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CLINICAL TRIAL REPORT

A Randomized Controlled Trial Comparing STREAMLINE Canaloplasty to Trabecular Micro-Bypass Stent Implantation in Primary Open-Angle Glaucoma

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Purpose: To report interim results of the VENICE study, a multi-center, randomized, controlled trial (RCT) comparing STREAMLINE Surgical System (STREAMLINE) canaloplasty with iStent inject W (iStent W) implantation in patients with mild-to-moderate primary open-angle glaucoma (POAG) undergoing phacoemulsification.

Patients and Methods: Safety and efficacy analyses involving the first 72 randomized eyes are included in this report. Following pre-(Screening) and post-medication washout (Eligibility) visits, one eye per subject was randomized 1:1 to STREAMLINE or iStent W after undergoing uncomplicated phacoemulsification. Subjects were evaluated postoperatively at Day 1, Week 1, Month 1, 3, and 6. Intraocular pressure (IOP) measurements, number of IOP-lowering medications, and adverse events (AEs) were assessed at each follow-up visit.

Results: Seventy-two eyes were randomized; 35 underwent STREAMLINE canaloplasty and 37 were implanted with the iStent W. Seventy eyes completed their 6-month follow-up. Both the mean morning post-washout Baseline IOP between STREAMLINE 24.86±3.05 mmHg and iStent W 25.16±3.41 mmHg and the mean IOP at 6 months between STREAMLINE eyes 16.52±3.63 mmHg and iStent W eyes 16.08±3.19 mmHg were not statistically significantly different (p=0.691 and 0.596, respectively). At 6 months, more eyes were on zero glaucoma medications in the STREAMLINE group (81.8%) compared to the iStent W group (78.4%). In medication-free eyes, the mean IOP was reduced from 24.80±2.79 mmHg to 16.00±3.40 mmHg and 24.60±3.18 mmHg to 15.80±2.21 mmHg in the STREAMLINE and iStent W groups, respectively (p=0.752). Both groups showed reduction in IOP-lowering medications at every visit, compared to pre-washout (Screening), with STREAMLINE resulting in numerically fewer medications 0.20±0.48 compared to iStent W 0.40±0.79 at 6 months (P=0.384). AEs were mild and self-limited.

Conclusion: To our knowledge, the VENICE trial is the first RCT involving canaloplasty. These interim findings demonstrated comparable IOP and medication reduction between STREAMLINE canaloplasty and iStent W implantation, when combined with phacoemulsification.

Keywords: primary open-angle glaucoma, POAG, STREAMLINE, iStent inject W, canaloplasty, microinvasive glaucoma surgery, MIGS

Introduction

According to a meta-analysis performed by the Vision Loss Expert Group of the Global Burden of Disease Study, glaucoma has remained the leading cause of irreversible blindness globally over the last two decades with 3.61 million people blind and 4.14 million visually impaired in 2020.[1] The risk factors and pathophysiology associated with glaucoma

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have been well-described in previous landmark studies, with intraocular pressure (IOP) being the only modifiable risk factor to slow or prevent visual field deterioration.[2,3] Historically, the first line of treatment for IOP control in glaucoma has been the use of topical pressure lowering medication drops followed by laser trabeculoplasty and eventually invasive surgery. The undesirable side effects and lack of compliance with topical drops, along with the adverse events (AEs) and economic burden of more invasive procedures, resulted in a desire for safer, less invasive, and predictably efficacious treatments for glaucoma.[4–6]

The introduction of micro-invasive glaucoma surgeries (MIGS) addressed the unmet need of safer IOP lowering with less invasive approaches compared to older filtration surgery techniques.[7–9] MIGS, as defined by the American Glaucoma Society (AGS), are a broad group of procedures "designed to lower IOP by improving aqueous outflow with minimal disruption to the sclera or conjunctiva with or without an implanted device, or by reducing aqueous production selectively".[10] Since the approval of Trabectome (NeoMedix, Tustin, CA) in 2004 and the first generation iStent in 2012 (Glaukos, Aliso Viejo, CA), MIGS have become a data-driven method of safely and effectively treating patients with various forms of glaucoma, both standalone as well as combined with cataract surgery.[11,12] Peer reviewed publications of MIGS treatments have documented safety and efficacy in patients with open-angle glaucoma (OAG), secondary glaucomas including pigmentary and pseudoexfoliative glaucoma,[12,13] and across the continuum from early to end-stage disease.[9,13–16]

MIGS studies have been reported on for over two decades and the data comparing the various procedures in head-to-head randomized clinical trials (RCTs) continues to mount with increasing information that guide treatment algorithms and clinical decision-making.[17,18] This report focuses on the RCT findings of the VENICE study which prospectively compares safety and efficacy of STREAMLINE Surgical System (STREAMLINE, New World Medical, Rancho Cucamonga, CA) canaloplasty to iStent inject W when combined with cataract extraction.

Materials and Methods

Study Design

The VENICE study was designed to evaluate the safety and efficacy of STREAMLINE canaloplasty compared to iStent inject W implantation at the time of cataract extraction. Both procedures were performed after successful uncomplicated cataract surgery with planned 24-Month follow-up. This study is currently enrolling with subjects recruited from approximately 20 sites in the United States and Latin America. The study protocol was reviewed and approved by a central Institutional Review Board in the US (Sterling IRB), and study was approved by the ethics committee in Costa Rica (Instituto Costarricense de Investigaciones Clinical Comite Etico Cientifico). The study conduct follows the tenets of the Declaration of Helsinki with written informed consent of subjects. The study is registered with the National Library of Medicine database (clinicaltrials.gov, NCT05280366).

The iStent inject W was approved by the FDA in 2018 and contains two preloaded trabecular meshwork (TM) bypass stents that are manufactured from titanium and are coated with heparin. The iStent inject W's two-stent system creates a patent pathway through the TM and into the canal of Schlemm (CS).[19] The STREAMLINE Surgical System (Figure 1A) received FDA clearance in 2021. This single-use disposable device consists of a surgical grade stainless-steel dispensing inner cannula with a retractable outer sleeve and a hand-held body that houses a pump for dispensing ophthalmic viscoelastic fluid. The STREAMLINE device is designed to perform up to 8 applications of viscoelastic fluid into the CS. Each application delivers approximately 7 µL of viscoelastic for a total volume of 56 µL.[20]

Inclusion and Exclusion Criteria

Only one eye per subject was randomized for this study. Patients were eligible to participate in the study if they met the following criteria: were able to understand a written informed consent and able and willing to comply with the protocol, were 22 years or older, had visually significant cataract scheduled for phacoemulsification surgery, diagnosed with mild-to-moderate primary open-angle glaucoma with angles that were non-occludable per Shafer grading, were on 1 to 3 topical glaucoma medications at Screening, and potential for improvement in best corrected visual acuity (BCVA) after cataract surgery.

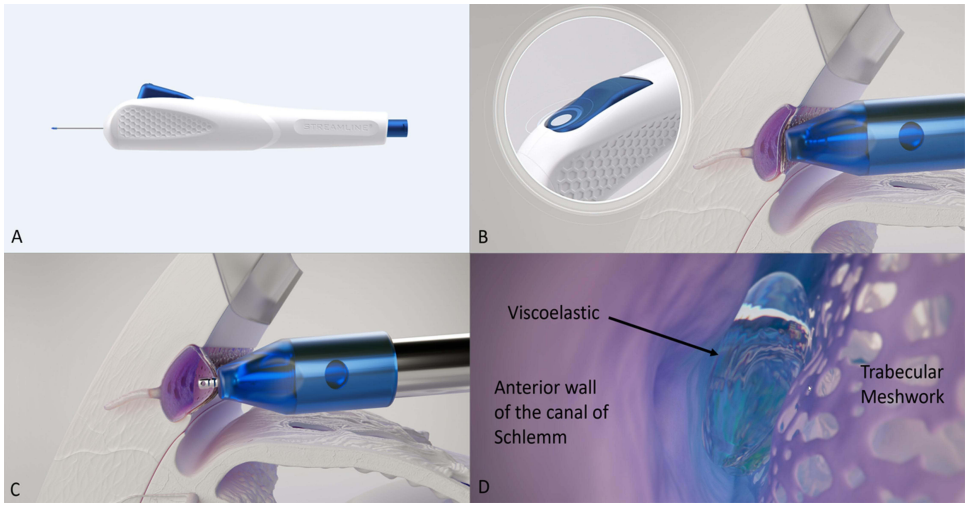

Figure 1 The STREAMLINE® Surgical System (**A**) is designed with a retractable sleeve that indents the trabecular meshwork (**B**) followed by actuation of the button leading to the inner cannula catheterizing the canal of Schlemm (**C**) and delivering ~7ul of viscoelastic across several clock hours of the canal through two outlets on either side of the cannula (**D**).

Eyes that had prior glaucoma surgery (CyPass, Xen, iStent, Express, Hydrus, glaucoma drainage device, canaloplasty, goniotomy, deep sclerotomy, trabeculotomy, trabeculectomy, endoscopic cyclophotocoagulation or cyclophotocoagulation), filtering or implantable glaucoma devices, previous laser peripheral iridotomy or Argon Laser Trabeculoplasty (ALT) were excluded from the study. Selective Laser Trabeculoplasty (SLT) was permitted if performed >3 months prior. Eyes with central corneal thickness less than 480µm or more than 620µm, previous intraocular surgery within the last 6 months, use of any medication that would be contraindicated for a glaucoma surgical procedure, use of oral hypotensive medication treatment for glaucoma, participation (≤30 days prior to Baseline) in an interventional trial which could have a potential effect on the study outcome or any condition, in the investigator's judgement, that would predispose the subject to significant risk of complications or significant vision loss at medication washout and throughout the study were also excluded. Additional exclusion criteria included eyes with severe or advanced glaucoma in the study eye characterized by: cup/disc ratio (C/D) greater than 0.80 (horizontal or vertical measurement); severe central visual field loss defined as a sensitivity ≤10 dB in at least 2 of the 4 visual field test points closest to the point of fixation; and anyone who could not safely undergo a washout of previously used IOP-lowering medication. Lastly, the non-study eye could not have a BCVA worse than 20/80.

Study participants were consented and examined at a Screening visit to determine if they met inclusion and exclusion criteria before washing out of medications. Table 1 shows the required minimum washout period for each IOP-lowering medication classification. After appropriate washout, subjects returned for an Eligibility visit where diurnal IOP, Goldmann applanation tonometry measurements taken 4 ± 1 hours apart between 8AM and 4PM, was measured. Subjects that reached an IOP of 22–34 mmHg (inclusive) were randomized 1:1 to either the STREAMLINE or iStent inject W group combined with cataract surgery. Subjects who did not meet the inclusion and exclusion criteria were categorized as screen failure.

Table 1 IOP-Lowering Medication Washout Schedule

Medication Class	Minimum Washout Period
Miotics and topical CAI	5 days ± 1 day
Alpha agonists	14 days ± 1 day
Beta antagonists, Prostaglandin analogues, Rho Kinase Inhibitors, Nitric Oxide	28 days ± 1 day
Combination drugs – Use longest washout period of the individual components	Up to 28 days ± 1 day

Abbreviations: IOP, Intraocular Pressure; CAI, Carbonic Anhydrase Inhibitor.

Randomization

All eligible subjects were given a randomization number which dictated the treatment group and randomization numbers could not be reused. On the day of surgery, after successful uncomplicated cataract extraction, subjects were randomized to either STREAMLINE canaloplasty or iStent inject W implantation based on their randomization number. STREAMLINE canaloplasty and iStent inject W implantation were performed per the instructions for use (IFU) as described below. All surgical procedures were performed by trained ophthalmologists with experience in angle-based surgical procedures.

Procedures

For the iStent inject W implantation, the microscope was tilted 35–45 degrees towards the surgeon and the patient's head was turned approximately 35–45 degrees away from the surgeon. After proper positioning, a gonioprism was used to visualize the TM. The injector was inserted through the same temporal corneal incision used to perform cataract surgery and centered on the nasal TM. Light pressure was applied and the delivery button was held down to penetrate the tissue with the trocar and deploy the implant. A second implant was inserted at least two clock hours away from the first stent implant in all iStent cases.[19]

For the STREAMLINE Surgical System (Figure 1A) canaloplasty, viscoelastic was loaded into the handpiece and the microscope was tilted 35–45 degrees towards the surgeon and the patient's head was turned approximately 35–45 degrees away from the surgeon. The handpiece was introduced through the cataract surgery incision and advanced across the anterior chamber to the nasal angle. The outer sleeve was positioned against the TM under direct gonioscopic visualization to indent the tissue (Figure 1B). The actuator button was then fully depressed, retracting the outer sleeve and allowing the inner cannula to enter the CS (Figure 1C). The button was held in the depressed position for 2 seconds to allow the viscoelastic to be delivered (Figure 1C and D). The tip was then withdrawn from the TM and the actuator button released. The procedure was repeated, spacing each application approximately one clock hour away from prior applications with 3–8 applications performed in each eye.[20] While STREAMLINE is a multiple function device and allows for incisions in the TM to be performed in addition to the canaloplasty, the VENICE trial was done exclusively with canaloplasty without additional incisions made in the TM.

Visit Assessments

The study was designed to include follow-up visits on Day 1, Week 1, Months 1, 3, 6, 9, 12, 18 and 24. Additional study exam procedures included BCVA, slit lamp, gonioscopy, dilated fundus exam, automated perimetry, pachymetry and endothelial cell density (ECD). All serious non-ocular and all study eye AEs were collected. Any changes in medical or ocular history from Screening and all concomitant systemic and ocular medications were recorded. This manuscript will report findings from Screening, Eligibility, Surgery Day, Day 1, Week 1, and Months 1 through 6 for the first 72 randomized subjects that are eligible for analysis.

Intraocular Pressure & Masking

IOP measurements were performed in both eyes using a calibrated Goldmann applanation tonometer at all visits. To minimize bias, a 2-person method that involved an operator and a reader was used to measure IOP. The operator was responsible for measuring IOP, while the reader recorded the results and was masked to the subject's treatment group for the entire study. An alternate IOP reader was required for each site should the main IOP reader become unmasked. Two consecutive IOP measurements were taken for each eye, and the applanation probe was withdrawn from the eye between the two measurements. If the difference between the 2 measurements differed by ≤4 mmHg, the average of the measurements was determined to be the mean IOP for that eye. If the two measurements for the same eye differed by >4 mmHg, a third measurement was taken. The two IOP measurements closest to each other were averaged. If the three measurements differed by equal amounts, all 3 measurements were averaged. Mean IOP values were rounded up to the next whole number if the value was equal to or greater than 0.5 mmHg and rounded down if less than 0.5 mmHg.

Statistical Analysis

In this interim report, data were analyzed as part of the planned safety monitoring after at least 60 subjects completed the Month 6 visit. IOP and number of ocular hypotensive medications were summarized by visit. Safety outcomes included intraoperative and postoperative AEs, as well as assessments of BCVA, slit-lamp exam, and ECD data. Subject demographics and Baseline characteristics were compared between the two treatment groups. Continuous variables (e.g., age) were summarized as the mean and standard deviation. The *t*-test was used to compare the means of two treatment groups for each continuous variable to see if there was a significant difference (*t*-test p-value less than 0.05). Categorical variables (e.g., sex) were summarized as counts and percentages. The chi-square test was used to examine the association or discrepancy between two treatment groups and the testing p-value was reported.

Results

IOP and IOP-Lowering Medications

At the time of this 6-month analysis, 105 subjects were enrolled (screened), of whom 72 met the inclusion/exclusion criteria. Each of the 72 subjects had one eye randomized, totaling 35 eyes in the STREAMLINE group and 37 eyes in the iStent inject W group. STREAMLINE eyes received an average of 4.43 ± 0.96 applications, each spaced at least one clock hour apart and all iStent inject W eyes successfully received two stent implants. The demographic (Table 2) and preoperative (Table 3) characteristics for both study groups were similar. The mean age was 70.10 ± 7.67 and 70.60 ± 7.07 years in the STREAMLINE and iStent groups, respectively (p = 0.628). The unmedicated diurnal IOP at Eligibility (the Baseline post-

Table 2 Subject Demographics

	STREAMLINE (n = 35) Mean (SD)	iStent inject W (n = 37) Mean (SD)	P Value
Age (years)	70.10 (7.67)	70.60 (7.07)	0.628
Sex			0.768
Male	13 (37.1%)	15 (40.5%)	
Female	22 (62.9%)	22 (59.5%)	
Race			0.460
Black	5 (14.3%)	2 (5.4%)	
Asian	2 (5.7%)	3 (8.1%)	
Native Hawaiian / Other Pacific Islander	0	1 (2.7%)	
White	28 (80.0%)	31 (83.8%)	
Eye			0.632
Right	19 (54.3%)	18 (48.6%)	
Left	16 (45.7%)	19 (51.4%)	

Abbreviation: SD, Standard Deviation.

Table 3 Pre-op Characteristics in Study Eyes at Screening (Visit 1, Before Medication Washout)

	STREAMLINE (n = 35) Mean (SD)	iStent inject W (n = 37) Mean (SD)	P Value
BCVA (logMAR)	0.60 (0.24)	0.60 (0.22)	0.762
CCT (μm)	545.70 (33.91)	546.90 (30.22)	0.882
Vertical C/D	0.60 (0.17)	0.60 (0.15)	0.734
Humphrey Visual Field, MD, (dB)	−3.50 (3.01)	−2.90 (3.20)	0.362

Abbreviations: SD, standard deviation; BCVA, Best Corrected Visual Acuity; logMAR, logarithm of the Minimum Angle of Resolution; CCT, central corneal thickness; μm, micrometers; C/D, cup to disc ratio; MD, Mean Deviation; dB, decibels.

washout IOP), calculated as the mean and standard deviation of all IOP measurements taken throughout the entire day, was 24.50 ± 3.02 mmHg in the STREAMLINE group and 25.00 ± 3.23 mmHg in the iStent inject W group, with no statistically significant difference between groups (p = 0.465). Analysis of IOP across study visits (Table 4) compared morning IOP values at Eligibility to morning IOP values at 6 months since full diurnal IOP was not obtained at Month 6 (planned at Month 12). The mean morning Baseline post-washout IOP values were 24.86 ± 3.05 mmHg for STREAMLINE and 25.16 ± 3.41 mmHg for iStent inject W. Overall, the IOP lowering efficacy and reduction in dependence on IOP lowering medications were similar between the two groups throughout the 6-month follow-up period (Table 4 and Figure 2).

The STREAMLINE group required numerically less medications for IOP control at every postoperative follow-up visit (Table 5 and Figure 3). At Week 1, more eyes were on zero medications in the STREAMLINE group (34/35, 97.1%) compared to the iStent inject W group (33/37, 89.2%). At Month 1, 33/35 (94.3%) of the STREAMLINE group eyes were on zero or one medication, compared to 33/37 (89.2%) of the iStent inject W group. At Month 3, 33/34 (97.1%) of the STREAMLINE group eyes were on zero or one medication compared to 34/37 (91.9%) in the iStent inject W group. At Month 6, the STREAMLINE group maintained a higher proportion of eyes on zero or one medication (32/33, 97.0%) compared to in the iStent Inject W group (34/37, 91.9%) and 2/37 (5.4%) eyes were on 3 medications in the iStent inject W group while none of the STREAMLINE eyes required 3 medications for IOP control. Both the STREAMLINE and iStent inject W groups had a statistically significant decrease in number of medications from Screening to Month 6 ($p<0.0001$ for each group). An analysis of eyes that were off of all IOP-lowering medications at 6 months is shown in Table 6. These data show that 81.8% (27/33) of STREAMLINE eyes and 78.4% (29/37) of iStent inject W eyes were on zero IOP-lowering medications. The mean IOP was reduced from 24.80 ± 2.79 to 16.00 ± 3.40 and from 24.60 ± 3.18 to 15.80 ± 2.21 in the STREAMLINE and iStent inject W groups, respectively (p = 0.752). This equates to a total IOP reduction of 8.8 mmHg for both groups and highlights that eyes remaining off all medications experienced the same level of pressure decrease regardless of the surgical approach.

Safety

LogMAR BCVA at Screening for STREAMLINE was 0.60 ± 0.24 and iStent was 0.60 ± 0.22, (p = 0.762). All subjects underwent uncomplicated cataract surgery before the randomization and BCVA improved to 0.90 ± 0.21 for STREAMLINE and 0.90 ± 0.19 for iStent inject W. ECD measurements were completed at a subset of sites using an Automated Non-contact Specular Microscope. There were 21 subjects in the STREAMLINE group and 25 subjects in the

Table 4 Intraocular Pressure Measurements at Each Study Visit

	STREAMLINE **n** **Mean (SD) mmHg**	**iStent inject W** **n** **Mean (SD) mmHg**	**P Value**
Screening	35	37	
	16.86 (4.30)	18.27 (5.57)	0.234
Baseline	35	37	0.691
Post Washout	24.86 (3.05)	25.16 (3.41)	
Day 1	35	37	
	16.54 (6.91)	18.86 (6.81)	0.156
Day 7	35	37	
	17.71 (6.97)	19.43 (5.25)	0.240
Month 1	35	37	
	15.69 (3.67)	17.24 (4.32)	0.104
Month 3	34*	37	
	15.62 (3.10)	15.49 (3.02)	0.858
Month 6	33**	37	
	16.52 (3.63)	16.08 (3.19)	0.596

Notes: *Subject missed visit. **One subject died and one subject missed visit.
Abbreviations: mmHg, millimeters of mercury; SD, standard deviation.

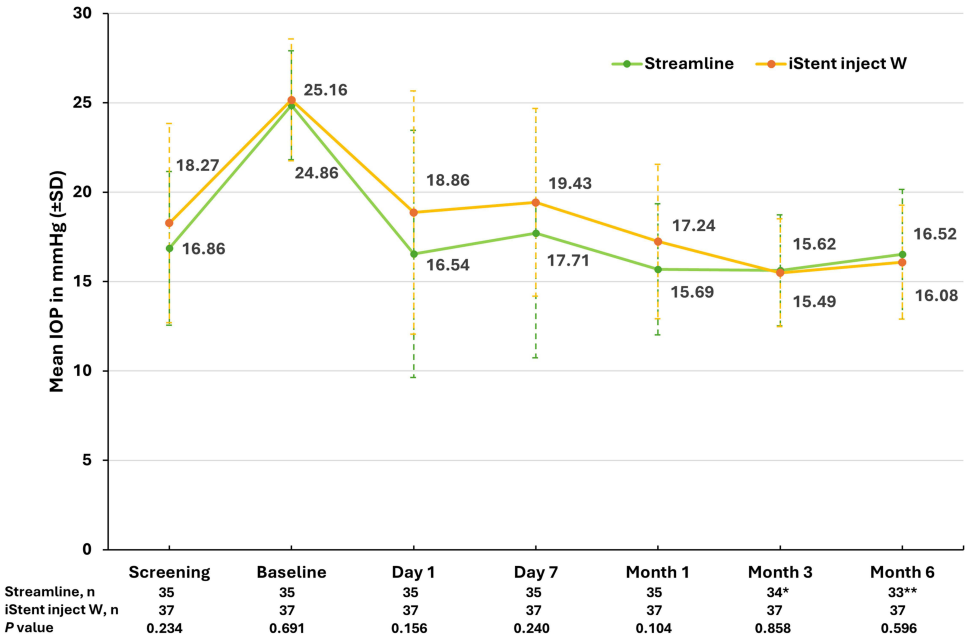

Figure 2 Mean IOP at pre-washout Screening, post-washout Baseline and postoperative visits. Error bars represent the standard deviation. There was no statistically significant difference between the STREAMLINE and iStent inject W groups across all visits up to postoperative Month 6 follow-up visit. *Subject missed visit. **One subject died and one subject missed visit.
Abbreviation: IOP, intraocular pressure.

iStent inject W group that were able to have ECD measured at Screening. For STREAMLINE, the mean ECD was 2642.20 ± 218.98 cells per square millimeter (cells/mm^2) at Screening and decreased to 2158.10 ± 537.18 cells/mm^2 by Month 6. Three eyes in the STREAMLINE group did not have ECD measurements at Month 6. For iStent inject W, 25 eyes had ECD measurements, with a mean of 2570.00 ± 264.65 cells/mm^2 at Screening decreasing to 2181.90 ± 499.77 cells/mm^2 at Month 6. These findings are consistent with ECD changes after cataract surgery alone and also in line with past MIGS studies.[21]

Table 5 Medication Use at Each Study Visit

Parameter	STREAMLINE n Mean (SD)	iStent inject W n Mean (SD)	P Value
Screening	35 1.90 (0.81)	37 1.70 (0.90)	0.531
Baseline	35	37	
Post Washout	0.00 (0.00)	0.00 (0.00)	N/A
Day 1	35 0.00 (0.00)	37 0.10 (0.49)	0.334
Day 7	35 0.10 (0.34)	37 0.20 (0.67)	0.213
Month 1	35 0.20 (0.65)	37 0.30 (0.81)	0.693
Month 3	34* 0.10 (0.44)	37 0.30 (0.78)	0.249
Month 6	33** 0.20 (0.48)	37 0.40 (0.79)	0.384

Notes: *Subject missed visit. **One subject died and one subject missed visit.
Abbreviations: SD, standard deviation; N/A, not applicable.

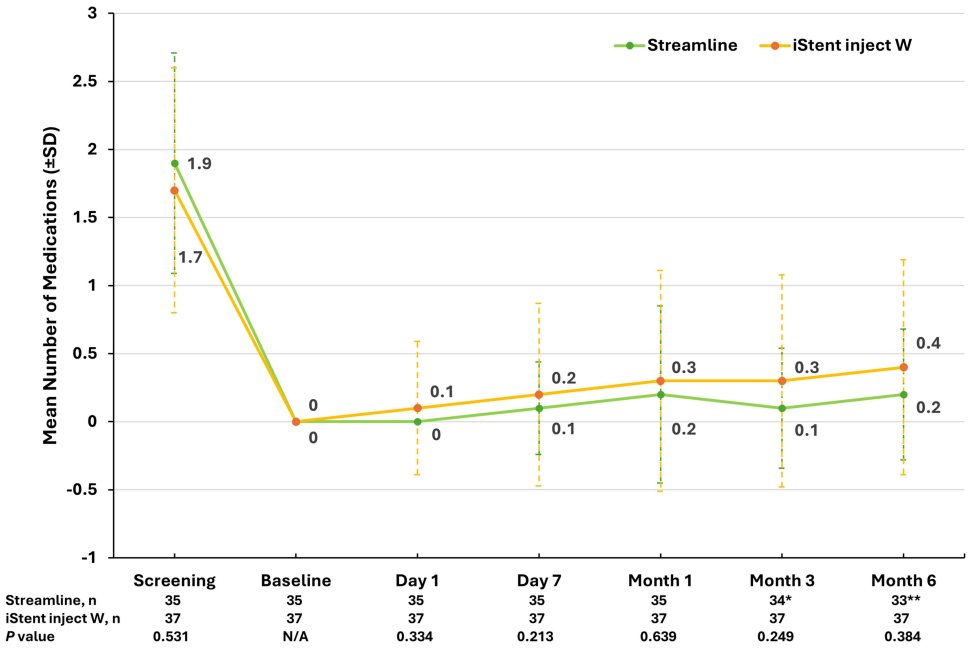

Figure 3 Mean number of IOP-lowering medications at pre-washout Screening and each postoperative visit. Error bars represent standard deviation. There was no statistically significant difference between the STREAMLINE and iStent inject W groups in mean glaucoma medication reduction from pre-washout Screening to post-operative Month 6 follow-up visit. *Subject missed visit. **One subject died and one subject missed visit.
Abbreviation: IOP, intraocular pressure.

AEs were generally mild and self-limited. Two eyes (one in the STREAMLINE group and one in the iStent inject W group) had early mild corneal edema with transiently elevated IOP and resolved with short-term use of topical therapeutics. One eye in the STREAMLINE group had late corneal edema with elevated eye pressure that occurred 30 days postoperatively and also resolved with short-term use of topical therapeutics. Two eyes (one in the STREAMLINE goup and one in the iStent inject W group) had early elevated IOP which resolved without sequelae after paracentesis tap and topical medication. Four study eyes in the STREAMLINE group were noted to have cell and flare 4 to 9 weeks after surgery. The inflammation was unrelated to the STREAMLINE device or canaloplasty procedure per the investigator; 3 eyes responded to topical therapy and AE was resolved. One eye experienced recurrent iritis post-surgery with continued close follow-up and work-up with rheumatology for etiology. One eye in the STREAMLINE group was noted to have blood in the angle at postoperative Day 1, but this resolved without sequela. Another eye in the STREAMLINE group was noted to have a vitreous floater postoperatively that was unrelated to the device or procedure. Lastly, one subject in the STREAMLINE group died for reasons unrelated to the study (cancer-related) after their Month 3 visit. One eye in the

Table 6 Analysis of IOP for Subjects off of All IOP-Lowering Medications

	STREAMLINE (n = 27)* Mean (SD)	**iStent inject W (n = 29)* Mean (SD)**	**P value**
Baseline Mean (SD)	24.80 (2.79)	24.60 (3.18)	0.744
Month 6 Mean (SD)	16.00 (3.40)	15.80 (2.21)	0.752

Notes: *At Month 6, 81.8% (27/33) of STREAMLINE subjects were off all IOP-lowering medications and 78.4% (29/37) of iStent inject W subjects were off all IOP-lowering medications.
Abbreviations: IOP, Intraocular Pressure; SD, Standard Deviation.

iStent inject W group had mild cystoid macular edema which resolved with topical treatment. A second eye in the iStent inject W group was diagnosed with a branch retinal vein occlusion, epiretinal membrane, and moderate cystoid macular edema occurring 3 months postoperatively (deemed by the investigator to be unrelated to the procedure).

Discussion

In this analysis, we evaluated the short-term, 6-month, safety and IOP-lowering efficacy of the STREAMLINE Surgical System versus iStent inject W when combined with cataract surgery in patients with mild to moderate, primary open-angle glaucoma (POAG). The IOP-lowering efficacy and reduction of IOP-lowering medications were similar between groups. AEs were also similar between groups and generally categorized as minor and unrelated to the devices used. These findings are similar to data reported on other MIGS devices with 6 months of follow-up and indicate that both STREAMLINE canaloplasty and iStent inject W are effective options for treating mild-to-moderate POAG when combined with cataract extraction (Table 7).[15,22–28]

The American Academy of Ophthalmology (AAO) describes canaloplasty as "Cannulation of Schlemm's canal (SC) with a catheter or stent with either an internal or external approach for at least three clock hours with an injection of viscoelastic while removing the stent to dilate the canal would be a canaloplasty. Alternatively, viscoelastic injections made via three or more punctures of the TM spanning at least three clock hours (90 degrees) to dilate SC should also qualify as canaloplasty."[29] The STREAMLINE Surgical System administers approximately 7 µl of ophthalmic viscoelastic device (OVD) per application, with 3–8 applications spaced about one clock hour apart, resulting in a total OVD

Table 7 Comparison of Month 6 IOP & Glaucoma Medication Reduction in Other MIGS Studies

	Treatment n at Month 6	Mean IOP (SD) Mean Medications (SD)	Screening	Baseline (Post Washout)	Month 6
VENICE†	STREAMLINE 33	IOP Meds	17.10 (3.82) 1.90 (0.81)	24.86 (3.05)*	16.52 (3.63) 0.20 (0.48)
	iStent inject W 37	IOP Meds	18.20 (3.29) 1.70 (0.90)	25.16 (3.41)*	16.08 (3.19) 0.40 (0.79)
Lazcano et al[15] – Streamline Single Site†	STREAMLINE 36	IOP Meds	16.9 (3.2) 2.1 (0.9)	23.2 (2.3)	15.4 (2.1) 0.8 (1.0)
Gallardo et al[22] – GEMINI†	OMNI-Phaco 134	IOP Meds	17.3 (3.1) 1.8 (0.9)	23.8 (3.1)**	15.1 (3.9) 0.6 (1.0)
Hirsch et al[23] – ROMEO	OMNI-Phaco 40	IOP Meds	19.5 (3.8) 1.8 (1.3)	N/A	15.1 (2.9) 1.1 (1.2)
Louanchi et al[24]	iStent inject W-Phaco 52	IOP Meds	16.1 (2.0) 2.3 (0.5)	N/A	13.0 (1.5) 1.8 (0.5)
Deneri et al[25]	iStent inject W-Phaco 32	IOP Meds	16.08 (3.27) 2.69 (1.03)	N/A	13.88 (2.57) 2.06 (1.34)
Hirabayashi – King[26]	KDB-Phaco 42	IOP Meds	17.1 (4.8) 2.4 (1.3)	N/A	15.0 (no SD) 1.2 (1.4)
Hirabayashi – Lee[27]	KDB-Phaco 97	IOP Meds	17.3 (4.8) 2.1 (1.3)	N/A	15.0 (3.5) 1.1 (1.3)
Mechleb et al[28]	KDB-Phaco 28	IOP Meds	18.11 (6.79) 2.86 (1.04)	N/A	13.57 (2.35) 1.56 (1.28)

Notes: †Screening visits for these were before IOP-lowering medication washout. *Morning average IOP at Eligibility. **Mean diurnal IOP of the entire Eligibility Day.
Abbreviations: IOP, Intraocular Pressure; Meds, Medication; SD, Standard deviation; MIGS, Microinvasive Glaucoma Surgery; IOP, Intraocular Pressure; N/A, not applicable; KDB, Kahook Dual Blade.

volume of 21 to 56 µl.[20] This volume is comparable to or exceeds that used by other canaloplasty devices.[30,31] The goal of using the STREAMLINE Surgical System for canaloplasty is to lower IOP and reduce reliance on IOP-lowering medications by addressing the main blockage points in the TM, SC, and the distal collector channels. The canaloplasty procedure has been found to be safe and effective, and similar to other MIGS procedures, both standalone and combined with cataract extraction, in multiple studies and in various forms of glaucoma.[15,22–28]

Table 7 contains information about various MIGS procedures including both IOP-lowering efficacy and efficiency at decreasing dependence on IOP-lowering medications. One example is from the GEMINI study, reporting prospective safety and efficacy outcomes of 360° canaloplasty and 180° trabeculotomy using the OMNI surgical system with concomitant phacoemulsification in 137 patients with OAG. Results at 6 months revealed 78% of patients were medication-free with IOP of 14.5 mmHg and a mean reduction of 9 mmHg from Baseline. They reported non-serious AEs such as hyphema in 7 (4.6%) patients, IOP elevation in 3 (2.0%), blepharitis in 2 (1.3%), cystoid macular edema in 1 (0.7%) and vitreous hemorrhage in 1 (0.7%) patient.[22] Hirsch and colleagues reported similar findings with a retrospective review of the OMNI system, in which case both canaloplasty and trabeculotomy were completed, showing effective IOP reduction and meaningful medication reduction for up to 12 months postoperatively.[23] They included two groups (overall n=81) in the study: Group 1 (Baseline IOP over 18mmHg) and Group 2 (Baseline IOP equal to or under 18mmHg). The mean IOP was reduced in Group 1 from 21.9 to 15.1 mmHg ($P < 0.0001$) and in Group 2 from 14.1 to 13.4 mmHg ($p = 0.318$). Mean medication use decreased from 2.0 ± 1.3 to 1.1 ± 1.1 and from 1.6 ± 1.3 to 0.9 ± 1.2 in Groups 1 and 2, respectively. AEs were typical for cataract or angle surgery: mild inflammation (11%), IOP spikes (IOP >10 mmHg above Baseline at >1 month, 5%), and hyphema (4%). It is noteworthy that both the ROMEO and GEMINI studies combined canaloplasty with trabeculotomy;[22,23] whereas, the prospective RCT data from this report (VENICE) only involved canaloplasty using the STREAMLINE device while achieving similar IOP-lowering effect and medication reduction across all three studies at the 6-month timepoint.

Limitations of this report include the relatively shorter follow-up period, while its strengths include the RCT design, comparison of two commonly used canal-based MIGS approaches and the use of surgeons from across various regions of the world and a diverse patient population. This study is ongoing and 12-month results for this cohort will be reported in the future to help better understand the long-term efficacy and safety for both STREAMLINE canaloplasty and iStent inject W implantation to treat glaucoma when combined with cataract surgery.

Conclusion

The 6-month results of the first 72 subjects randomized in the VENICE prospective RCT comparing STREAMLINE canaloplasty to iStent inject W implantation when combined with cataract extraction show similar safety and IOP lowering efficacy. Overall reduction in dependence on IOP-lowering medications was comparable with a numerically larger reduction in the STREAMLINE group. To our knowledge, this study is the first to directly compare the safety and efficacy of STREAMLINE canaloplasty to iStent inject W implantation at the time of cataract extraction.

Data Sharing Statement

Study data are available from the corresponding author upon reasonable request.

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Disclosure

EMI, HR, and MH are employees of New World Medical. Inc. and participated in the design and conduct of the study, the collection, management, and analysis of data, and the preparation of the manuscript. DFG has financial interests and/or receives consulting fees with New World Medical, Glaukos, AbbVie, Alcon, Johnson & Johnson and Ocular Science. CO receives consulting fees from New World Medical. BEF receives consulting from New World Medical, Glaukos, Alcon, Sight Sciences, iStar Medical, Iantrek and Sanoculis, and research grants from NiCox; IPS receives consulting, research and/or speaker fees from New World Medical, Glaukos, AVG, Alcon, Allergan, B+L, Elios, IStar Medical, Lumibird, Nova Eye, Ocular Therapeutix, Radius, Rayner, Sight Sciences, Tarsus and Thea. LKS receives consulting fees from New World Medical, Allergan and Oculus Surgical. MKE receives research support from New World Medical and Glaukos. MYK is a consultant to New World Medical and his university receives fees on his behalf for this consultancy. MYK also has a patent (No. 10,729,584) related to the STREAMLINE Surgical System technology and a patent (US 2021/0322218 A1) owned by New World Medical. The authors report no other conflicts of interest in this work.

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