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A comparison of iStent combined with phacoemulsification and endocyclophotocoagulation (ICE2) with the PreserFlo MicroShunt and XEN-45 implants

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Umair Qidwai, Lee Jones and Gokulan Ratnarajan

Abstract

Background: Minimally invasive glaucoma surgery (MIGS), including minimally invasive bleb surgery (MIBS), is a rapidly evolving area of research and clinical interest in ophthalmology. The growing number of devices has necessitated evaluations to identify subtle differences in outcomes between treatments.

Objectives: To compare clinical effectiveness and safety outcomes of iStent combined with endoscopic cyclophotocoagulation (ICE2) with bleb forming PreserFlo MicroShunt (PMS) and XEN-45 gel implant in a 24-month retrospective review.

Design: A retrospective review of patient records.

Methods: We compared outcomes of 247 patients undergoing one of three glaucoma procedures (ICE2 = 162; PMS = 48; XEN-45 = 37) at a single facility in the United Kingdom. Clinical records were reviewed retrospectively between July 2016 and May 2020. Pairwise comparisons and within group analyses were performed to assess intraocular pressure (IOP), best-corrected LogMAR visual acuity (BCVA), the Humphrey visual fields and antiglaucoma medication outcomes across the three treatment groups.

Results: No statistically significantly differences in IOP between the groups at day 7, 6 months, 12 months and 24 months. PMS had statistically significantly change in IOP between baseline and day 7 compared with ICE2 ($p = 0.003$). BCVA was statistically significant different at 24 months between the ICE2 compared with PMS group (0.12 *versus* 0.33 LogMAR; $p = 0.002$). PMS group achieved the largest decline in medication usage between baseline a 24-month follow-up (2.9 *versus* 0.9; $p < 0.001$), with no statistically significant difference in the number of antiglaucoma medications being used between groups at 24 months. Postoperative complications in all three groups were transient and could be resolved with office-based interventions.

Conclusion: Real-world outcomes after 24 months were similar between patients undergoing MIGS and MIBS procedures.

Keywords: clinical effectiveness, minimally invasive glaucoma surgery, safety

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Correspondence to:
Gokulan Ratnarajan
Consultant Ophthalmologist, Corneo-Plastic Unit and Eye Bank, Queen Victoria Hospital NHS Foundation Trust, East Grinstead RH19 3DZ, West Sussex, UK.
gokulan.ratnarajan@nhs.net

Umair Qidwai
Corneo-Plastic Unit and Eye Bank, Queen Victoria Hospital NHS Foundation Trust, East Grinstead, UK

Lee Jones
Corneo-Plastic Unit and Eye Bank, Queen Victoria Hospital NHS Foundation Trust, East Grinstead, UK

UCL Institute of Ophthalmology, London, UK

Introduction

Glaucoma affects approximately 57.5 million people globally, with a projected increase to 111 million people by the year 2040.[1] Early diagnosis is essential for avoiding irreversible visual field loss by sustainably reducing intraocular pressure (IOP). Multiple treatment options are available following diagnosis including medical, laser and surgical approaches. Drops can be effective in controlling and stabilising IOP but are

associated with side effects and discomfort.[2,3] Patients experiencing ocular surface disease have a propensity for medication discontinuation, and thus are at risk of glaucomatous progression.[4,5]

Minimally invasive glaucoma surgeries (MIGS) have gained popularity as a treatment strategy because of their clinical efficacy and safety profile.[6] Furthermore, MIGS are an attractive management approach because of the reduced requirement for antiglaucoma medications, preserving the health and functionality of the ocular surface.[7] The first MIGS device approved by the US Food and Drug Administration (FDA) was the iStent Trabecular MicroBypass Stent (Glaukos, Laguna Hills, CA, USA) for treatment of mild-to-moderate open-angle glaucoma.[8] Multiple studies have demonstrated the safety and efficacy of iStent when combined with phacoemulsification cataract surgery.[9] The iStent has also been combined with endoscopic cyclophotocoagulation (ECP) along with phacoemulsification cataract surgery in a triple procedure referred to as ICE2 which demonstrates superior short-term safety and efficacy compared with iStent and phacoemulsification alone.[10]

MIGS have become a rapidly evolving area of research and clinical interest with new devices entering the market, including newer approaches referred to as 'Minimally invasive bleb surgery' (MIBS). The first of this type to be approved by FDA was XEN-45 Gel Stent (Allergan, Inc., Dublin, Ireland).[11] It is an ab interno implantation device with a length of 6 mm and a lumen of 45 µm, and creates a passage for aqueous humour from the anterior chamber to the subconjunctival space, thus forming a bleb.[12,13] Similarly, another successfully used system is the PreserFlo MicroShunt (PMS; Santen, Osaka, Japan) (formerly known as the InnFocus MicroShunt). The device is composed of poly(styrene-block-isobutylene-block-styrene) which is the bioinert synthetic substance known as SIBS. It has an *ab externo* technique of implantation, and has a length of 8.5 mm, an outer diameter of 350 µm and a lumen of 70 µm. PMS has been evidenced as a safe and effective device for reducing IOP as well as the need for antiglaucoma medications.[14]

The growing number of devices has necessitated evaluations to identify subtle differences in outcomes between treatments. Such evaluations may help provide indications for the most suitable approaches on a case-by-case basis. For example, the goal should be to individualise the treatment by matching the surgical benefits with the disease stage. Few direct comparisons are available in the literature. One such study comparing iStent and ICE2 showed that ICE2 offered superior IOP-reducing properties.[10] Similarly, two bleb-forming procedures (PMS and XEN-45) have been compared in a single study, which showed both to equally effective and safe.[15] To date, no comparison has been made between MIGS *versus* MIBS. The aim of this study was to compare the safety and clinical effectiveness of ICE2 procedure with the bleb-forming XEN-45 and PMS.

Methods

This report is a retrospective review of patients undergoing either of the three MIGS/MIBS procedures, with or without combined phacoemulsification surgery from July 2016 to May 2020 by a single surgeon at Queen Victoria Hospital National Health Service (NHS) Foundation Trust, UK. The study was approved by Queen Victoria Hospital Clinical Research and Audit Department (ID: QVH503; date: 7 May 2020) and adhered to the tenets of Helsinki declaration. As this review uses retrospective data from routine clinical practice, the need for consent was waived by the institutional review board.

Inclusion criteria to list patients for MIGS or MIBS were as follows: treated (on topical medication or previous selective laser trabeculoplasty) ocular hypertension or mild-to-moderate glaucoma. All patients attended a baseline visit prior to surgery. Clinical measurements at this visit included IOP using the Goldmann Applanation Tonometry, visual field examination with the Humphrey Field Analyser (Carl Zeiss Meditec, Dublin, CA, USA) and best-corrected visual acuity (BCVA) in LogMAR. Detailed history was also recorded including number of antiglaucoma medications, lens status, glaucoma type and patient demographics. Clinical decision-making regarding the type of device selected for surgery is complex and based on a range of factors, including but not limited to clinical features, device availability and patient preferences. In general, when a lower target IOP is required, then PMS or XEN-45 is the preferred candidates, whereas if a slightly higher IOP is acceptable, then ICE2 is usually preferred. In addition, ICE2 is often preferred when combined cataract removal is required. The latest generation of iStent (iStent inject W) was used in ICE2 procedures.

Table 1. Baseline distribution of categorical variables including sex, eye, concurrent cataract surgery, lens status and type of glaucoma is compared between the three treatment groups.

		ICE2 (*N* = 162)	PMS (*N* = 48)	XEN-45 (*N* = 37)	Total
Sex	Female	95 (58.6%)	23 (48%)	20 (54%)	138
	Male	67 (41.4%)	25 (52%)	17 (46%)	109
Eye	Left	75 (46.3%)	24 (50%)	20 (54%)	119
	Right	87 (53.7%)	24 (50%)	17 (46%)	128
Concurrent cataract surgery	Yes	159 (98.1%)	7 (14.6%)	8 (21.6%)	174
	No	3 (1.9%)	41 (85.4%)	29 (78.4%)	73
Lens status	Phakic	159 (98.1%)	9 (18.75)	21 (56.8%)	189
	Pseudophakia	3 (1.9%)	38 (79.1%)	16 (43.2%)	57
	Aphakic	0	1 (2.08%)	0	1
Type of glaucoma	POAG	126 (77.7%)	36 (75%)	29 (78%)	191
	SOAG	2 (1.2%)	8 (16.6%)	3 (8%)	13
	NTG	10 (6.2%)	2 (4.2%)	0	12
	OHT	4 (2.5%)	0	0	4
	PACG	20 (12.3%)	2 (4.2%)	3 (8%)	25

ICE2, iStent combined with endoscopic cyclophotocoagulation; NTG, normal tension glaucoma; OHT, ocular hypertension; PACG, primary angle closure glaucoma; PMS, PreserFlo MicroShunt; POAG, primary open-angle glaucoma; SOAG, secondary open-angle glaucoma.

Concentration of mitomycin C (MMC) used in PMS and XEN-45 was 0.2 or 0.4 mg/ml. MMC was given by subconjunctival injection for XEN-45 and was applied directly to the area with sponges after dissection in PMS.

Patients were followed over a 2-year period with clinic visits scheduled at 7 days, 1 month, 3 months, 6 months, 12 months, 18 months and 24 months from the date of surgery. IOP, BCVA and number of medications were recorded at each visit, whereas visual fields were completed at 12 and 24 months.

Statistical analysis was performed using SPSS version 27.0 (SPSS Inc., Chicago, IL, USA), and the data were plotted using RStudio ggplot2 packages (Boston, MA, USA). Average IOP, BCVA, number of drops and mean deviation (MD) visual field were compared between the groups (ICE2 *versus* PMS *versus* XEN-45) using the Kruskal–Wallis test. Within group, comparisons were performed using paired *t* tests or the Wilcoxon signed-rank test.

Results

Overall, 247 eyes of 247 patients were included in the analysis. Of these, 162 eyes (65.6%) had the ICE2 procedure with iStent inject W, 48 eyes (19.4%) had PMS implanted *ab externo* and 37 eyes (15%) had XEN-45 implanted *ab interno*. Patient demographic and baseline details are shown in Table 1.

Concurrent cataract surgery was performed in only 14.5% and 22% of patients in PMS and XEN-45 groups, respectively, compared with 98% undergoing ICE2. Most patients in the PMS group (79.1%) were pseudophakic, whereas almost all patients undergoing ICE2 (98.1%) were phakic at the time of surgery. The distribution of phakic and pseudophakic was mostly balanced in the XEN-45 group (56.8% *versus* 43.2%). Primary open-angle glaucoma (POAG) was the most common type of glaucoma indication for all three procedures.

As shown in Table 2, age profiles were similar across the three treatment groups (Kruskal–Wallis

Table 2. Average (mean value and standard deviation) measurements at baseline across treatment groups.

	ICE2 (*N* = 162)	PMS (*N* = 48)	XEN-45 (*N* = 37)	*p* value
Age (years)	77.4 ± 6.9	74.6 ± 11.9	76.3 ± 8.3	0.16
IOP (mmHg)	18.5 ± 4.1	20.5 ± 7.4	19.9 ± 4.5	0.17
BCVA	0.28 ± 0.2	0.36 ± 0.4	0.23 ± 0.2	0.25
Visual field MD (dB)	−7.2 ± 6.2	−14.7 ± 7.7	−9.4 ± 5.8	<0.001*
Number of drops	2.0 ± 1.0	2.9 ± 0.8	2.9 ± 0.7	<0.001*
Acetazolamide	3 (1.8%)	6 (12.5%)	1 (5%)	

BCVA, best-corrected visual acuity; dB, decibels; ICE2, iStent combined with endoscopic cyclophotocoagulation; IOP, intraocular pressure; MD, mean deviation; mmHg, millimetre of mercury; PMS, PreserFlo MicroShunt. * denotes statisitcally significant *p* value (< 0.05).

Table 3. Prior glaucoma treatments between the three treatment groups.

	ICE2 (*N* = 162)	PMS (*N* = 48)	XEN-45 (*N* = 37)
SLT	20 (12%)	5 (10.4%)	1 (2.7%)
Trabeculectomy	1 (0.6%)	6 (12.5%)	1 (2.7%)
CYPASS	1 (0.6%)	2 (4%)	0
ICE2	0	1 (2%)	0
XEN-45	0	1 (2%)	0
Drainage device	0	1 (2%)	0

ICE2, iStent combined with endoscopic cyclophotocoagulation; PMS, PreserFlo MicroShunt; SLT, selective laser trabeculoplasty.

test; $p = 0.16$). BCVA at baseline was also similar on average between the groups (Kruskal–Wallis test; $p = 0.25$). Baseline IOP was higher on average for patients in the XEN-45 and PMS groups compared with ICE2; however, measurements across the groups were not statistically significantly different (Kruskal–Wallis test; $p = 0.17$). Patients in the ICE2 group were taking less antiglaucoma medications at baseline compared with the XEN-45 and PMS groups (Kruskal–Wallis test; $p < 0.001$). Patients in the PMS group had greater visual field damage as determined by the Humphrey MD (−14.7 ± 7.7 dB) compared with patients undergoing ICE2 (−7.2 ± 6.2 dB) or XEN-45 (−9.4 ± 5.8 dB) which was statistically significant ($p < 0.001$).

A higher proportion of patients undergoing PMS had undergone prior glaucoma treatments. For example, 12.5% of patients had experienced failed filtration surgery compared with just 2.7% and 0.6% in the XEN-45 and ICE2 groups, respectively. Prior glaucoma treatments are shown in Table 3.

All three procedures had good safety intraoperatively profile. In the PMS group, one patient had conjunctival buttonhole during the surgery which was successfully managed without any postoperative leak. None of the patients had any postoperative spikes of IOP.

As shown in Table 4, 1 week postoperatively, all three groups experienced a reduction in IOP with no statistically significant differences in IOP values between the groups at day 7 (Kruskal–Wallis test; $p = 0.33$). Pairwise comparison of change in IOP between baseline and day 7 showed the only statistically significant difference to be between the ICE2 and PMS groups (median reduction = 5 mmHg *versus* 9 mmHg, respectively; $p = 0.003$). Similarly, average percentage change in IOP from baseline was statistically significantly greater for the PMS group (42 ± 53%) compared with the ICE2 group (28 ± 19%) at day 7 (Kruskal–Wallis test; $p < 0.001$). Percentage change in IOP from baseline was comparable across all groups at 6, 12 and 24 months. As shown in Figure 1, reduction in IOP was consistent for all treatment groups across the 24 months. IOP reduction in ICE2, PMS and XEN-45 groups at 12 months was 4.6, 7.0 and 5.6 mmHg, respectively. IOP reduction at 24 months remained stable across all groups, in which average values were 5.1, 8.2 and 6.8 mmHg for ICE2, PMS and XEN-45 groups, respectively.

BCVA remained mostly stable over the 2-year time frame across treatment groups (Table 5 and

Table 4. Mean value and standard deviation (±) IOP values (mmHg) between groups over 24 months.

		ICE2	PMS	XEN-45
Timepoint	Baseline	18.5 ± 4.1	20.5 ± 7.4	19.9 ± 4.5
	Day 7	13.1 ± 3.3	10.1 ± 6.2	10.0 ± 4.2
	Month 1	13.7 ± 4.5	11.9 ± 5.5	13.1 ± 5.3
	Month 3	13.5 ± 2.7	10.0 ± 3.9	16.3 ± 5.0
	Month 6	13.9 ± 2.9	12.6 ± 1.5	14.4 ± 3.7
	Month 12	13.9 ± 3.1	13.5 ± 4.4	14.3 ± 1.8
	Month 18	14.3 ± 3.3	13.6 ± 3.0	16.0 ± 5.2
	Month 24	13.4 ± 3.0	12.3 ± 4.0	13.1 ± 4.3
Average reduction from baseline	Day 7	5.4 $p < 0.001$*	10.4 $p < 0.001$*	9.9 $p < 0.001$*
	Month 6	4.6 $p < 0.001$*	7.9 $p < 0.001$*	5.5 $p = 0.002$*
	Month 12	4.6 $p < 0.001$*	7.0 $p < 0.001$*	5.6 $p < 0.001$*
	Month 24	5.1 $p < 0.001$*	8.2 $p < 0.001$*	6.8 $p < 0.001$*

ICE2, iStent combined with endoscopic cyclophotocoagulation; PMS, PreserFlo MicroShunt.
* denotes statisitcally significant p value (< 0.05).

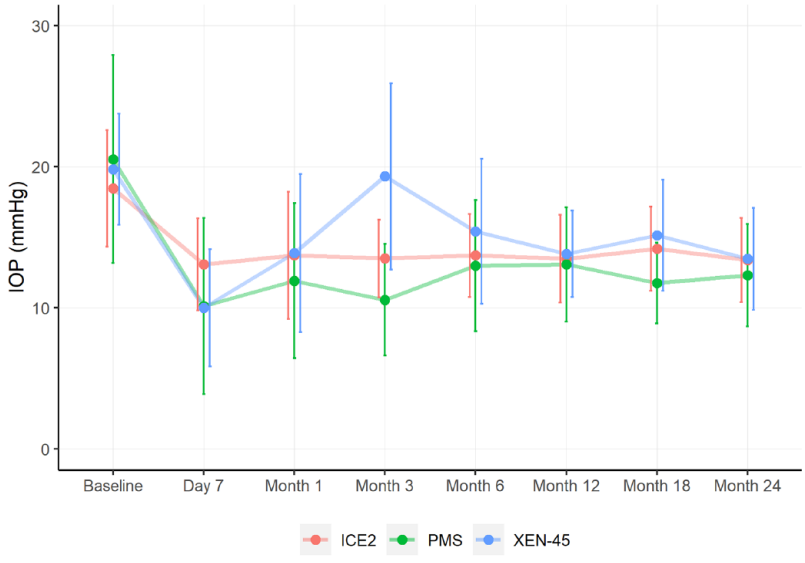

Figure 1. Average and standard deviation IOP measurements (mmHg) across treatment groups over the 24-month study period.
ICE2, iStent combined with endoscopic cyclophotocoagulation; IOP, intraocular pressure; PMS, PreserFlo MicroShunt.

Table 5. Mean value and standard deviation (±) best-corrected visual acuity (BCVA) in LogMAR between groups over 24 months.

		ICE2	PMS	XEN-45
Timepoint	Baseline	0.28 ± 0.2	0.36 ± 0.4	0.27 ± 0.3
	Day 7	0.14 ± 0.1	0.45 ± 0.4	0.20 ± 0.2
	Month 1	0.16 ± 0.2	0.36 ± 0.3	0.17 ± 0.2
	Month 3	0.13 ± 0.1	0.39 ± 0.2	0.17 ± 0.2
	Month 6	0.13 ± 0.2	0.34 ± 0.3	0.21 ± 0.25
	Month 12	0.12 ± 0.1	0.40 ± 0.4	0.18 ± 0.2
	Month 18	0.10 ± 0.1	0.33 ± 0.14	0.16 ± 0.1
	Month 24	0.12 ± 0.1	0.33 ± 0.3	0.20 ± 0.2
Average change from baseline	Day 7	0.14 $p < 0.001$*	−0.09 $p < 0.001$*	0.07 $p = 0.34$
	Month 12	0.16 $p < 0.001$*	−0.04 $p = 0.23$	0.09 $p < 0.006$*
	Month 24	0.16 $p < 0.001$*	0.03 $p = 0.44$	0.07 $p < 0.04$*

ICE2, iStent combined with endoscopic cyclophotocoagulation; PMS, PreserFlo MicroShunt. * denotes statisitcally significant p value (< 0.05).

Figure 2). An initial decline in BCVA was observed in patients receiving PMS which was regained after 1 month and remained stable at 24 months. There was a statistically significant difference in BCVA at 24 months between patients in the ICE2 compared with the PMS group (0.12 *versus* 0.33 LogMAR; $p = 0.002$). This could be explained by a larger proportion of PMS patients being pseudophakic at baseline (79.1%) compared with the ICE2 group (1.9%); thus, patients in the latter group are likely to yield greater improvement in BCVA because of the removal of clinically significant cataract.

As shown in Table 6, a mean reduction in number of antiglaucoma medications was observed across all groups at 24 months. The PMS group achieved the largest decline in medication usage between baseline a 24-month follow-up (2.9 *versus* 0.9; $p < 0.001$). There was no statistically significant difference in the number of antiglaucoma medications being used between groups at 24 months (Kruskal–Wallis test; $p = 0.43$). Although there was a reduction in the average number of drops in the XEN-45 group, drop usage gradually increased after 12 months. At 12 months, the proportion of patients who were drop-free was 18%, 47% and 31% for the ICE2, PMS and XEN-45 groups, respectively. Similarly, the proportion of patients drop-free at 24 months was 20%, 39% and 32% between the groups.

Visual fields were maintained during the 24-month period across all groups. Average [95% confidence interval] MD values at baseline and 24 months were −7.2 [−8.2 to −6.2] dB and −5.7 [−6.9 to −4.4] dB in the ICE2 group (Wilcoxon signed-rank test; $p = 0.48$). Similarly, MD values between baseline and 24 months were comparable for the PMS (−14.7 [−17.2 to −12.1] dB *versus* −14.0 [−18.9 to −9.2]; $p = 0.99$) and XEN-45 (−10.0 [−12.6 to −7.5] *versus* ± 10.8 [−14.5 to −7.0]; $p = 0.22$) groups. Twenty-four-month visual field follow-up data, however, were available for only 47.5%, 27.1% and 51.4% of patients undergoing ICE2, PMS and XEN-45, respectively.

As shown in Table 7, 12 (27.2%) patients required five Fluro Uracil (5-FU) injections in the PMS groups after 3 months. There were four (8.3%) occasions in which bleb needling was required and four (8.3%) instances of bleb

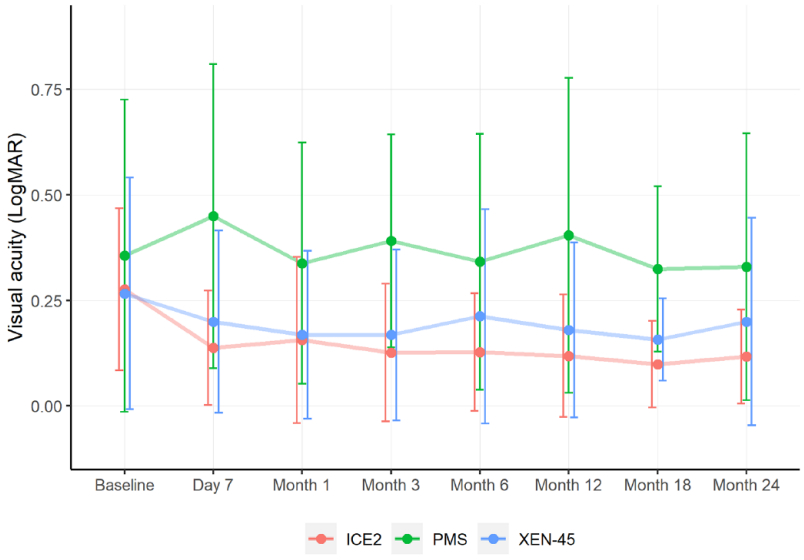

Figure 2. Average and standard deviation BCVA measurements (LogMAR) across treatment groups over the 24-month study period.

Table 6. Mean value and standard deviation (±) number of antiglaucoma medications between groups over 24 months.

		ICE2	PMS	XEN-45
Timepoint	Baseline	2.0 ± 1.0	2.9 ± 0.8	2.9 ± 0.7
	Day 7	1.8 ± 1.1	0.3 ± 0.1	0.0 ± 0.0
	Week 5	1.6 ± 1.1	0.4 ± 0.9	0.3 ± 0.5
	Month 3	1.5 ± 1.1	0.7 ± 1.2	0.3 ± 0.8
	Month 6	1.7 ± 1.1	1.5 ± 1.3	1.1 ± 1.0
	Month 12	1.3 ± 1.1	0.8 ± 1.1	1.6 ± 0.8
	Month 18	1.2 ± 1.1	1.6 ± 0.9	1.0 ± 1.7
	Month 24	1.4 ± 1.1	0.9 ± 1.1	1.9 ± 1.1
Average reduction from baseline	Day 7	0.6 $p = 0.001$*	2.6 $p < 0.001$*	2.9 $p < 0.001$*
	Month 12	0.7 $p < 0.001$*	1.3 $p < 0.001$*	1.3 $p < 0.001$*
	Month 24	0.6 $p < 0.001$*	2.0 $p < 0.001$*	1.0 $p = 0.001$*

ICE2, iStent combined with endoscopic cyclophotocoagulation; PMS, PreserFlo MicroShunt. * denotes statisitcally significant p value (< 0.05).

revision among PMS patients. In the XEN-45 group, 10 (27%) patients underwent 5-FU injections and a higher proportion ($N = 12$; 32%) required bleb needling. Bleb revision was comparable with PMS, and only one (2.7%) patient needed replacement of XEN with PMS.

Table 7. Postoperative surgical/laser interventions between groups.

	ICE2 (*N* = 162)	PMS (*N* = 48)	XEN-45 (*N* = 37)
Day 7	0	0	5-FU – 1 (2.7%)
Months 1–3	0	5-FU – 12 (27.2%) Bleb revision – 2 (4.2%)	5-FU – 6 (16.2%) Bleb needling – 6 (16.2%) Bleb revision – 2 (5.2%) XEN ligation – 1 (2.7%)
Month 6	0	Bleb needling – 2 (4.2%) Bleb revision – 1 (2.1%)	5-FU – 3 (8.1%) Bleb needling – 4 (10.8%) SLT – 1 (2.7%)
Month 12	0	Baerveldt tube – 1 (2.1%) Bleb revision –1 (2.1%) Replacement – 1 (2.1%)	Bleb revision – 1 (2.7%) Bleb needling – 1 (2.7%) SLT – 1 (2.7%)
Month 18	0	0	Bleb needling – 1 (2.7%) SLT – 1 (2.7%)
Month 24	SLT – 1 (0.6%)	0	SLT – 1 (2.7%) XEN removal plus PMS – 1 (2.7%)

5-FU, five Fluro Uracil; ICE2, iStent combined with endoscopic cyclophotocoagulation; PMS, PreserFlo MicroShunt; SLT, selective laser trabeculoplasty.

In terms of postoperative complications, six patients in the ICE2 group had cystoid macular oedema (CMO), which successfully resolved after 4 weeks with nonsteroid anti-inflammatory drops. One case had prolonged postoperative inflammation which successfully resolved with good vision and IOP with topical steroid which was slowly tapered. One XEN-45 patient had CMO, which also resolved after 4 weeks. In the PMS group, one patient developed suture-related keratitis which was successfully treated. One patient had CMO, which also resolved without any persistent effect on vision. One patient developed branch retinal vein occlusion, which was deemed unlikely to be as a direct complication of the procedure.

No data on endothelial cell count were available in this retrospective case series for patients receiving ICE2 or XEN-45. Two-year follow-up data for central endothelial cell count were available for 14 (29.2%) PMS patients. For these patients, average central endothelial cell count was 1963.2 ± 429 at baseline and remained mostly stable by the end of the study observation at 1930.1 ± 538 (Wilcoxon signed-rank test; $p = 0.98$).

Discussion

While glaucoma surgery has evolved significantly over the last 20 years, trabeculectomy predominantly remains the treatment of choice for progressing moderate to advanced POAG.[16–18] The National Institute for Health and Care Excellence (NICE) has recently recognised the role of MIGS devices in glaucoma management and has published guidance on their usage, with special arrangements for clinical governance, consent and audit. Within the evidence-based recommendations, however, NICE highlights that there are many devices available on the market; yet, evidence on the safety and efficacy of the procedure is predominantly from one device.[19,20] Introduction of different MIGS/MIBS now offers a substitute for trabeculectomy with a growing body of evidence supporting clinical adoption of the procedures.[21] There, however, remain significant subjectivity and an absence of research data,[22] highlighting the need for comparative studies to better assess outcomes. The purpose of this analysis was to compare outcomes related to safety and clinical effectiveness between patients undergoing ICE2, XEN-45 and PMS.

Our analysis showed greater average IOP reduction was observed in the PMS and XEN-45 groups at the first week follow-up compared with ICE2. At the 1-month visit, however, the initial decline in IOP among these groups had diminished, and average measurements were similar across all treatment groups beyond 6 months.

These findings are similar to a retrospective comparative case series which demonstrated XEN-45 and PMS to have similar IOP-lowering profiles in glaucoma patients experiencing visual field progression on maximum tolerated therapy.[15] Moreover, average IOP reduction of 5.5 mmHg at 6 months in the PMS group is similar to recently published comparison between PMS and trabeculectomy in patients with inadequately controlled IOP on maximum therapy.[21]

Previous studies have shown PMS and XEN-45 to be effective surgical approaches in eyes with previously failed trabeculectomy.[23,24] In this analysis, PMS was performed after failed trabeculectomy in 12.5% of cases. IOP-lowering at 12 and 24 months was 7.0 and 7.1 mmHg (PMS group), respectively, and 5.6 and 6.8 mmHg (XEN-45 group), respectively. These findings suggest PMS could be effective in lowering IOP in eyes in which previous surgical intervention has been unsuccessful, therefore representing a viable choice as a second surgery. Further research, however, is needed to understand the impact of previous laser and surgical interventions on clinical outcomes across all of the devices in this study. Notwithstanding, careful preoperative assessment and targeted stent placement remain important factors in the IOP-lowering properties of the procedures.[23]

Although IOP-lowering was effective after failed trabeculectomy in both PMS and XEN-45 groups, a higher rate of postoperative surgical manipulation (i.e. bleb needling or revision) was required for XEN-45 patients compared with PMS. This finding aligns with previous retrospective studies which indicate bleb needling or surgical revision is required in over 40% of cases within 1 year of XEN-45 implantation.[25] Possible complications associated with bleb needling include flat anterior chamber, hyphema, choroidal effusion, conjunctival buttonhole and blebitis.[26] Postoperative IOP reduction at day 1 is a good predictor for needling in patients undergoing XEN-45, whereas type or severity of glaucoma does not influence the probability of needling or the number of needling interventions required.[27] Patients considering XEN-45 should be cautioned about the high probability of requiring postoperative bleb intervention and the risks associated with this procedure.

Subconjunctival injections (5-FU) were most commonly performed between 1- and 3-month follow-up, administered in 27.2% and 16.2% patients in the PMS and XEN-45 groups, respectively. 5-FU injections were not considered complications of surgery, but rather a strategy for postoperative optimisation to reduce the scarring process. This is because of growing evidence that the use of antimetabolites such as 5-FU for bleb management following MIBS improves wound healing,[28] and as a result is becoming the standard of care.[29]

At both 12- and 24-month follow-ups, patients in the ICE2 and XEN-45 groups had improved BCVA compared with baseline. There were no changes in BCVA for PMS patients, except for a statistically significant worsening of BCVA at day 7 compared with baseline which was regained at subsequent visits. On average, patients undergoing PMS had worse BCVA at baseline and had more advanced visual field loss. PMS is typically performed independently of phacoemulsification; in this analysis, concurrent cataract surgery was performed in only 14.6% of cases. BCVA outcomes in this analysis can also be explained by the majority of PMS patients being pseudophakic (79.1%) at the time of surgery.

A reduction in the average number of antiglaucoma medications was observed across all three treatment groups. Patients undergoing ICE2 were typically using less medications prior to surgery than PMS and XEN-45 patients which was expected given the more advanced glaucoma severity in the latter groups. Average reduction in medications was initially most pronounced in the PMS and XEN-45 groups. After 24 months, however, average medication usage was 1.9 ± 1.1 in the XEN-45 group compared with 1.4 ± 1.1 and 0.9 ± 1.1 in the ICE2 and PMS groups, respectively. Previous studies have demonstrated XEN-45 and PMS to have a similar impact on the number of antiglaucoma medications required postoperatively at 1 and 2 years, with no differences in the proportions of patients achieving drop-free status.[15] This finding highlights the requirement for further comparative studies with larger sample sizes and longer follow-up.

Postoperative complications in all three treatment groups were transient and could be resolved with office-based interventions without implications for residual vision. This finding provides further evidence to compliment the emerging literature supporting PMS, XEN-45 and ICE2 as safe procedures with minimal vision–threatening complications.[10,30,31]

This study had a number of limitations. Data were collected from a single centre in which all surgeries were performed by the same surgeon, limiting the generalisability of the findings. Because of the retrospective design and real-world nature of this study, the loss to follow-up between baseline and 24 months in some cases was considerable. For example, of the 162 patients undergoing ICE2, follow-up data were available for 150 (92.6%) patients at 12 months and 87 (53.7%) patients at 24 months. Of 48 PMS patients, data were available for 47 (97.9%) patients at 12 months and 27 (56.3%) patients at 24 months. Finally, of 37 XEN-45 patients, data were available for 35 (94.6%) patients at 12 months and 34 (91.9%) patients at 24 months. Data relating to endothelial cell count were unavailable for the majority of patients preventing comparisons between treatment groups. Consideration for the health of the corneal endothelial cell health has a role in the decision-making process when planning glaucoma management; therefore, the absence of this analysis is a limitation. Moreover, the retrospective nature of this study means that a power calculation was not possible; rather, our aim was to assess outcomes in a real-world sample of consecutive patients attending the Queen Victoria Hospital glaucoma service. This article will provide useful data to help power future trials in this area of glaucoma surgery. A further limitation is the differences in glaucoma severity among the treatment groups, for example, patients in the PMS group had more advanced glaucoma than the XEN-45 and ICE2 groups. As such, it is recommended that the findings are best interpreted within the context of a patients' particular disease stage at the time of surgery.

Multicentre randomised clinical trials remain the gold standard for obtaining high-quality evidence on the safety and efficacy of medical interventions, and there is currently an unmet need for more comparative data in the literature surrounding MIGS.[22] In the absence of this level of evidence, real-world studies can provide complementary evidence which better reflect clinical experience across a broader and more diverse distribution of patients. Moreover, given the proliferation of devices entering the market, analyses such as these can aid postmarketing pharmacovigilance by providing surveillance of the devices which are becoming available to patients.

In summary, this retrospective review demonstrates the clinical effectiveness and safety profile of PMS, XEN-45 and ICE2. PMS showed the maximum effect in reducing IOP among patients with more severe stage disease. ICE2 was associated with less postoperative complications compared with PMS and XEN-45 but is typically performed in patients with less severe visual field damage using less antiglaucoma medications. PMS was associated with less postoperative bleb manipulations compared with XEN-45 after 24 months, suggesting it is advisable to warn patients undergoing XEN-45 about the likelihood of repeated intervention. In light of our results, ICE2 may be the first choice of intervention in phakic patients who have moderate uncontrolled glaucoma. PMS may be the preferred candidate in pseudophakic patients with moderate or advanced uncontrolled glaucoma as a standalone procedure, or in phakic patients with advanced uncontrolled glaucoma as a standalone or combined procedure. The research team are currently working on developing a smartphone application to guide surgeon decision-making when selecting the most appropriate MIGS/MIBS devices to enable clinicians to make faster and more comprehensive decision about glaucoma surgery.

Declarations

Ethics approval and consent to participate

The study was approved by Queen Victoria Hospital Clinical Research and Audit Department (ID: QVH503). Written consent for surgery was obtained from each patient.

Consent for publication

Not applicable.

Author contributions

Umair Qidwai: Conceptualisation; Data curation; Project administration; Writing – review & editing.

Lee Jones: Formal analysis; Project administration; Visualisation; Writing – original draft.

Gokulan Ratnarajan: Conceptualisation; Resources; Supervision; Writing – review & editing.

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ORCID iD

Lee Jones https://orcid.org/0000-0002-8030-1211

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