approximately a 2-point benefit in IOP reduction for the CyPass Micro-Stent. Although the XEN gel stent may be considered a MIGS procedure, it is

indicated for more severe refractory glaucoma in which prior surgery or medications have failed, rather than mild-moderate glaucoma.[24] Made of a porcine gelatin material, it is implanted ab interno and creates a conduit from the anterior chamber into the subconjunctival space to allow for aqueous outflow.[24] Studies of the current Xen model have demonstrated an IOP lowering effect from 29% to 45% with anywhere from 39% to 90% of patients medication free postoperatively.[25] This is in line with the current study in which there was a 39% drop in IOP along with 61% of patients being medication free postoperatively. Additionally, there is no chance of conjunctival fibrosis following implantation of the CyPass Micro-Stent as there is with the Xen implant, leaving room for future filtering surgery if needed.

Glaucoma surgery must not only be efficacious but demonstrate adequate safety over a period of time. This is especially true for MIGS procedures, as they are utilized earlier in the disease process. One of many safety parameters measured during FDA clinical trials involving MIGS procedures is endothelial cell loss (ECL). At the time of this writing (early September 2018), Alcon globally withdrew the CyPass Micro-Stent based on concerns of progressive ECL shown in the COMPASS-XT trial. Performed at the request of the FDA, the COMPASS-XT trial was a 3-year extension of the 2-year COMPASS trial and included 282 of the 505 patients enrolled in the COMPASS trial, with 253 patients completing the 60-month visit. At the end of the 24-month COMPASS trial, the treatment and control group demonstrated similar mean and percentage of eyes with > 30% ECL. However, by the 60-month follow up visit, the CyPass group had shown a significantly higher mean and percentage of eyes with ECL (Figures 7 and 8, data available at (www.alcon.com/cypass). The only variable found to be correlated with progressive ECL was device positioning (Figure 9). Based on this data, it seems as though the ideal position of the device is with no retention rings visible, with the anterior position of the device at or below the trabecular meshwork. When positioned in this manner, an ECL of 1.39% per year occurred, which is more in line with what is expected for patients with glaucoma, although this is still higher than control group loss of 0.36% per year.[26] During the clinical trial, surgeons were instructed to implant the device with an optimal position of 1 ring visible, which is reflected in FDA "directions for use" (DFU). Only 1 patient developed mild corneal edema at 51 months during COMPASS-XT, and this was successfully resolved with device trimming a subsequent resolution of edema. The CyPass Micro-Stent compares favorably with ECL after traditional glaucoma surgery, with tube shunts demonstrating up to

24.6% reduction in mean ECL at 4 years, and trabeculectomy up to 28% at 1 year.[27,28] Compared with other MIGS procedures, the CyPass has shown greater ECL although the follow period in other trials has not been as long. In example, the Hydrus Microstent exhibited 14% mean ECL at 2 years versus 18.4 % for CyPass at 5 years. Our group is currently working on a trial to reexamine all original COMPASS patients from our site and revaluate stent positioning and ECL.

A major strength of this study is the significant length of follow up. To our knowledge it represents the longest follow up data available on the CyPass Micro-Stent and of all MIGS procedures in general. Furthermore, this subset of patients was part of the COMPASS study meaning we have valuable baseline data from a randomized clinical trial. This data clearly demonstrates the sustained efficacy of the CyPass Micro-Stent in terms of IOP lowering capability. There are several weaknesses to this study. This was a retrospective chart review and not a randomized controlled clinical trial. Medication reintroduction was not strictly controlled once patients were returned to general clinic, and there was no postoperative washout IOP in all patients, making it difficult to compare our results with other trials that have this parameter. The IOP used for analysis at follow up only represents one time point, and there was likely some IOP fluctuation post surgically. This limits our ability to determine IOP change over time to some degree. Some patients underwent secondary surgical procedures for IOP control, which confounds our true ability to determine true postoperative IOP and medication usage in that subset of patients. All patients underwent concurrent cataract surgery, which has also been shown to affect IOP with a significant lowering effect.[29,30] Despite these drawbacks, this study provides quality long-term data for this MIGS device.

Conclusion

In conclusion, the CyPass Micro-Stent combined with cataract surgery demonstrates good long-term efficacy over cataract surgery alone in patients with mild-moderate POAG. Further study is needed to determine the long-term safety of the procedure.

Tables and Figures:

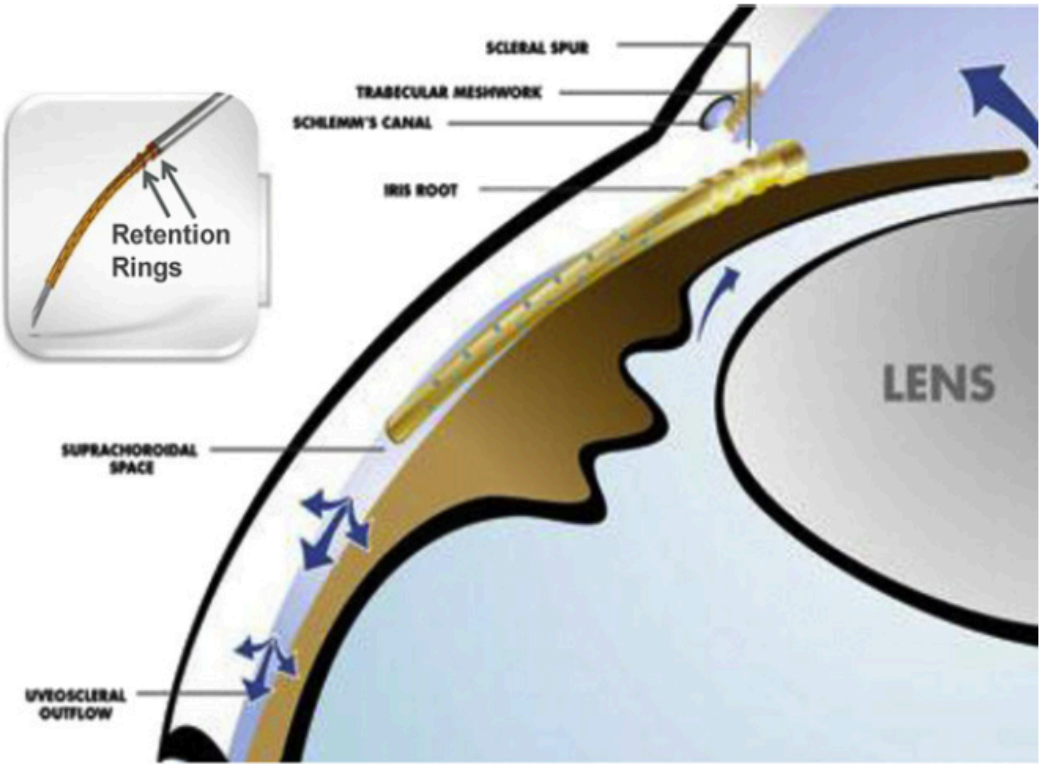


Figure 1: CyPass within supraciliary space, increasing non-trabecular flow (Hoeh, H)

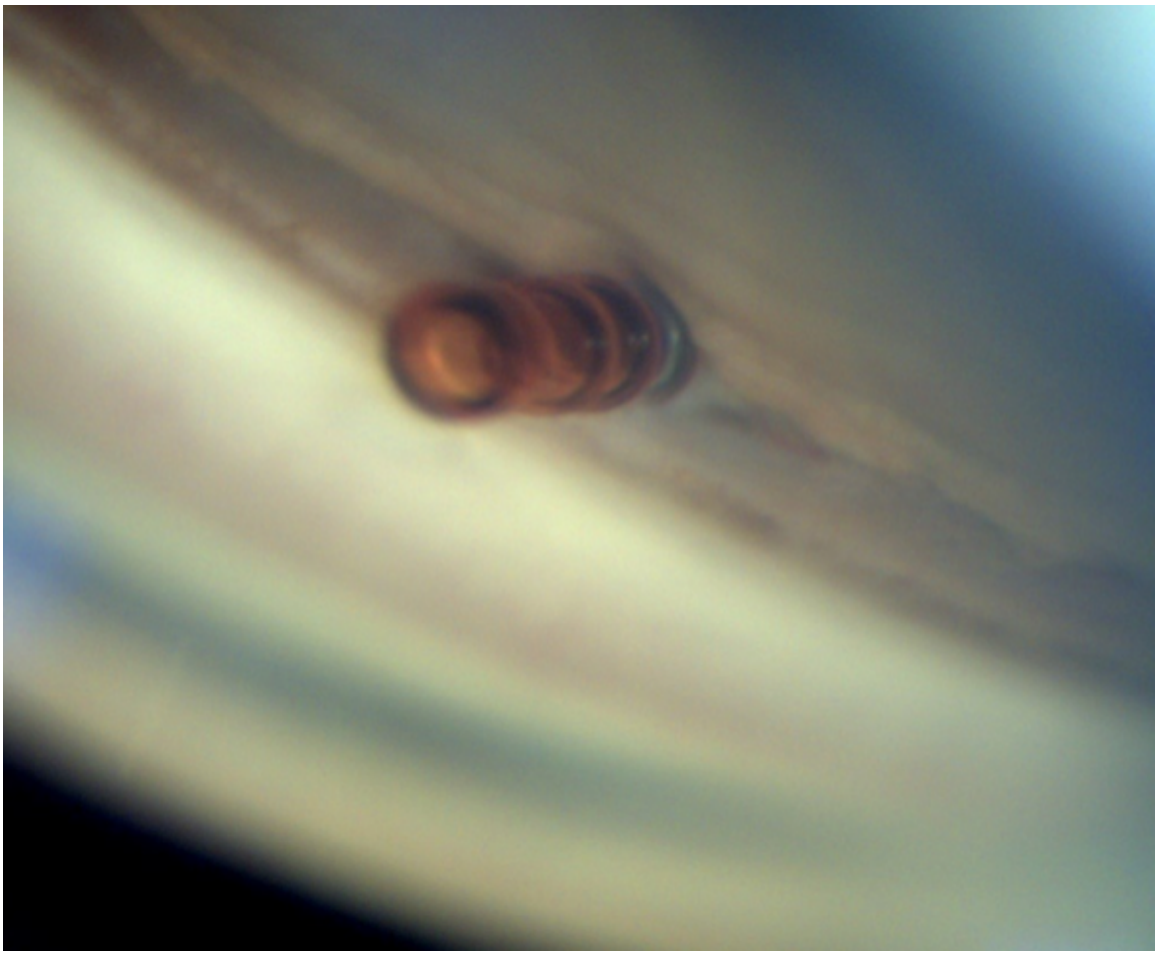


Figure 2: CyPass Micro-Stent in situ. (Photo by Mike McFarland, OD)

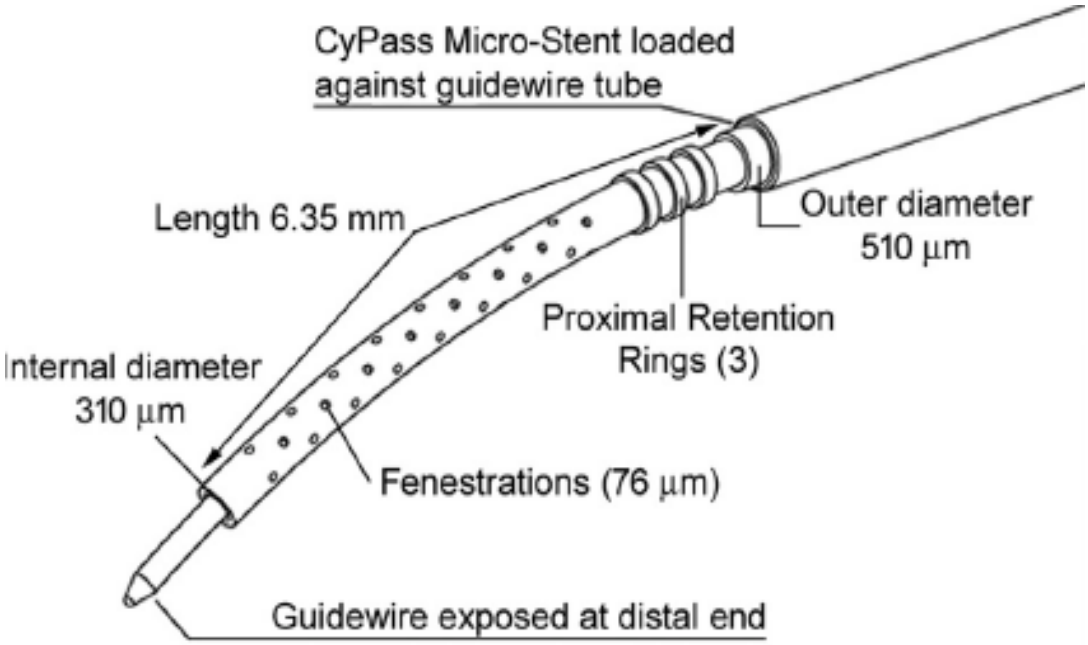


Figure 3: CyPass Micro-Stent on guidewire with visible fenestrations. Blunt guidewire at distal end facilitates dissection of plane between ciliary body and sclera (Vold, SD)

RANDOMIZATION BY INVESTIGATIONAL SITE
ITT POPULATION

Site	Randomized Group		Total
	Cataract Surgery with CyPass n (%)	Cataract Surgery Only n (%)	
Site 01	25 (5.0%)	10 (20%)	35 (6.9%)
Site 02	18 (3.6%)	8 (1.6%)	26 (5.1%)
Site 03	9 (1.8%)	3 (0.6%)	12 (2.4%)
Site 04	21 (4.2%)	8 (1.6%)	29 (5.7%)
Site 05	64 (12.7%)	24 (4.8%)	88 (17.4%)
Site 14	16 (3.2%)	5 (1.0%)	21 (4.2%)
Site 30	16 (3.2%)	5 (1.0%)	21 (4.2%)
Site 31	13 (2.6%)	5 (1.0%)	18 (3,6%)
Site 32	14 (2.8%)	5 (1.0%)	19 (3.8%)
Site 33	22 (4.4%)	7 (1.4%)	29 (5.7%)
Site 35	11 (2.2%)	3 (0.6.%)	14 (2.8%)
Site 36	23 (4.6%)	6 (1.2%)	29 (5.7%)
Site 37	12 (2.4%)	4 (0.8%)	16 (3.2%)
Site 38	3 (0.6%)	1 (0.2%)	4 (0.8%)
Site 39	20 (4.0%)	6 (1.2%)	26 (5.1%)
Site 40	14 (2.8%)	4 (1.8%)	18 (3.6%)
Site 42	11 (2.2%)	5 (1.0%)	16 (3.2%)
Site 43	10 (2.0%)	4 (0.8%)	14 (2.8%)
Site 44	4 (0.8%)	1 (0.2%)	5 (1.0%)
Site 45	5 (1.0%)	1 (0.2%)	6 (1.2%)
Site 46	26 (5.1%)	10 (2.0%)	36 (7.1%)
Site 47	6 (1.2%)	2 (0.4%)	8 (1.6%)
Site 50	5 (1.0%)	2 (0.4%)	7 (1.4%)
Site 51	6 (1.2%)	2 (0.4%)	8 (1.6%)
All sites	374 (74.1%)	131 (25.9%)	505 (100.0%)

% = n ¸ (Total Randomized) ´ 100%.

Figure 4: COMPASS enrollment by site. Current study subjects a long-term subgroup of site 05

Figure 5. Medication usage by treatment group

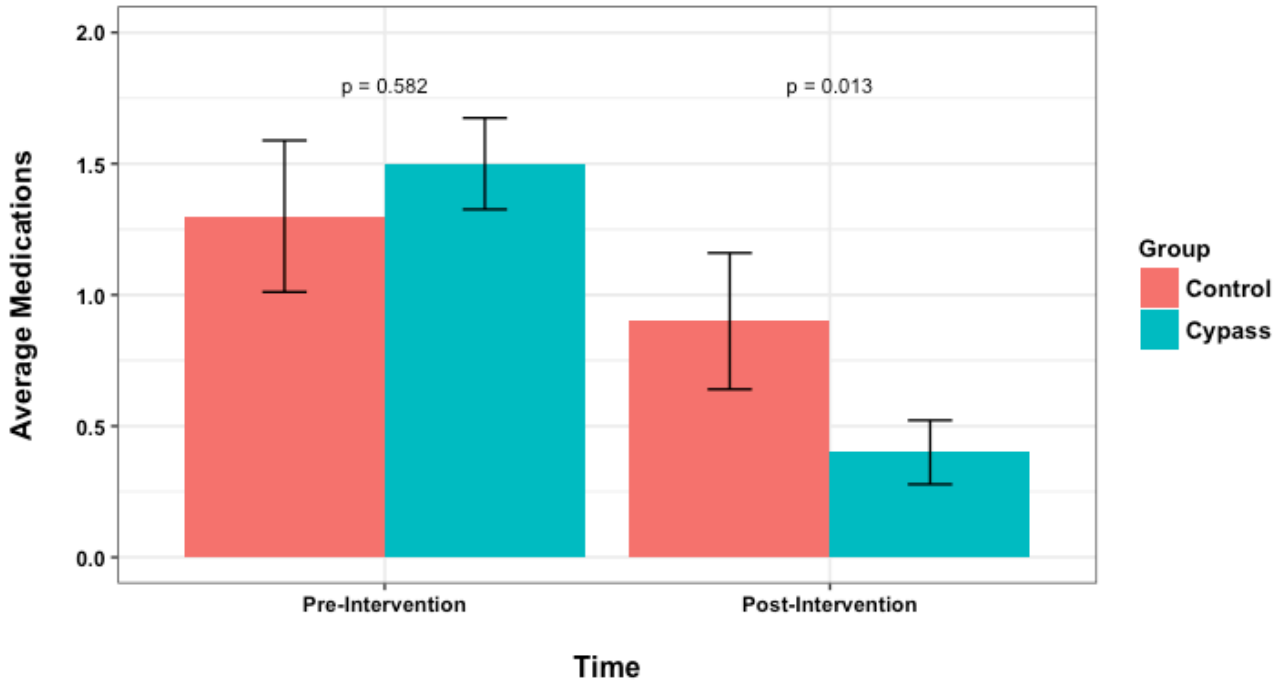
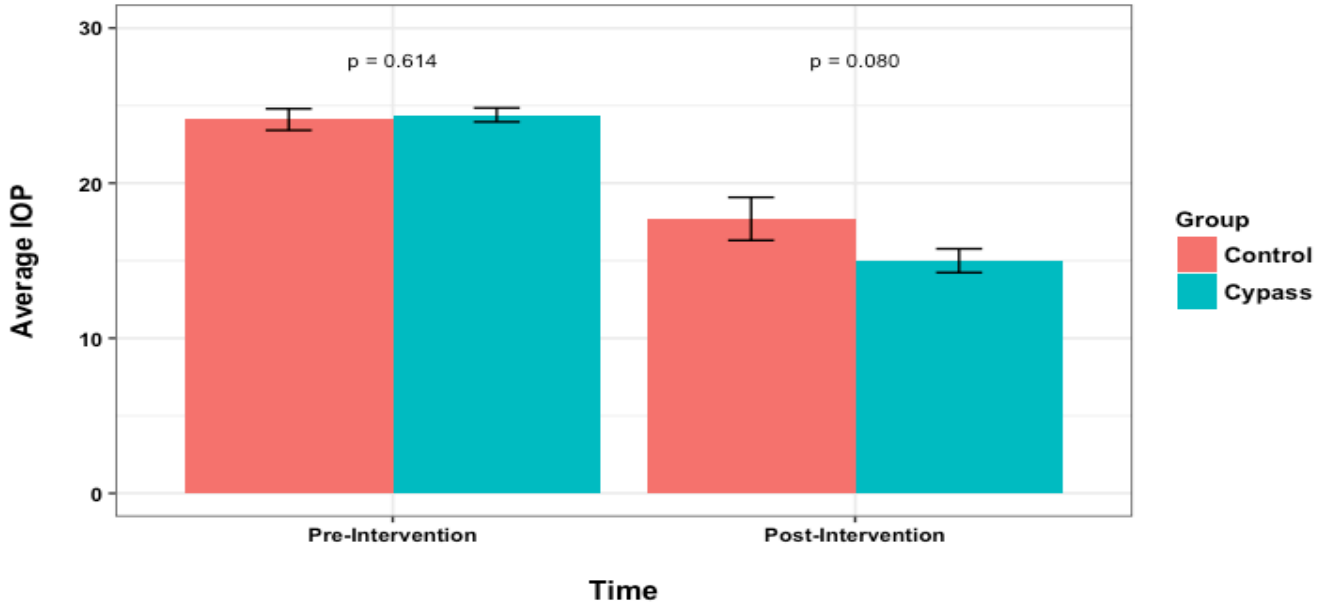


Figure 6. IOP by treatment group



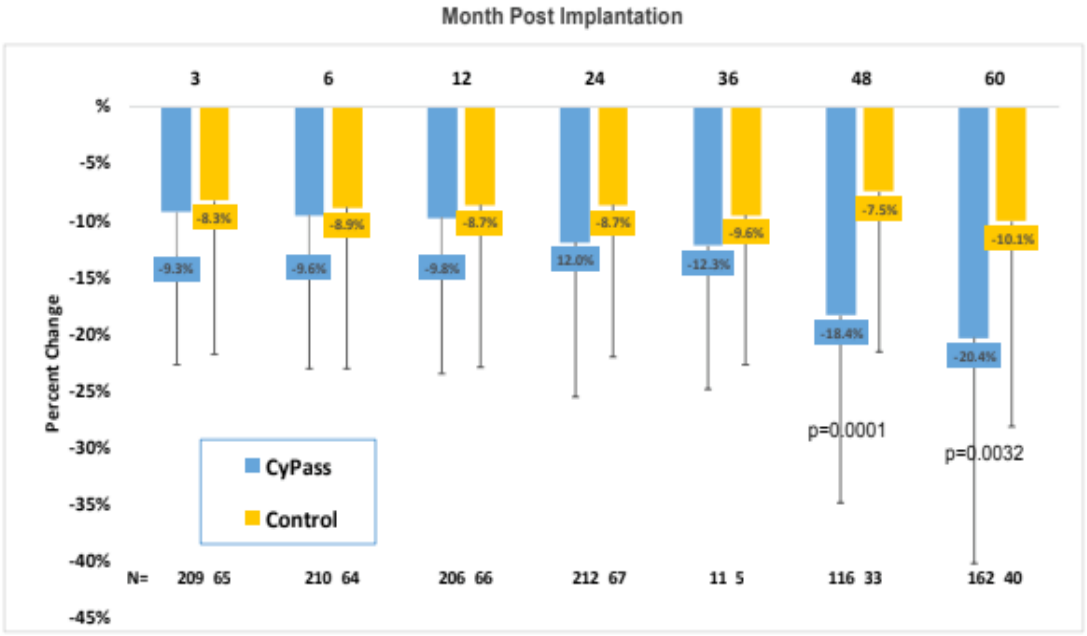


Figure 7. Mean change in ECD from baseline (Data provided by Alcon)

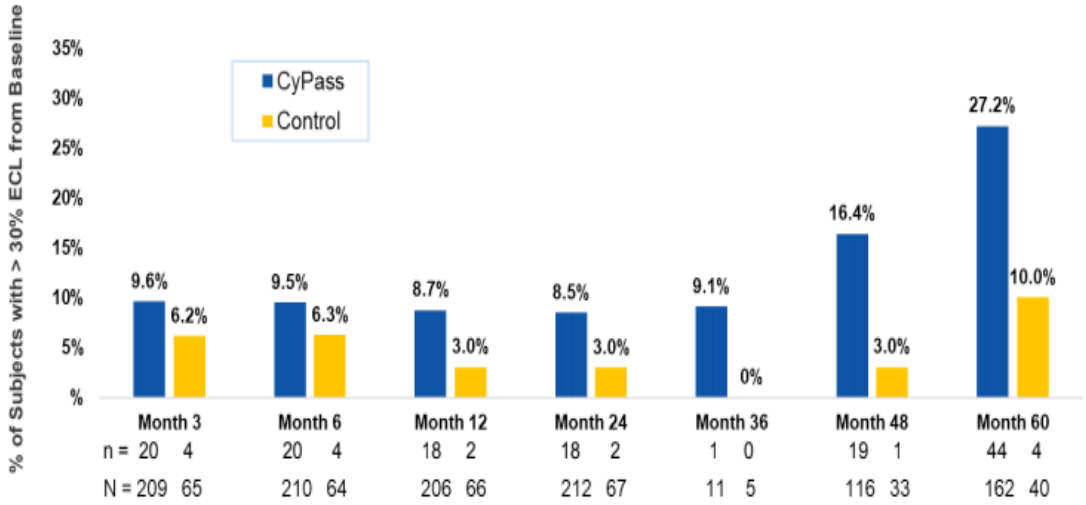


Figure 8. Percentage of patients > 30% ECL from baseline (Data provided by Alcon)

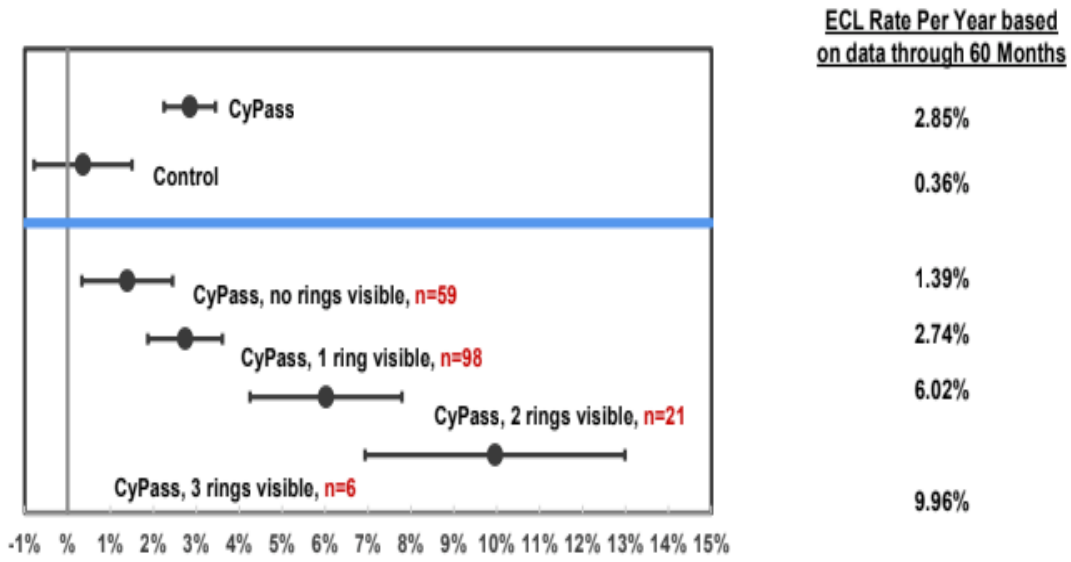


Figure 9: Annual ECL based on stent positioning

Table 1. Baseline, preoperative, and postoperative data

Parameter	CyPass	Control	P-Value
N (eyes)	33	12	–
Female Count (Percent)	19 (57.6)	14 (42.4)	–
Right Eyes Count (Percent)	16 (48.5)	8 (66.7)	–
Mean Age ± SD	66.8 ± 7.3	65.9 ± 5.5	0.53
Mean Pre VF ± SD	-3.1 ± 2.3	-3.3 ± 2.5	0.73
Mean Post VF ± SD	-3.7 ± 2.7	-3.6 ± 2.2	0.93
Mean Pre IOP WO ± SD	24.4 ± 2.6	24.1 ± 2.4	0.61
Mean Pre IOP ± SD	17.7 ± 3.3	18.6 ± 4.4	0.76
Mean Post IOP ± SD	15.0 ± 4.4	17.7 ± 4.8	0.08
Mean Pre Med ± SD	1.5 ± 1.0	1.3 ± 1.0	0.58
Mean Post Med ± SD	0.4 ± 0.7	0.9 ± 0.7	0.01*
Mean Days PO ± SD	2298.1 ± 433	2419.3 ± 469.2	0.43

Pre VF=preoperative Humphrey mean deviation; Post VF=postoperative Humphrey mean deviation; Pre IOP WO=preoperative washout IOP found in COMPASS trial; Pre IOP= preoperative intraocular pressure at COMPASS screening; Post IOP= postoperative intraocular pressure at last clinic exam; Pre Med= preoperative glaucoma medication usage at COMPASS screening; Post Med= postoperative glaucoma medication usage at last clinic exam; Days PO= days since surgery;*P<0.05

Table 2. Success, Qualified Success, and Failure	CyPass Count (Percent)	Control Count (Percent)	P-Value
Complete Success	20 (60.6)	2 (16.7)	0.008
Qualified Success	9 (27.3)	5 (41.7)	
Failure	4 (24.2)	5 (41.7)	

Table 3. Reasons for "Qualified Success" or "Failure".	Qualified			Failure			
	SLT	Med	Mult	IOP	Med	Sx	Mult
CyPass	2	5	2	1	1	0	2
Control	1	4	0	1	1	3	0

SLT=selective laser trabeculoplasty; Med=medication; Multi=combination; IOP=intraocular pressure; Sx=incisional surgical intervention

Raw Data

Sub ID	Sex	Age	Eye	TxGroup	PreVF	PostVF	PreIOP	PreIOP WO	PostIOP	PreMed	PostMed	Days PO	Secondary Ocular Procedures	Comments
003-01	M	70	OS	CyPass	-1.85	0.46	18	22	14	1	0	3104	N	
003-02	F	63	OS	CyPass	-2.17	-6.32	22	23	15	1	0	2701	N	
003-03	F	68	OS	CyPass	-2.73	-7.18	14	22	18	1	0	3030	N	
003-04	M	67	OS	CyPass	-2.85	-2.23	19	24	6	1	0	3023	N	
003-05	F	71	OD	CyPass	-1.25	-0.46	18	22	11	1	0	2933	N	
003-06	F	53	OS	CyPass	-4.78	-3.2	23	22	15	0	0	2982	N	
003-07	M	72	OD	CyPass	-0.26	-0.74	16	26	13	2	2	2901	N	
003-08	F	55	OS	CyPass	-3.7	-5.9	15	33	33	2	2	2817	YM	MLT, Hydrus VII
003-09	M	55	OS	CyPass	-7.9	-7.97	21	31	17	1	1	2514	N	
003-10	F	65	OS	CyPass	-2.2	-1.56	19	23	18	2	1	2224	Y	SLT
003-11	F	61	OS	CyPass	-2.06	-3.85	11	25	19	3	0	2435	Y	SLT
003-12	F	72	OD	CyPass	-3.64	-3.07	13	23	11	1	0	2332	N	
003-13	F	65	OS	CyPass	-4.15	-3.12	17	25	14	1	1	2416	N	
003-14	F	65	OS	CyPass	-5.99	-9.4	17	22	14	1	1	2351	N	
003-15	M	67	OD	CyPass	-2.79	-6.9	20	26	19	3	2	1794	N	
003-16	M	79	OD	CyPass	-1.79	-5.93	16	22	17	2	0	2330	N	
003-17	M	64	OD	CyPass	-1.45	-1.91	23	27	14	0	0	2374	N	
003-18	F	77	OD	CyPass	-3.23	-6.02	15	24	11	2	0	2265	Y	SLT
003-19	F	66	OS	CyPass	-8.15	-4.88	26	23	10	0	1	2253	N	
003-20	M	77	OS	CyPass	-4.22	-5.26	16	22	10	2	1	2099	N	
003-21	F	71	OD	CyPass	-0.45	-1.32	16	23	14	3	0	2198	N	
003-22	F	79	OS	CyPass	-0.05	-2.73	14	25	16	3	0	2102	N	
003-23	F	64	OS	CyPass	-5.78	-3.92	16	24	14	1	0	1493	N	
003-24	M	71	OD	CyPass	-6.22	-7.01	17	24	14	0	0	2086	N	
003-25	M	73	OS	CyPass	0.54	0.5	15	26	16	2	0	1896	N	
003-26	M	58	OD	CyPass	-8.64	-3.48	18	26	17	3	1	2032	Y	SLT
003-27	M	68	OD	CyPass	-3.01	0.14	21	24	13	0	0	1932	Y	SLT
003-28	M	73	OD	CyPass	-0.2	0.47	16	22	16	2	0	1905	N	
003-29	F	75	OD	CyPass	-2.1	-1.42	16	23	16	2	0	1884	N	
003-30	F	61	OD	CyPass	-2.62	-4.08	19	25	17	2	0	1869	N	
003-31	M	54	OD	CyPass	-2.55	-3.95	14	23	15	2	0	1961	N	
003-32	F	57	OD	CyPass	-2.37	-6.25	22	24	17	0	0	1767	N	
003-33	F	68	OS	CyPass	-2.79	-4.99	21	28	10	2	0	1834	N	
003-34	M	69	OS	Control	-3.08	-4.53	16	24	19	1	1	2531	N	
003-35	F	62	OD	Control	-3.83	-1.45	22	24	16	0	0	3131	Y	MLT, SLT
003-36	M	71	OS	Control	-1.15	-4.49	20	28	18	1	2	3073	Y	SLT
003-37	M	65	OD	Control	-0.08	-1.23	19	27	16	1	1	2013	N	
003-38	F	61	OS	Control	-2.6	0.79	19	23	16	3	1	2835	N	
003-39	F	63	OD	Control	-2.66	-5.84	17	21	21	1	1	2902	YM	trabecular outflow
003-40	M	61	OD	Control	-5.4	-5.31	18	22	14	1	1	2224	N	
003-41	F	76	OD	Control	-4.41	-4.06	14	22	16	2	0	1904	N	
003-42	F	74	OS	Control	-3.91	-3.84	13	22	11	3	0	2378	N	
003-43	M	59	OD	Control	-0.92	-2.56	30	28	28	0	1	2277	YM	trabecular outflow
003-44	M	64	OD	Control	-9.62	-6.8	16	24	13	1	1	1911	N	
003-45	M	66	OD	Control	-2.46	-4.33	19	24	24	2	2	1853	YM	Trabeculectomy

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