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ORIGINAL RESEARCH

Comparative Effectiveness and Safety of Two Different Trabecular MIGS Devices With and Without Ab Interno Canaloplasty in Patients with Primary Open-Angle Glaucoma

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ABSTRACT

Introduction: This study compared outcomes of the iStent *inject* trabecular micro-bypass system versus the Hydrus Microstent in patients with primary open-angle glaucoma (POAG).

Methods: Forty subjects (80 eyes) with POAG were included in this single-center, retrospective, contralateral-eye analysis. All patients underwent phacoemulsification with either iStent *inject* or Hydrus implantation in one eye and the other device in the contralateral eye, with $\geq$ 3-month follow-up. In 58 eyes (27 iStent *inject*, 31 Hydrus) the surgery also included ab interno canaloplasty (ABiC). Twelve-month outcomes included intraocular pressure (IOP), medications, and adverse events. Subgroup analyses were completed for iStent *inject* versus Hydrus, and with versus without ABiC.

Results: At 12 months versus baseline, mean IOP reduced from 16.8 ± 3.7 to 13.6 ± 2.9 ($p = 0.003$) in iStent *inject* eyes, and from 18.1 ± 4.5 to 14.9 ± 3.2 mmHg ($p = 0.003$) in Hydrus eyes (between-group IOP reduction $p = 0.582$). Mean number of glaucoma medications reduced from 1.23 ± 0.97 to 0.30 ± 0.76 ($p < 0.001$) in iStent *inject* eyes and from 1.20 ± 1.02 to 0.39 ± 0.72 ($p = 0.001$) in Hydrus eyes (between-group medication reduction $p = 0.943$). At 12 months, 82.6% of iStent *inject* eyes and 73.9% of Hydrus eyes were medication-free versus 20.0% preoperatively in both groups ($p < 0.0001$ both groups). There were no statistically significant IOP or medication differences between iStent *inject* and Hydrus pre- or postoperatively, both in the overall cohort and in the with/without ABiC subgroups. Outcomes also were similar between eyes with/without ABiC in the overall cohort and in the iStent *inject*/Hydrus subgroups. There were no adverse events in the iStent *inject* group; two eyes in the Hydrus group had device-related complications requiring five additional surgeries (one Hydrus repositioning, one Hydrus exchange, one Hydrus removal, two goniotomies).

Conclusion: In this contralateral-eye comparison of iStent *inject* versus Hydrus, the groups had similar IOP and medication outcomes, regardless of stratification by ABiC completion. Eyes receiving Hydrus had more complications and subsequent surgeries.

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PLAIN LANGUAGE SUMMARY

The present study contributes some of the first real-world data comparing iStent *inject* versus Hydrus Microstent implantation in combination with cataract surgery in opposite eyes (right or left) of the same patient (i.e., contralateral-eye study). The report also includes subgroup analyses of eyes with versus without ab interno canaloplasty (ABiC). There were no significant between-group differences in mean intraocular pressure or medication burden preoperatively or postoperatively for iStent *inject* versus Hydrus. The intraocular pressure and medication reductions versus the groups' respective baselines were statistically similar as well. Finally, results remained similar for iStent *inject* versus Hydrus regardless of whether ABiC was completed, and were also similar when comparing eyes with ABiC versus without ABiC. In eyes receiving Hydrus, there was a greater incidence of complications and need for further surgery.

Keywords: iStent inject; Hydrus; Trabecular; Micro-bypass; Micro-invasive; MIGS; Canaloplasty; ABiC; Pairing

Key Summary Points

Why carry out this study?

Interventions to treat glaucoma, a major cause of blindness worldwide, must be evaluated for both their effectiveness and safety profiles.

This dual-arm contralateral-eye retrospective dataset assessed 12-month outcomes following cataract surgery combined with either iStent *inject* (W) or Hydrus Microstent implantation in one eye and the other device in the opposite eye in patients with primary open-angle glaucoma.

The iStent *inject* versus Hydrus results were stratified by whether concomitant ab interno canaloplasty (ABiC) was completed, and a comparison of eyes with versus without ABiC was performed as well.

What was learned from the study?

Significant intraocular pressure (IOP) and medication reductions versus baseline were achieved by both groups through 12 months.

No significant between-group differences existed in the mean IOP or medication burden preoperatively or postoperatively. The IOP and medication reductions versus the groups' respective baselines were statistically similar as well.

iStent *inject* versus Hydrus outcomes remained similar after stratification for ABiC completion. Results were also similar when comparing eyes with or without ABiC. In eyes receiving Hydrus, there was a greater incidence of complications and need for further surgery.

INTRODUCTION

Glaucoma is the leading cause of irreversible blindness worldwide, affecting an estimated 76 million people [1, 2]. The primary treatment aim in glaucoma is the reduction of intraocular pressure (IOP). Even small decreases in IOP can significantly reduce the risk of glaucoma progression [3, 4], with the Early Manifest Glaucoma Trial showing an 11% decrease in disease progression risk per 1 mmHg of IOP reduction [5]. Historically, topical medications have been the first-line method to reduce IOP [6]. Topical treatments such as prostaglandin analogues and beta-blockers have the advantages of being relatively safe, cost-effective, and rapid-onset. However topical treatment has several limitations, including poor compliance, ocular surface discomfort [7], dry eye [8], pigmentary changes, hyperemia, orbital fat atrophy, and

systemic side effects such as bradycardia and bronchospasm [9, 10].

An increasing number of surgical options are now available to treat glaucoma patients. Subconjunctival filtration surgeries such as trabeculectomy [11] and tube shunts [12] remain very effective in reducing IOP, particularly in advanced or secondary forms of glaucoma or in patients who cannot tolerate or are poorly compliant with topical glaucoma treatments. However, these procedures carry serious risks such as bleb-related infections and endophthalmitis, flat anterior chamber, corneal decompensation, suprachoroidal hemorrhage, bleb dysesthesia, hypotony maculopathy, conjunctival scarring, and bleb failure. For these reasons, they are often reserved for refractory and advanced glaucoma cases [13]. Patients who progress despite topical treatment can therefore be therapeutically challenging, as they require an escalation of treatment but may not warrant surgery with the aforementioned risks [14, 15].

Minimally invasive glaucoma surgery (MIGS) offers a potential solution to this treatment gap by providing a surgical option with a more favorable side effect profile than traditional filtration surgeries [16]. MIGS procedures can be classified based on their intended target tissue: trabecular, suprachoroidal, or subconjunctival [17]. Ab interno trabecular MIGS in particular, which acts upon the natural physiologic aqueous outflow pathway, can provide a surgical intervention with a favorable benefit-to-risk profile [16, 17] that takes into account patient comorbidities [18] and does not preclude future glaucoma surgery if needed [19].

In this retrospective contralateral study, we compared the clinical outcomes and safety profile of two trabecular bypass MIGS devices that improve aqueous outflow through the trabecular meshwork: the iStent *inject* trabecular micro-bypass system (either iStent *inject* or wide-flange iStent *inject* W; Glaukos Corporation, Aliso Viejo, CA, USA) and the Hydrus Microstent (Alcon, Fort Worth, TX, USA) when combined with phacoemulsification and in some cases ab interno canaloplasty (ABiC). Although there are some studies in the literature pertaining to iStent technologies and Hydrus in general, we are aware of only one study that compares two on-label uses of current-generation technology (i.e., iStent *inject* + phacoemulsification vs. Hydrus + phacoemulsification): the scientifically rigorous Fight Glaucoma Blindness Registry study [20]. Most of the other studies (such as the popularized COMPARE study [21]) are off-label (e.g., in standalone use) and/or include older-generation technology (i.e., iStent rather than iStent *inject*), so they are of limited clinical relevance to practicing surgeons. Moreover, the existing research has minimal to no comparative contralateral-eye data for the two technologies. To our knowledge, there are no contralateral studies to date that compare these two current technologies in on-label usage. The present study aims to fill this gap in the scientific literature.

METHODS

Study Design

This retrospective analysis is a single-center, single-surgeon comparison of patients who underwent phacoemulsification cataract surgery combined with implantation of iStent *inject* or iStent *inject* W in the right eye or Hydrus Microstent in the left eye. In eyes with greater preoperative disease burden (characterized by one or more of the following: unmedicated IOP $>$ 18 mmHg, treatment with two or more medications, and/or concerning visual field or optic nerve abnormalities), ABiC was completed prior to iStent *inject* or Hydrus implantation.

All patients were reviewed preoperatively and at 3, 6, and 12 months postoperatively. The primary outcome measures were mean IOP and mean number of glaucoma medications. Secondary outcomes included the proportions of eyes with IOP $\leq$ 15 mmHg, IOP $\leq$ 18 mmHg, and IOP reduction $\geq$ 20% from baseline, and on zero medications. Safety data consisted of intraoperative complications, postoperative adverse events, and secondary surgeries. The study was conducted according to the tenets of the Helsinki Declaration of 1964, local ethics guidelines (Western Institutional Review Board [IRB]), and HIPAA [Health Insurance Portability

and Accountability Act] privacy practices. All patients gave informed consent prior to undergoing surgery, and their data were analyzed in a retrospective anonymized fashion.

Subject Selection

Subjects were included from a single center in this retrospective contralateral-eye analysis. All patients aged 18 years or above with a diagnosis of POAG were eligible for inclusion. Preoperatively, patients were reviewed for best-corrected visual acuity (BCVA), IOP measured with Goldman applanation tonometry, gonioscopy, slit lamp exam, and examination of the fundus and optic disc. Exclusion criteria included evidence of a comorbid ocular pathology that could confound study outcomes, and abnormalities of the anterior chamber angle such as peripheral anterior synechiae or angle recession.

Surgical Technique

All surgeries were performed by a single surgeon (MS). Phacoemulsification was performed as standard using a clear corneal temporal incision. Where applicable, ABiC was performed as described previously [22]. First, a small goniotomy was created, and then the canaloplasty catheter (either iTrack, Nova Eye Medical, Fremont, CA, USA; or OMNI Surgical System, Sight Sciences, Menlo Park, CA, USA) was advanced into Schlemm's canal. The catheter was withdrawn while injecting viscoelastic to distend Schlemm's canal and the orifices of collector channels. After phacoemulsification with or without canaloplasty, two iStent *inject* stents or one Hydrus stent were implanted in the right or left eye, respectively. The surgeries were not completed in any particular order. That is, the first operation was based on which eye the patient preferred to have done first. Then, approximately 2–3 weeks after the first surgery, surgery was completed in the contralateral eye.

Implantation of the two iStent *inject* stents (either original iStent *inject* or wide-flange iStent *inject* W; Fig. 1) was completed as described previously [23]. After insertion through the temporal clear corneal incision, the injector was advanced across the anterior chamber to the nasal angle. The protective sleeve was retracted and the injector tip was used to engage the trabecular meshwork perpendicularly and lightly dimple it. The implant was then released. The steps were repeated for the second implant.

Insertion of the Hydrus device (Fig. 1) was completed using a hand-held injector through a temporal clear corneal incision as described previously [24]. The surgical microscope and the patient's head were adjusted to allow a clear view of the nasal angle using a surgical gonioprism, and then viscoelastic was injected into the anterior chamber to distend it and expand the angle. The Microstent was introduced using the injector into the anterior chamber, and the cannula tip was used to incise the trabecular meshwork. The Hydrus Microstent was advanced through Schlemm's canal to span three clock hours, with the 1–2 mm inlet segment remaining in the anterior chamber.

Following device implantation in either group, appropriate device positioning was confirmed, the injector was withdrawn, viscoelastic was removed, and the anterior chamber was filled with balanced salt solution. Postoperatively, patients received topical antibiotics for 10 days (besifloxacin or ofloxacin), and topical anti-inflammatory medication for 4–6 weeks (loteprednol and bromfenac).

Statistical Analysis

Statistical analysis was performed using a commercially available statistical software package (IBM SPSS Statistics for Windows, Version 20.0, released 2015. IBM Corp., Armonk, NY, USA.). Outcomes were reported as mean ± SD unless otherwise indicated. Within each group (iStent *inject* or Hydrus), postoperative IOP and medications versus baseline were compared using paired *t* tests (for continuous variables) or *z* tests (for categorical variables). The mean IOP and medications were compared between the two treatment groups (iStent *inject* versus Hydrus) using two-sample *t* tests. The amount of IOP and medication reduction from baseline for iStent *inject* versus Hydrus was compared with

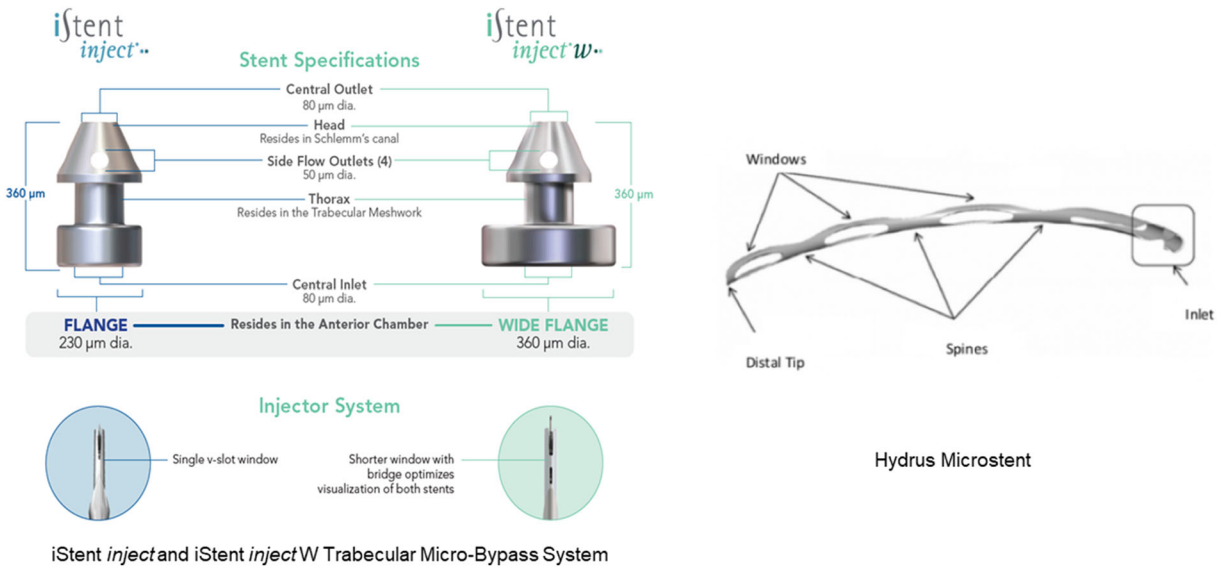

Fig. 1 iStent *inject* and iStent *inject* W Trabecular Micro-Bypass System; Hydrus Microstent*. *Not actual size

nonparametric tests. Subgroup analyses were completed for eyes with or without concomitant ABiC, including comparisons between the two devices (iStent inject or Hydrus), as well as between eyes with or without ABiC. A p value of < 0.05 was considered statistically significant.

RESULTS

Demographics

A total of 40 patients (80 eyes) with mean age of 74.2 ± 8.4 years were included in this study; 69, 51, and 46 eyes had follow-up data available at 3, 6, and 12 months, respectively. Concomitant ABiC was completed in 27 eyes in the iStent *inject* group and 31 eyes in the Hydrus group. Table 1 shows the baseline ocular parameters of the two groups.

IOP and Medication Outcomes

The primary outcome measures, mean IOP and mean number of glaucoma medications, were measured preoperatively and at 3, 6, and 12 months. At 12 months postoperatively versus baseline, the mean IOP reduced from 16.8 ± 3.7 to 13.6 ± 2.9 ($p = 0.003$) in iStent *inject* eyes, and from 18.1 ± 4.5 to 14.9 ± 3.2 mmHg ($p = 0.003$) in Hydrus eyes (Table 2, Fig. 2). The mean number of glaucoma medications reduced from 1.23 ± 0.97 to 0.30 ± 0.76 ($p < 0.001$) in iStent *inject* eyes, and from 1.20 ± 1.02 to 0.39 ± 0.72 ($p = 0.001$) in Hydrus eyes (Table 2, Fig. 3). There was no statistically significant difference between the two devices in mean IOP pre- or postoperatively ($p = 0.245$ and 0.132, respectively), or in mean number of glaucoma medications pre- or postoperatively ($p = 0.854$ and $p = 0.522$, respectively). There also was no difference in the amount of IOP or medication reduction experienced by the two groups versus their respective preoperative values (between-group $p = 0.582$ and $p = 0.943$, respectively).

At 12 months, the percentage of eyes with IOP ≤ 15 mmHg was 78.3% for iStent *inject* (vs. 40.0% preoperatively, $p = 0.0076$) and 52.2% for Hydrus (vs. 27.5% preoperatively, $p = 0.0917$). At 12 months, 82.6% of iStent *inject* eyes and 73.9% of Hydrus eyes were medication-free, versus 20.0% in both groups preoperatively ($p < 0.0001$ both groups). Table 3 and Fig. 4 summarize the proportional IOP and medication changes at baseline versus 12 months.

Table 1 Baseline ocular parameters of patients in the iStent *inject* and Hydrus groups

	All eyes (*N* = 80)	**iStent *inject* (*N* = 40)**	**Hydrus (*N* = 40)**	***p* value* (iStent *inject* vs. Hydrus)**
BCVA (logMAR)				
Mean (SD)	0.62 (0.43)	0.52 (0.34)	0.71 (0.50)	*0.057*
Median [min, max]	0.51 [0, 2.30]	0.44 [0, 1.30]	0.54 [0.18, 2.30]	
CD ratio				
Mean (SD)	0.53 (0.19)	0.53 (0.20)	0.53 (0.19)	*0.927*
Median [min, max]	0.55 [0.20, 0.90]	0.52 [0.20, 0.90]	0.55 [0.20, 0.80]	
	N = 78	*N* = 39	*N* = 39	
Visual field MD				
Mean (SD)	−2.65 (3.76)	−2.84 (4.05)	−2.47 (3.55)	*0.895*
Median [min, max]	−2.31 [−17.2, 5.57]	−2.31 [−17.2, 1.78]	−2.16 [−12.0, 5.57]	
	N = 43	*N* = 21	*N* = 22	
Corneal thickness				
Mean (SD)	527 (25.2)	524 (25.5)	531 (24.9)	*0.226*
Median [min, max]	524 [476, 597]	520 [483, 597]	529 [476, 589]	
	N = 46	*N* = 22	*N* = 24	
OCT RNFL				
Mean (SD)	82.6 (14.8)	81.4 (16.7)	83.6 (13.2)	*0.841*
Median [min, max]	85.0 [52.0, 109]	82.0 [52.0, 105]	85.5 [60.0, 109]	
	N = 49	*N* = 23	*N* = 26	

All procedures were combined with phacoemulsification cataract surgery and intraocular lens implantation
BCVA best-corrected visual acuity, *SD* standard deviation, *OCT* optical coherence tomography, *RNFL* retinal nerve fiber layer, *MD* mean deviation, *ABiC* ab interno canaloplasty
*Two-sample *t* test

Comparison of iStent *inject* versus Hydrus, with Stratification by Ab Interno Canaloplasty

Approximately three-fourths of eyes (27 iStent *inject*, 31 Hydrus) underwent ABiC prior to iStent *inject* or Hydrus implantation, so the dataset was further stratified to compare outcomes without/with ABiC (Table 4a and b). At baseline and 12 months, in cases without ABiC, IOP reduced from 19.5 ± 2.6 to 14.8 ± 3.6 (iStent *inject*) and from 18.0 ± 4.9 to 16.4 ± 2.4 (Hydrus). The mean number of medications reduced from 0.69 ± 0.63 to 0.12 ± 0.35 (iStent *inject*) and from 0.89 ± 0.60 to 0.14 ± 0.38 (Hydrus). There were no statistically significant differences between the iStent *inject* and Hydrus subgroups pre- or postoperatively, either in the mean IOP and medications (Table 4a) or in the amount of reduction versus baseline (Table 4b).

In cases with concomitant ABiC, mean IOP reduced from 15.5 ± 3.5 to 12.9 ± 2.3 (iStent

Table 2 iStent *inject* vs. Hydrus: intraocular pressure and glaucoma medications through 12 months

	Preop	3 M	6 M	12 M
IOP				
iStent inject				
IOP *n*	40	36	26	23
Mean ± SD	16.8 ± 3.7	14.5 ± 4.7	14.6 ± 3.6	13.6 ± 2.9
Mean IOP vs. preop *p* value*	–	***< 0.001***	*0.056*	***0.003***
IOP reduction from preop (mmHg)	–	−2.17	−1.54	−2.78
Hydrus				
IOP *n*	40	33	25	23
Mean ± SD	18.1 ± 4.5	15.4 ± 2.6	15.4 ± 3.5	14.9 ± 3.2
Mean IOP vs. preop *p* value*	–	***< 0.001***	***0.013***	***0.003***
IOP reduction from preop (mmHg)	–	−2.55	−2.44	−3.96
p values, iStent *inject* vs. Hydrus				
Mean IOP at time points**	*0.245*	***0.034***	*0.292*	*0.132*
IOP reduction¥	–	0.439	0.557	0.582
Number of medications				
iStent inject				
Meds *n*	40	36	26	23
Mean ± SD	1.23 ± 0.97	0.11 ± 0.52	0.23 ± 0.71	0.30 ± 0.76
Mean no. of meds vs. preop *p* value*	–	***< 0.001***	***< 0.001***	***< 0.001***
No. of meds reduction from preop	–	−1.17	−0.92	−0.83
Hydrus				
Meds *n*	40	33	25	23
Mean ± SD	1.20 ± 1.02	0.24 ± 0.71	0.28 ± 0.74	0.39 ± 0.72
Mean no. of meds vs. preop *p* value*	–	***< 0.001***	***< 0.001***	***0.001***
No. of meds reduction from preop	–	−1.03	−0.92	−0.87
p values, iStent *inject* vs. Hydrus				
Mean no. of meds at time points**	*0.854*	*0.344*	*0.682*	*0.522*
No. of meds reduction¥	–	0.392	0.759	0.943

All procedures were combined with phacoemulsification cataract surgery and intraocular lens implantation
Preop preoperative, *M* months, *Meds* medications, *IOP* intraocular pressure
*Paired *t* test (Wilcoxon) for continuous variables
**Two-sample *t* test comparing mean IOP or mean number of medications
¥Nonparametric test comparing the *degree* of IOP or medication reduction from preoperative values for iStent *inject* vs. Hydrus

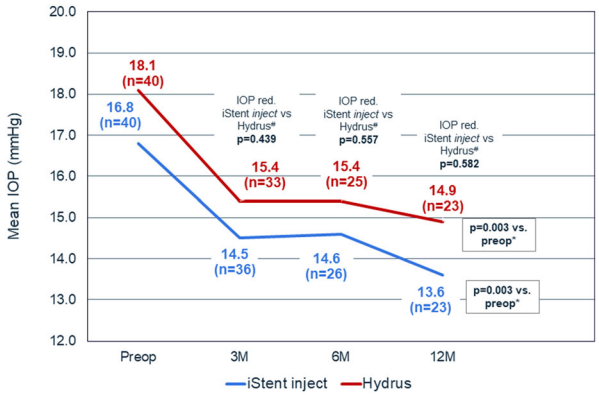

Fig. 2 Mean intraocular pressure for iStent *inject* and Hydrus groups through 12 months. *Paired *t* test (Wilcoxon) for continuous variables. #Nonparametric test comparing the degree of IOP reduction from preoperative values for iStent *inject* vs. Hydrus. All procedures were combined with phacoemulsification cataract surgery and intraocular lens implantation. *Preop* preoperative, *M* months, *IOP* intraocular pressure

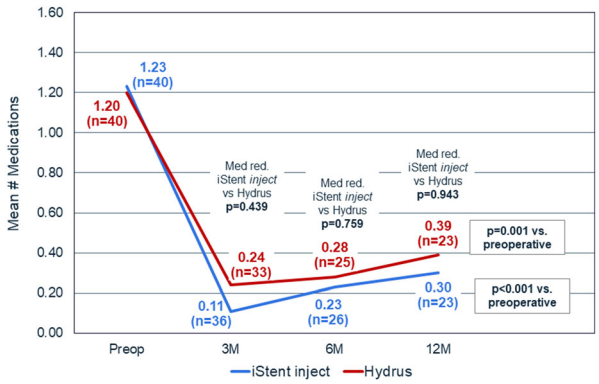

Fig. 3 Mean number of medications for iStent *inject* and Hydrus groups through 12 months. *Paired *t* test (Wilcoxon) for continuous variables. #Nonparametric test comparing the degree of medication reduction from preoperative values for iStent *inject* vs. Hydrus. All procedures were combined with phacoemulsification cataract surgery and intraocular lens implantation. *Preop* preoperative, *M* months, *Meds* medications

inject) and from 18.1 ± 4.5 to 14.3 ± 3.3 (Hydrus), mean number of medications reduced from 1.48 ± 1.01 to 0.40 ± 0.91 (iStent *inject*) and from 1.29 ± 1.1 to 0.50 ± 0.82 (Hydrus). No statistically significant postoperative differences existed between the two subgroups, either in the mean IOP and medications (Table 4a) or in the amount of reduction versus baseline (Table 4b).

Comparison of Eyes With or Without Ab Interno Canaloplasty for Each Device

In addition to comparing iStent *inject* versus Hydrus in the overall cohort and in the subgroups with or without ABiC, a separate analysis was completed to compare eyes with or without ABiC. Results are shown in Table 5 for the overall cohort and for the iStent *inject* and Hydrus subgroups. No statistically significant differences were observed in the amount of IOP or medication reduction experienced by the with ABiC versus without ABiC subgroups.

Adverse Events and Secondary Surgeries

No intraoperative complications occurred in either group. Postoperatively, no adverse events occurred in the iStent *inject* group. Postoperatively in the Hydrus group, there was one device dislocation and one device malposition. The case of dislocated Hydrus was noted at 1 week postoperatively and was accompanied by IOP of 24 mmHg (versus 20 mmHg preoperatively and 11 mmHg on day 1). The dislocation was managed with Hydrus repositioning at 1 week, followed by Hydrus exchange with goniotomy at 1 month; IOP remained ≤ 18 mmHg at study visits thereafter. The case of malposition was noted at month 1 and was accompanied by IOP elevation to 26 mmHg (versus 16 mmHg preoperatively, 13 mmHg on day 1, and 21 mmHg at week 1). The malposition required Hydrus removal with goniotomy; IOP was 17 mmHg at the subsequent visit. Based on prior experience, in both of these cases, it is likely there were areas within Schlemm's canal that were blocked. In such areas, the viscodilation catheter could have broken through trabecular meshwork into an area of Schlemm's canal that was not visualized by the gonioprism during catheterization, thereby creating a space for the Hydrus to inadvertently enter.

Table 3 Mean intraocular pressure and medication burden at 12 months vs. preoperative, *n* (%)

	iStent *inject*			Hydrus		
	Preop *(n = 40)*	**12 M *(n = 23)***	***p* value vs. preop**	**Preop *(n = 40)***	**12 M *(n = 23)***	***p* value vs. preop**
IOP						
Percentage of eyes with IOP ≤ 15 mmHg	16 (40.0%)	18 (78.3%)	***0.0076***	11 (27.5%)	12 (52.2%)	*0.0917*
Percentage of eyes with IOP ≤ 18 mmHg	27 (67.5%)	21 (91.3%)	*0.0675*	21 (52.5%)	19 (82.6%)	***0.0342***
Percentage of eyes with > 20% reduction in IOP	10 (43.5%)			11 (47.8%)		
Percentage reduction in mean IOP	19.4%			17.4%		
Number of medications						
Percentage of eyes medication-free	8 (20.0%)	19 (82.6%)	< ***0.0001***	8 (20.0%)	17 (73.9%)	< ***0.0001***
Percentage of eyes on ≤ 1 medication	29 (72.5%)	21 (91.3%)	*0.1464*	30 (75.0%)	20 (87.0%)	*0.4204*
Percentage reduction in mean number of medications	75.2%			67.4%		

All procedures were combined with phacoemulsification cataract surgery and intraocular lens implantation
Preop preoperative, *M* months, *IOP* intraocular pressure
*Two-proportions *Z* test

DISCUSSION

The use of MIGS in the treatment of glaucoma has significantly changed the way glaucoma is managed. MIGS is particularly useful in those patients who are not controlled on topical treatment alone but for whom more invasive filtration surgeries are either not appropriate or present an unfavorable side effect profile. There is now a wide array of potential MIGS therapies with varying mechanisms of action. The majority of clinical studies investigating MIGS have focused on individual devices, with fewer studies of paired procedures or comparisons of different procedures [20, 21, 25, 26]. A greater understanding of how MIGS procedures can be combined, or their comparative utility, may reveal potential [27] new treatment approaches for patients who might otherwise experience disease progression requiring invasive filtration surgery. To that end, the present study supplies data on the paired use of trabecular micro-bypass and ABiC, as well as a comparison of two MIGS devices (iStent *inject* vs. Hydrus). The study is, to our knowledge, the first published contralateral-eye data to compare the iStent *inject* and Hydrus devices.

The comparative IOP and medication outcomes of the two devices in this study are consistent with prior studies of iStent or iStent *inject* versus Hydrus. For example, a 24-month large multicenter independent comparison study by Holmes et al. of iStent *inject* versus Hydrus demonstrated no statistically significant differences in IOP lowering at 24 months, and a potential additional medication reduction with iStent *inject* [20]. A prospective comparative study of iStent *inject* versus Hydrus with phacoemulsification showed similar IOP and medication reductions with the two devices [28]. A study by Lee et al. comparing iStent versus Hydrus in combination with phacoemulsification also showed no difference in IOP outcomes [29]. Overall safety profiles in these studies were generally similar or slightly more favorable for iStent or iStent *inject* than Hydrus, including more device-related adverse events and secondary surgeries with Hydrus [28], and more

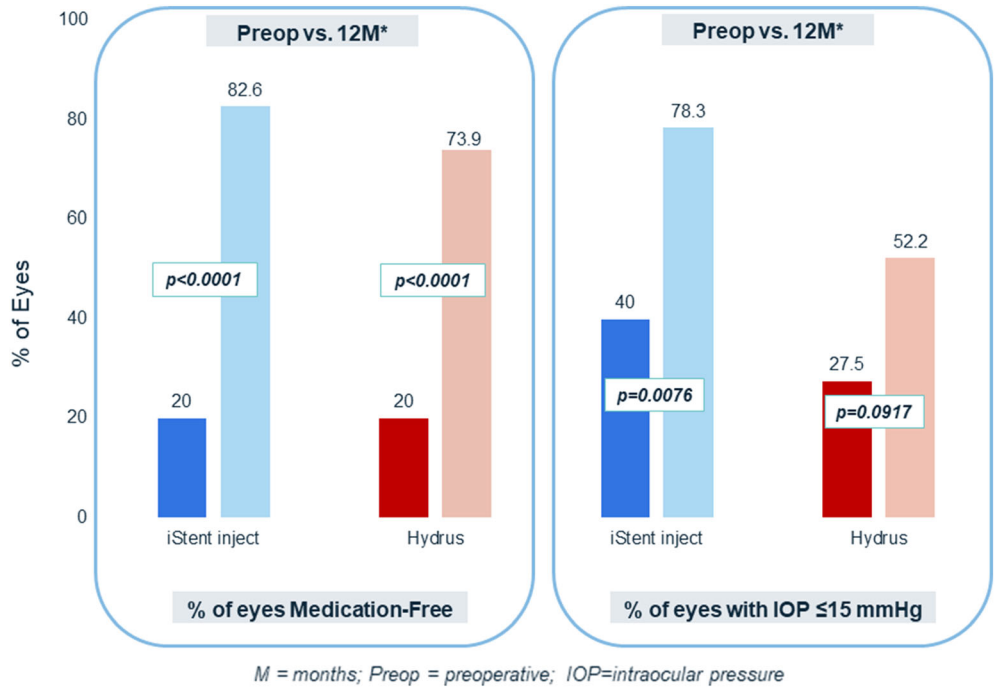

Fig. 4 Preoperative vs. month 12 proportion of eyes medication-free and proportion of eyes with IOP $\leq$ 15 mmHg, iStent *inject* vs. Hydrus. *Two-proportion Z test. All procedures were combined with phacoemulsification cataract surgery and intraocular lens implantation. *Preop* preoperative, *M* months, *Meds* medications, *IOP* intraocular pressure

intraoperative complications such as device repositioning needed with Hydrus [29].

The present study demonstrated comparable IOP outcomes and medication reduction in both groups, suggesting that the two devices have comparable efficacy when treating glaucoma. More adverse events and additional surgeries were required in the Hydrus group, including one case requiring Hydrus repositioning and another case requiring Hydrus removal. Meanwhile, no adverse events occurred in the iStent *inject* group. These findings are consistent with the study by Lee et al., which reported device repositioning in 9/52 Hydrus eyes versus 0/50 iStent eyes [29]. Malposition of stents can result in significant ocular damage including corneal decompensation, uveitis, iris trauma, and pigment dispersion syndrome. Not surprisingly, in the 5-year extension study of the Hydrus pivotal trial, approximately 20% of eyes had corneal endothelial cell loss $\geq$ 30% versus preoperative values [30].

In addition to comparing the iStent *inject* and Hydrus devices, the current study contributes data on the paired use of ABiC with either device in approximately three-fourths of eyes [31, 32]. Canaloplasty can be performed as a standalone procedure or in combination with other surgeries [33, 34]. In our experience, canaloplasty can be used to open the angle, allowing easier visualization of the trabecular meshwork and facilitating MIGS placement, and it may be combined with stent implantation to further lower the IOP [35]. In the current study, although sample sizes were limited, there appeared to be a preliminary trend toward lower final IOP when pairing either device with canaloplasty compared to either device alone (Table 4a); this coincides with the recently published findings of Gallardo et al. [36]. However, given the baseline differences between subgroups, any such trends are to be interpreted with caution. Regardless of whether canaloplasty had been performed, there was still

Table 4 a. iStent *inject* vs. Hydrus: Mean intraocular pressure and medications, stratified by ab interno canaloplasty (ABiC)

	iStent *inject*	Hydrus	iStent *inject* vs. Hydrus *p* value*
Without ABiC			
IOP			
Baseline	19.5 ± 2.6 (n = 13)	18.0 ± 4.9 (n = 9)	*0.545*
3 mos	14.2 ± 2.8 (n = 10)	15.6 ± 4.4 (n = 8)	*0.370*
6 mos	14.5 ± 2.3 (n = 8)	16.8 ± 3.0 (n = 6)	*0.121*
12 mos	14.8 ± 3.6 (n = 8)	16.4 ± 2.4 (n = 7)	*0.381*
Number of meds			
Baseline	0.69 ± 0.63 (n = 13)	0.89 ± 0.60 (n = 9)	*0.467*
3 mos	0 ± 0 (n = 10)	0.12 ± 0.35 (n = 8)	*0.314*
6 mos	0 ± 0 (n = 8)	0.17 ± 0.41 (n = 6)	*0.312*
12 mos	0.12 ± 0.35 (n = 8)	0.14 ± 0.38 (n = 7)	*1.000*
With ABiC			
IOP			
Baseline	15.5 ± 3.5 (n = 27)	18.1 ± 4.5 (n = 31)	***0.020***
3 mos	14.6 ± 5.3 (n = 26)	15.4 ± 1.9 (n = 25)	*0.058*
6 mos	14.6 ± 4.1 (n = 18)	14.9 ± 3.6 (n = 19)	*0.725*
12 mos	12.9 ± 2.3 (n = 15)	14.3 ± 3.3 (n = 16)	*0.279*
Number of meds			
Baseline	1.48 ± 1.01 (n = 27)	1.29 ± 1.10 (n = 31)	*0.375*
3 mos	0.15 ± 0.61 (n = 26)	0.28 ± 0.79 (n = 25)	*0.609*
6 mos	0.33 ± 0.84 (n = 18)	0.32 ± 0.82 (n = 19)	*0.962*
12 mos	0.40 ± 0.91 (n = 15)	0.50 ± 0.82 (n = 16)	*0.571*

b. iStent *inject* vs. Hydrus: *Reduction* in intraocular pressure and medications, stratified by ab interno canaloplasty (ABiC)

	iStent *inject* + cataract surgery	Hydrus + cataract surgery	iStent *inject* vs. Hydrus *p* value**
Without ABiC			
IOP reduction from baseline			
3 mos	−5.10 (n = 10)	−1.37 (n = 8)	***0.036***
6 mos	−4.00 (n = 8)	−3.17 (n = 6)	*0.558*
12 mos	−4.00 (n = 8)	−2.57 (n = 7)	*0.382*

Table 4 continued

b. iStent *inject* vs. Hydrus: *Reduction* in intraocular pressure and medications, stratified by ab interno canaloplasty (ABiC)

	iStent *inject* + cataract surgery	Hydrus + cataract surgery	iStent *inject* vs. Hydrus *p* value**
Meds reduction from baseline			
3 mos	−0.70 (n = 10)	−0.75 (n = 8)	*0.922*
6 mos	−0.75 (n = 8)	−0.83 (n = 6)	*0.887*
12 mos	−0.62 (n = 8)	−0.86 (n = 7)	*0.366*
With ABiC			
IOP reduction from baseline			
3 mos	−1.04 (n = 26)	−2.92 (n = 25)	*0.762*
6 mos	−0.44 (n = 18)	−2.21 (n = 19)	*0.240*
12 mos	−2.13 (n = 15)	−4.56 (n = 16)	*0.276*
Meds reduction from baseline			
3 mos	−1.35 (n = 26)	−1.12 (n = 25)	*0.270*
6 mos	−1.00 (n = 18)	−0.95 (n = 19)	*0.622*
12 mos	−0.93 (n = 15)	−0.87 (n = 16)	*0.661*

All procedures were combined with phacoemulsification cataract surgery and intraocular lens implantation
Preop preoperative, *mos* months, *IOP* intraocular pressure, *med* medication, *ABiC* ab interno canaloplasty
*Two-sample t test comparing mean IOP or mean number of medications
**Mann–Whitney U test comparing the degree of IOP or medication reduction from preoperative values for iStent *inject* vs. Hydrus

no difference in effectiveness outcomes between the two devices.

Limitations in this real-world patient cohort include loss to follow-up, yielding diminishing sample sizes especially in later months of the study. The randomization scheme was based on the laterality of the eye; however, this would not be expected to impact outcomes given there is no biological mechanism for laterality to impact IOP. Sample size was modest, and no contralateral-eye adjustments were made. Approximately three-fourths of stent surgeries were performed in combination with ABiC, thereby introducing another variable into the study; however, given that a similar percentage of eyes in either group had ABiC, the between-group comparisons would remain valid. Additionally, any potential impact of ABiC was mitigated by stratifying for whether or not ABiC was completed, and these stratified outcomes remained similar between devices. The study was designed to minimize bias, but given the surgical nature of the intervention, masking for the surgical method was not possible. Future studies could include a multicenter multi-surgeon design to avoid any potential surgical methodological bias, along with larger sample size and statistical adjustments for contralateral eyes.

CONCLUSION

In conclusion, this study shows comparable IOP- and medication-reducing effectiveness of iStent *inject* or Hydrus in combination with

Table 5 With ab interno canaloplasty vs. without ab interno canaloplasty: all eyes, iStent *inject* subgroup, Hydrus subgroup

	With ABiC	Without ABiC	With ABiC vs. without ABiC *p* value*
All eyes			
IOP reduction from baseline			
3 mos	−1.96 (n = 51)	−3.44 (n = 18)	*0.161*
6 mos	−1.35 (n = 37)	−3.64 (n = 14)	*0.096*
12 mos	−3.39 (n = 31)	−3.33 (n = 15)	*0.716*
Meds reduction from baseline			
3 mos	−1.23 (n = 51)	−0.72 (n = 18)	*0.090*
6 mos	−0.97 (n = 37)	−0.79 (n = 14)	*0.748*
12 mos	−0.90 (n = 31)	−0.73 (n = 15)	*0.592*
iStent inject			
IOP reduction from baseline			
3 mos	−1.04 (n = 26)	−5.10 (n = 10)	***0.017***
6 mos	−0.44 (n = 18)	−4.00 (n = 8)	***0.034***
12 mos	−2.13 (n = 15)	−4.00 (n = 8)	*0.218*
Meds reduction from baseline			
3 mos	−1.35 (n = 26)	−0.70 (n = 10)	*0.073*
6 mos	−1.00 (n = 18)	−0.75 (n = 8)	*0.588*
12 mos	−0.93 (n = 15)	−0.62 (n = 8)	*0.306*
Hydrus			
IOP reduction from baseline			
3 mos	−2.92 (n = 25)	−1.37 (n = 8)	*0.540*
6 mos	−2.21 (n = 19)	−3.17 (n = 6)	*0.823*
12 mos	−4.56 (n = 16)	−2.57 (n = 7)	*0.524*
Meds reduction from baseline			
3 mos	−1.12 (n = 25)	−0.75 (n = 8)	*0.558*
6 mos	−0.95 (n = 19)	−0.83 (n = 6)	*0.945*
12 mos	−0.87 (n = 16)	−0.86 (n = 7)	*0.772*

All procedures were combined with phacoemulsification cataract surgery and intraocular lens implantation
Preop preoperative, *mos* months, *IOP* intraocular pressure, *med* medication, *ABiC* ab interno canaloplasty
*Mann Whitney *U* test comparing the *degree* of IOP or medication reduction from preoperative values for eyes with ABiC vs. eyes without ABiC

phacoemulsification. Effectiveness outcomes remained similar across subgroups regardless of whether concomitant ABiC had been completed. The main distinction between the devices was the different safety profile, as more complications and additional surgical procedures occurred with Hydrus than with iStent *inject*. These findings provide valuable real-world information to surgeons and patients who must weigh the benefits and risks of any given MIGS surgery.

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Author Contribution. Mitchell Shultz: Research design, data acquisition and research execution, data analysis, data interpretation, manuscript preparation. Abraham Chorbajian: Data acquisition and research execution, data analysis, manuscript preparation. Ala Zohouralen: Data acquisition and research execution, data analysis, manuscript preparation.

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Declarations

Conflict of Interest. Dr. Shultz: Aerie, R; Alchemy Vision, O; Allergan, C; Avellino Lab, C; Bausch and Lomb, C, R, L; BVI, R; Cloud Break, R; Glaukos, C, R, L; Glint Pharma, C; HDMD, C; HDMD, C; Imprimis/Harrow, C; Ivantis, C, L; New World Medical, C, R; Ocuphire Pharm, C; Sight Sciences, C, L; SOMED, C; SUN Pharm, C; Tarsus, R; Twenty Twenty, C; Zeiss, C. (C, consulting fees; R, research fees; L, lecture fees). Mr. Chorbajian: no competing interests. Ms. Zohouralen: no competing interests.

Ethical Approval. The study was conducted according to the tenets of the Helsinki Declaration of 1964, local ethics guidelines (Western IRB), and HIPAA privacy practices. All patients gave informed consent prior to undergoing surgery, and their data were analyzed in a retrospective anonymized fashion.

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