



Supplement
February 2022

GLAUKOS ISTENT *INJECT*[®] W SUPPLEMENT 2022



THE LONG-TERM DATA HAVE SPOKEN —
THE CASE FOR ISTENT *INJECT*[®] W FOR
MILD TO MODERATE PRIMARY OPEN-ANGLE GLAUCOMA

INTRODUCTION

Affecting an estimated 76 million people worldwide in 2020 (1), glaucoma is the leading cause of irreversible vision loss and the second leading cause of blindness worldwide (2). Open angle glaucoma (OAG) is the most common form, occurring in 74% of diagnosed glaucoma cases (3, 4). It is often seen in conjunction with cataract, with approximately one-in-five cataract patients also needing glaucoma medication (5).

These numbers present both a daunting challenge and a major opportunity. Elevated intraocular pressure (IOP) remains the major risk factor for glaucoma, and most current treatments, including pharmacological, laser and surgical interventions, focus on lowering IOP (6). Yet each have drawbacks.

Ocular hypotensive medications are reasonably safe and effective, but their pressure-reducing effects may wane over time, they can lead to ocular surface disease and conjunctival hyperemia, and adherence is notoriously problematic (7-11). Laser trabeculoplasty reliably reduces IOP but can lose effectiveness after three to five years (38-40) and some forms may induce inflammation in the intermediate term (12). And while incisional surgeries such as trabeculectomy and tube shunt implantation can reduce IOP dramatically, they expose patients to safety risks, including endophthalmitis and hypotony, that can persist for the lifespan of treatment (13-15).

TRABECULAR MICRO-BYPASS RESPONSE

These shortcomings sparked development of micro-invasive glaucoma surgery, including the original iStent®, the second generation iStent *inject*®, and the current iStent *inject*®W. Measuring 360 microns deep and wide, **iStent *inject* W is one of the smallest medical implants now available.** In bypassing the trabecular meshwork, which is often the major obstruction to fluid drainage in open-angle glaucoma (6), the stent is designed to restore physiological aqueous outflow directly to Schlemm's canal (16).

Multiple studies out five to eight years have shown that in select patients with ocular hypertension (OHT) or mild to moderate primary open-angle glaucoma (POAG) these devices reliably reduce IOP up to 40% or more while lessening the need for medications (6, 17, 23-25), and spare conjunctival tissue in the event incisional surgery is later needed. As a result, they are gaining popularity as an IOP-lowering option, according to Imran Masood Bsc, MB, ChB, MRCS(Ed), FRCOphth.

"The use of trabecular micro-bypass has increased massively over the last decade. There are **over 800,000 patients across the world who have been implanted with iStent technologies and it is the family of devices that has the largest evidence base behind it terms of efficacy and use** in various different scenarios; in combination with cataract surgery and as a standalone procedure (41)," said Mr Masood, who is a consultant ophthalmic surgeon and director of glaucoma service at Birmingham and Midland Eye Centre, director of the Birmingham

Institute of Glaucoma Research and honorary senior lecturer at the University of Birmingham, UK. He has extensive experience implanting the iStent, iStent *inject* and iStent *inject* W for patients with OHT and mild to moderate open-angle glaucoma.

REDUCED IOP, MEDICATION NEED

Whether **combined with cataract surgery or implanted as standalone procedure, studies show the iStent and iStent *inject* devices significantly reduce intraocular pressure (IOP) as well as the mean number of topical medications needed to control IOP.** In many cases, trabecular micro-bypass stenting eliminates the need for glaucoma medication entirely (3, 6, 17).

Reduced reliance on topical medications benefits patients in several ways. Taking fewer drops cuts the risk of ocular surface irritation, inflammation and tissue damage related to long-term exposure to topical medications and their preservatives, said Prof Cédric Schweitzer MD, of the Bordeaux University Hospital, France. Such complications are not only unpleasant but can even be debilitating for patients. They can reduce medication compliance and cut success rates for future glaucoma filtering procedures, increasing the risk of glaucoma progression and vision loss (7-11).

Trabecular micro-bypass stenting may also reduce diurnal IOP fluctuation, which may reduce progression risk (18). At the same time, **physiological episcleral backpressure may minimize the risk of hypotony** seen with more invasive glaucoma procedures including transscleral devices (18, 19).

Placed through a clear corneal incision, **iStent inject W is straightforward to implant** as a stand-alone glaucoma procedure or when combined with cataract surgery. With a wider base and improved injector, it is more elegant to implant than ever. For combined trabecular micro-bypass stenting with cataract surgery, **the procedure requires no additional scheduled follow up appointments over those of cataract surgery alone**, making it highly compatible with established cataract surgery workflow. And studies show adding iStent technologies to cataract surgery **is refractively neutral**, with visual outcomes similar to stand-alone cataract procedures (20). **They may also improve patients' quality of life** (21, 22).

"We know from a lot of studies and meta-analyses that the [iStent] is very useful in helping reduce medication burden and improve IOP control," Mr Masood said. "There has also been a lot of

work done on the issue of quality of life and ocular surface disease."

In this supplement we discuss the clinical cases and indications for stand-alone and combined cataract-iStent *inject W* surgery in select patients, including new five-year outcomes data from completed and ongoing studies of iStent *inject*. For qualified patients, iStent *inject W* may provide substantial clinical and lifestyle advantages, giving glaucoma and cataract surgeons a new tool to help prevent long-term vision loss while improving patient quality of life.

"We know from a lot of studies and meta-analyses that the [iStent] is very useful in helping reduce medication burden and improve IOP control," Mr Masood said. "There has also been a lot of work done on the issue of quality of life and ocular surface disease."

THE CASE FOR ISTENT *INJECT*® W PART 1 – LONG-TERM IOP REDUCTION

PROF HENGERER FINDS SUCCESS IN COMBINED AND STANDALONE PROCEDURES

Germany was the first country in which the iStent *inject*® was commercially available. As a result, "we are very happy that we can provide you with the insight of our five years' dataset because this is one of the longest running and most robust datasets to date," said Prof Fritz H Hengerer MD, PhD, Chief Medical Officer and Director of Ophthalmology at Bürgerhospital Eye Clinic, Frankfurt, Germany.

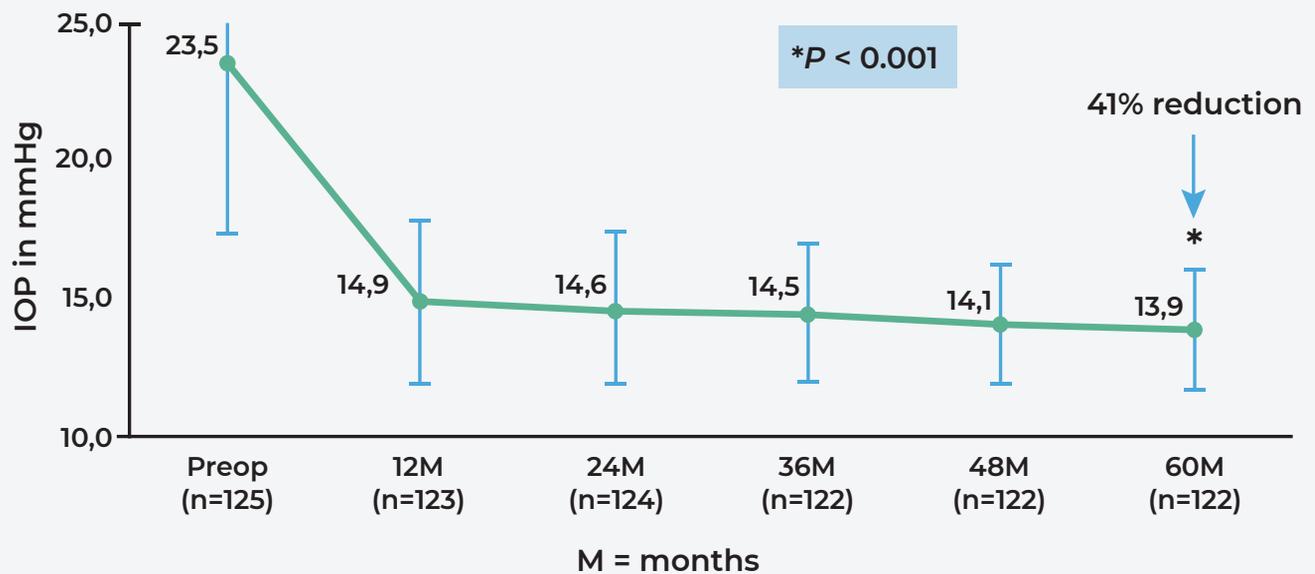
The ongoing results of the study were presented by Prof Hengerer during the Glaukos lunch symposium at the 2021 ESCRS Congress, at the World Glaucoma Congress and the American Academy of Ophthalmology, were compiled in conjunction with colleagues at the International Vision Correction Research Centre (IVCRC); the David J Apple International Laboratory of Ophthalmic Pathology; and the Dept of Ophthalmology of the University of Heidelberg.

The prospective **consecutive case series study evaluated 60-month efficacy and safety following iStent *inject* implantation in 125 glaucomatous eyes** with varying severities and surgical

histories at a large academic ophthalmology centre in Heidelberg, Germany (17). It is significant in part because it tracks data from a large cohort of patients who were implanted with the device either in combination with cataract surgery (combined, 81 eyes) or as a stand-alone procedure (standalone, 44 eyes) by the same surgeon, Prof Hengerer, in the same setting. As such, it **"enables validation of the long-term IOP- and medication-lowering potential of the stents independent from cataract extraction,"** Prof Hengerer said. Results of the same cohort have been previously reported (23-25).

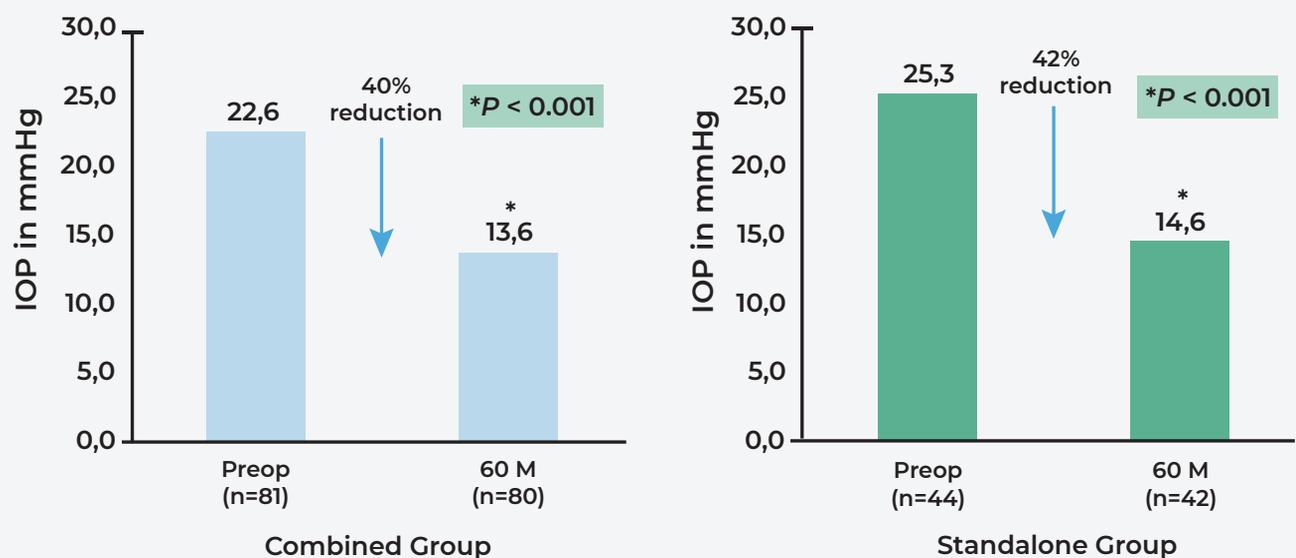
Demographics of the two groups were largely similar, though the stand-alone patients were more likely to have had previous glaucoma surgery than the combined patients, at 84.1% v 34.6% respectively. Most of both groups were on three to four IOP-lowering medications pre-operatively, at 70% v 56% for the stand-alone and combined groups respectively. Mean age for the overall cohort was about 72, varying from 40 to 88 years. Cup-to-disc ratios were similar at 0.8±0.1 for the stand-alone v 0.7±0.1 for the combined group, with visual fields -6.4±06.9dB for the stand-alone and -8.2.8±6.6dB for the combined.

Mean IOP Over 5 Years — Overall Cohort



Graphic 1. Mean IOP Over 5 Years – Overall Cohort (17)

Mean IOP at Preop and 60-Month Visits



Graphic 2. Mean IOP at Preop and 60-Month Visits by Group (17)

Mean five-year IOP reduction was similar for both groups. The combined cohort dropped to 13.9mmHg from 23.5mmHg preoperatively – a **reduction of 41%**. The standalone group saw a reduction to 14.6mmHg from 25.3mmHg, or 42%, while the combined group fell to 13.6mmHg from 22.6mmHg, or 40%.

“We can now see that IOP-lowering is not related to the cataract extraction alone; it is also related to the *iStent* technology,” Prof Hengerer said. His standalone data demonstrates that ***iStent inject***

works independently of cataract extraction. Further, his results in the cataract + *iStent inject* group are superior to published studies where only cataract extraction was performed.

“Importantly, these data were gathered prospectively in consecutive patients from the surgeon’s practice, making them broadly applicable in both combined and standalone surgical settings,” Prof Hengerer concluded.

“We can now see that IOP-lowering is not related to the cataract extraction alone; it is also related to the *iStent* technology.”

— Prof Hengerer

DR KLABE SEES REDUCED IOP OUT TO FIVE YEARS IN PRIVATE PRACTICE

Dr Hengerer’s results are mirrored by the experience of Dr Karsten Klabe MD, of Breyer, Kaymark and Klabe Eye Surgery in Dusseldorf, Germany, who is also a partner in the IVCRC. In a retrospective study of 164 eyes implanted with *iStent inject* followed for 2 to 5 years, mean IOP decreased from 18.5mmHg preoperatively to 16mmHg 1 month after surgery and to 15.5mmHg at month six, stabilising at that level for the remaining follow up (28).

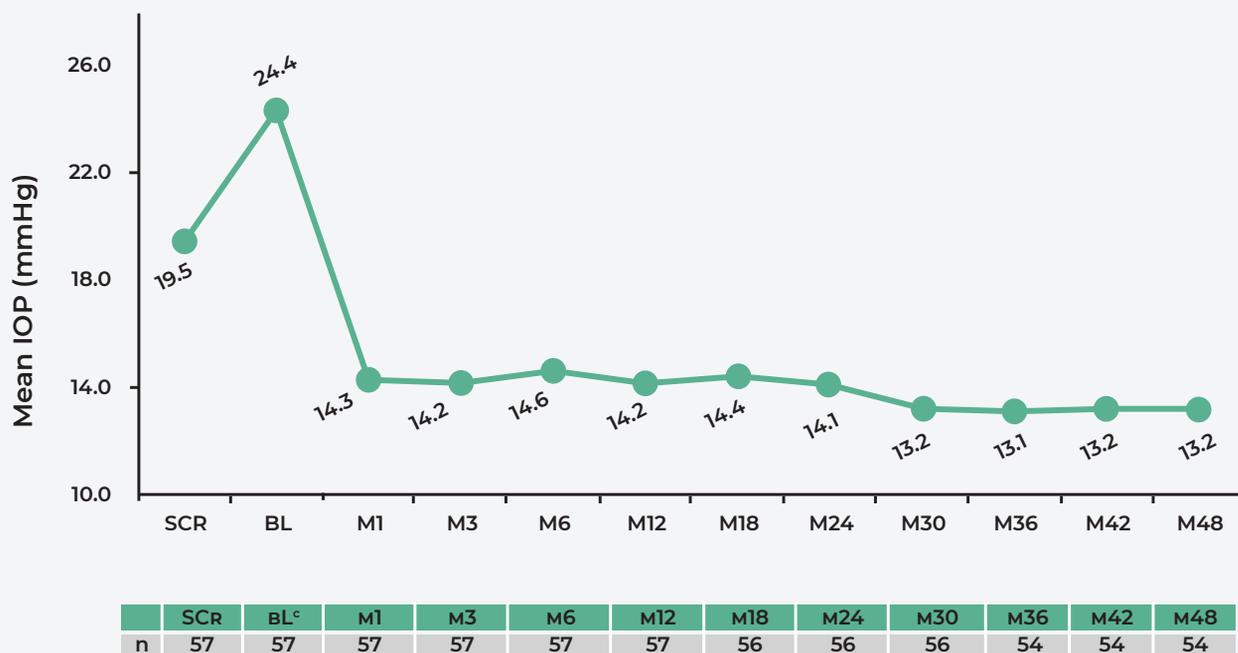
DR LINDSTROM SEES MEAN IOP DROP 46% AT 48 MONTHS IN STANDALONE IMPLANTS

In a prospective interventional study of 57 eyes in 57 patients on one pressure-lowering medication undergoing implantation of *iStent inject* without cataract surgery, mean IOP dropped 46% to 13.2±1.6 mmHg vs 24.4±1.3 mmHg preoperatively (p<0.0001) 48 months after surgery, according to a study published in 2020 by Dr Richard Lindstrom MD, of Minneapolis Eye Consultants, Minneapolis, USA. At month 48, eyes achieved an IOP reduction

“This prospective long-term study demonstrated safe and durable four-year IOP and medication reductions after implantation of second-generation *iStent inject* stents in eyes with OAG. Since stent implantation was completed as a standalone procedure, it was possible to assess the impact of the device alone, independent from the IOP-reducing impact of cataract surgery. The study intervention also included cessation of medication postoperatively. Due to these specifications, the observed 46% reduction in medication-free IOP can be attributed to the stents alone, without the confounding factors of cataract surgery or medication,” the report said.

“Outcomes were consistent with previous literature on *iStent inject* implantation either with or without concomitant cataract surgery,” the study concluded.

of ≥20% without medication versus preoperative washout IOP; and although they had eliminated medication, 81% of eyes still had an IOP reduction of ≥20% versus preoperative IOP on 1 medication. 95% of medication-free eyes had IOP ≤18mmHg and 82% had IOP ≤15mmHg (6).



Graphic 3. Mean intraocular pressure through 48 months postoperative (6)

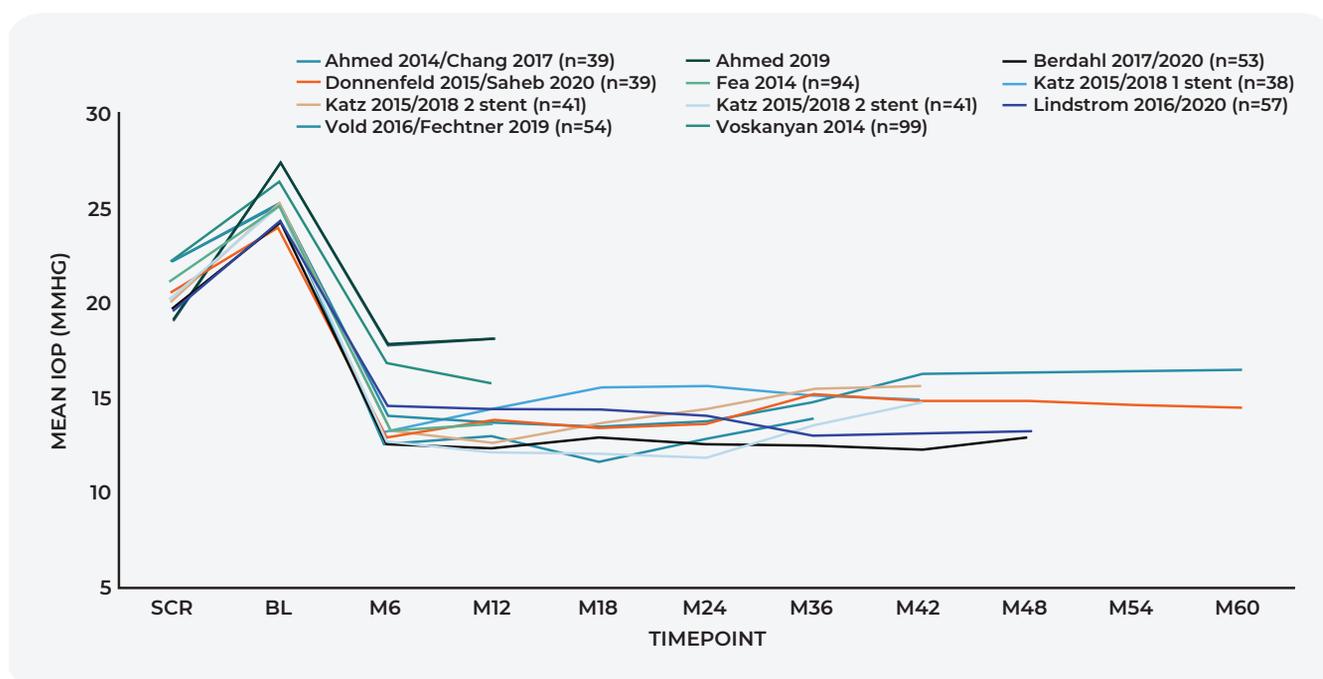
META-ANALYSIS FINDS MORE THAN 30% MEAN IOP REDUCTION IN STANDALONE ISTENT® IMPLANTATIONS FROM 6 TO 60 MONTHS

A review of **13 published studies involving a total of 778 eyes** by Prof Paul R Healey B(Med)Sc, MBBS (Hons) MMed (Clin epidemiology), PhD, of the University of Sydney Australia and colleagues, mean IOP fell 31.1% at 6 to 12 months post-operatively, 30.4% at 36 to 48 months, and 32.9% at 60 months. Eyes received either the first generation iStent or the second generation iStent *inject*. The pooled weighted mean reduction in intraocular pressure

from baseline across all studies at 6-12 months and 36-60 months post-stent implantation was 7.01mmHg and 6.59mmHg respectively (3).

“The results from these studies support the independent effect of the iStent Trabecular Micro-Bypass technology on intraocular pressure and medication burden over a duration of follow-up of up to five years,” the study said.

META-ANALYSIS SHOWS CONSISTENT IOP REDUCTION FOR STANDALONE ISTENT DEVICES.



Graphic 4. Mean IOP over time from included studies. BL indicates baseline (postwashout/medication free); IOP, intraocular pressure; M, month; SCR, screening (prewashout). Excludes data from 4 studies that did not perform a medication washout at baseline (3)

The weight of the evidence supporting IOP reduction using iStent technologies from these and other studies simply cannot be ignored. **“We have a lot of information on the long-term outcomes of iStent inject,”** said Prof José M. Martínez de la Casa MD, PhD, who heads the glaucoma department at Hospital Clínico San Carlos, Universidad Complutense, Madrid, Spain.

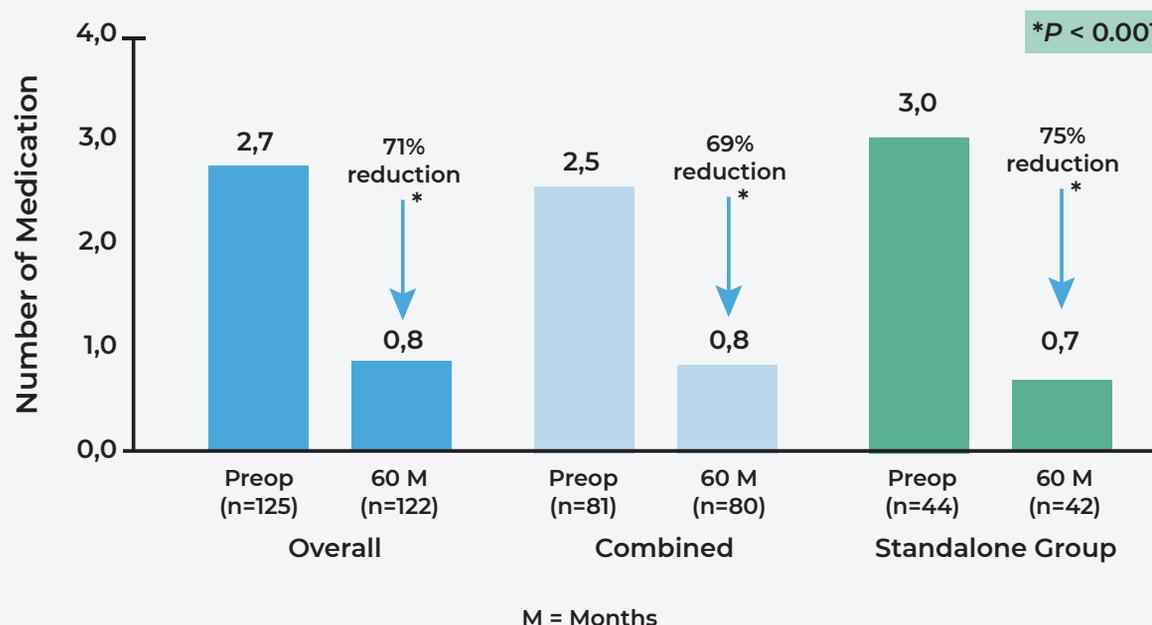
THE CASE FOR ISTENT INJECT® W PART 2 – LONG-TERM MEDICATION REDUCTION AND IMPROVED QUALITY OF LIFE

PROF HENGERER FINDS REDUCED MEDICATION BURDEN IN COMBINED AND STANDALONE CASES

In terms of long-term efficacy and improvements in patient quality of life, **reduction in medication burden may be just as important as the IOP reduction iStent inject and iStent inject W offer.** That’s because medication use – and with it, medication efficacy – decline as adherence drops (9-11) and reducing medications also may reduce OSD symptoms (8) and improve quality of life scores (21, 22).

In addition to a 41% reduction in IOP among a mixed cohort of 125 phaco-combined and stand-alone recipients of the iStent *inject*, Germany’s Prof Hengerer also observed a **71% reduction in the number of IOP-lowering medications required to control IOP.** Results were similar in the subgroups with mean medication use falling to 0.7 from 3.0, a 75% reduction, in the stand-alone group, and to 0.8 from 2.7 in the combined surgery group, a reduction of 69%.

Mean Glaucoma Medication Use Preop vs 60 Months



Graphic 5. Mean Glaucoma Medication Use Preop v 60 Months (17)

“Although the cohort had relatively high glaucoma medication burden preoperatively, nearly half of eyes were medication-free by 60 months, while mean IOP decreased by nearly 10mmHg,” Prof Hengerer said.

“So, we can conclude that the iStent *inject* implantation resulted in significant and sustained reductions in IOP and medication burden through five years. This is something which is very valuable for both our patients and for me as a surgeon, because this gives me the confidence that when we implant the iStent device, we are on a good side to reduce the IOP and can reduce the medications which lead to OSD,” Prof Hengerer said.

DR KLABE SEES MEDICATION USE DROP OUT TO 5 YEARS

Similarly, Dr Klabe saw a significant reduction in medication after implanting iStent *inject* in 164 eyes followed from 2 to 5 years. Pressure-reducing medications fell from a mean of 1.47, ranging from 0 to 4, before surgery to 0.17 to 0.23 at various points after surgery, with no patient requiring more than two medications, Dr Klabe said (28).

DR LINDSTROM SEES MEDICATION USE DROP TO 0 FROM 1 FOR 57 EYES OF 57 PATIENTS AT FOUR YEARS

In their four-year follow up of 57 patients on one medication receiving iStent *inject* as a standalone procedure, Dr Lindstrom and colleagues saw 3 subjects placed on medication at months 18, 30, and 32, respectively, but all remaining subjects remained free of medications (6).

ISTENT TECHNOLOGY IN A TYPICAL CASE AND AFTER FILTRATION SURGERY

PROF BECKERS LOWERS IOP AND IMPROVES VISUAL OUTCOMES

According to European Glaucoma Society guidelines, trabeculectomy is still the gold standard for treating open-angle glaucoma, but MIGS are an option at the surgeons’ choice. And iStent *inject* W is among the safest, said Prof Henny JM Beckers MD, PhD.

“It is a very straightforward procedure to do after a phacoemulsification,” said Prof Beckers, who heads the glaucoma clinic at the University Eye Clinic, Maastricht Medical Center, Netherlands. Compared with the second generation iStent *inject*, the new injector and wider flange of the iStent *inject* W device improve control during the procedure, enhancing the predictability of placement, which may improve results, she added.

Based on her extensive experience and research, Prof Beckers said the iStent *inject* W is most suitable for patients with mild to moderate stable OAG, and for patients on 2 or more IOP-lowering medications, particularly if non-adherence or intolerance are problems. Another procedure may be more suitable for fast progressing patients needing a very low IOP target, or for advanced cases, where IOP may spike post-op with the iStent, she said.

CASE STUDY – PSX GLAUCOMA

Prof Martínez de la Casa presented a case he said was representative of the results he sees with iStent *inject*.

A 73-year-old man with cataract and mild pseudoexfoliation glaucoma and OSD was treated with combined cataract surgery and iStent *inject* in October 2016. Five years after surgery his IOP was reduced to 18mmHg with one medication from 22mmHg with three medications before surgery, demonstrating the efficacy of the treatment. “He is quite stable and the quality of life of the patient has improved, too,” Prof Martínez de la Casa said.

PROF HEALEY’S META-ANALYSIS SEES REDUCTION OF ABOUT 1.0 MEDICATIONS FOR ISTENT IMPLANTS

While medication use was not consistently reported as an endpoint in the 13 studies of standalone iStent implants conducted by Australia’s Prof Healey, the study nevertheless estimated that medication use decline by 1.0 medication at 6-18 months and 1.2 medications at 36-60 months (3).

PIVOTAL STUDY SHOWS OSD AND VISION-RELATED ACTIVITIES IMPROVEMENT AFTER 24 MONTHS

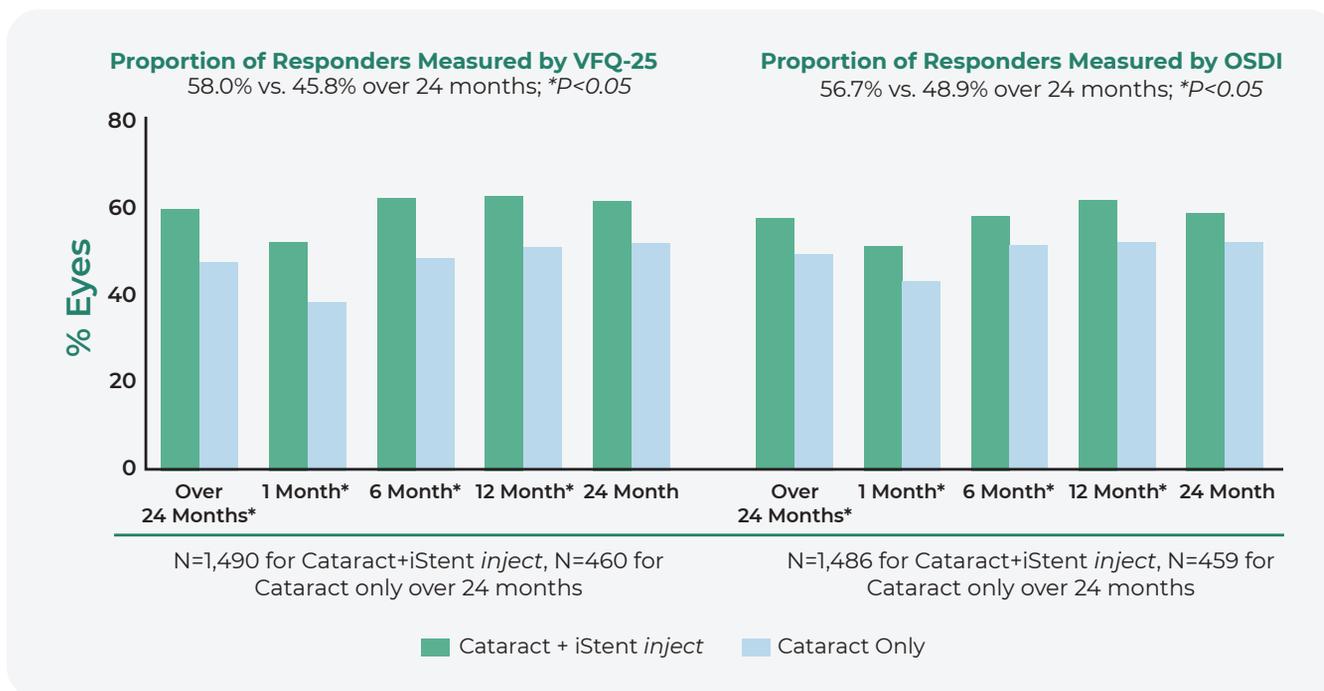
The reduction in medication commonly seen with iStent *inject* implantation may translate into improved quality of life.

In fact, a 24-month pivotal study comparing outcomes of iStent *inject* plus phaco to phaco alone by Thomas W Samuelson MD and colleagues found that the **combined procedure may improve ocular symptoms and vision-related activities more than cataract surgery alone.**

Involving 505 patients randomised three to one to combined or phaco alone surgery, the study found a higher percentage of responders reporting **improvement in the combined group on the Visual Function Questionnaire (VFQ-25) and the Ocular Surface Disease Index (OSDI)** at 1, 6, 12 and 24 months after surgery. Differences in response rates on the VFQ-25 were most pronounced in the General Vision, Ocular Pain and Driving subscales. (21)

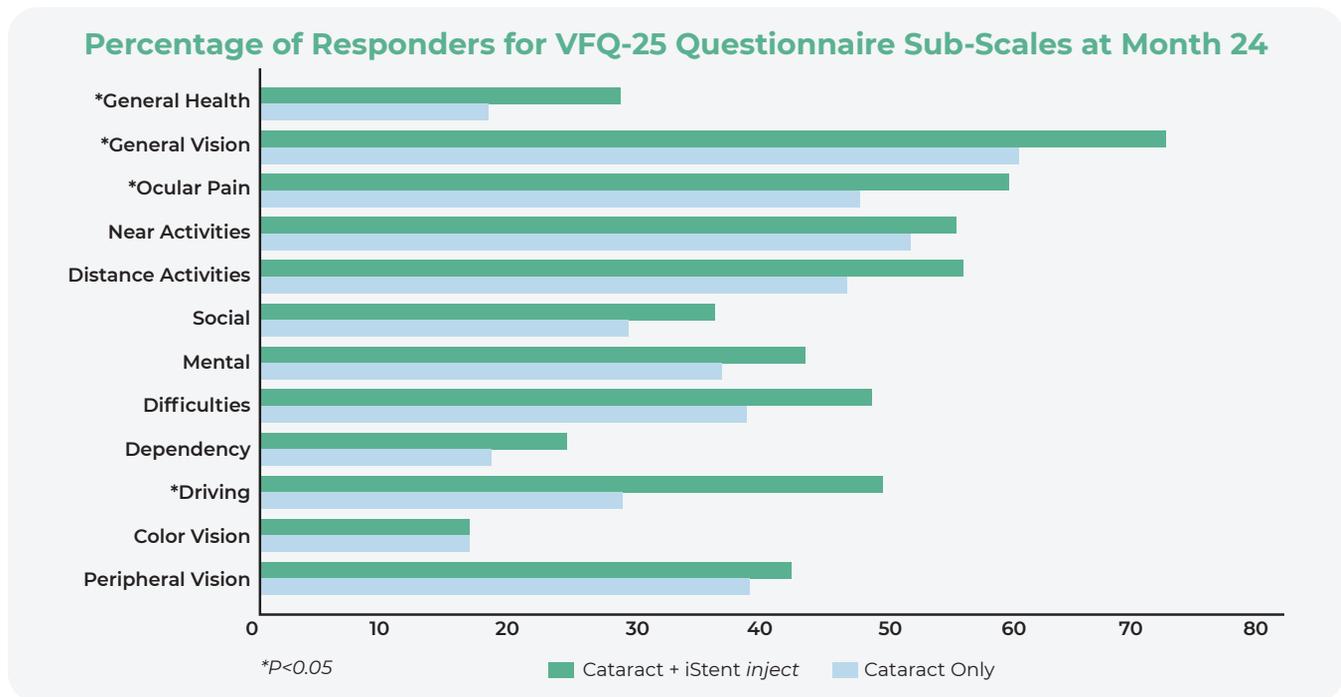
The study also found that **76.5% of combined surgery patients were completely medication free at month 24** compared with 62.6% in the phaco alone group. “Topical medication use increases ocular discomfort and fluctuating vision. **Improvements may be attributable to patients’ greater eye comfort from being medication-free,**” the study concluded (21).

PATIENT REPORTED OUTCOMES TO TWO YEARS



Graphic 6. Greater % of Patient Reported Outcomes Responders in iStent *inject* group vs. Cataract Only group(21)

SIGNIFICANT DIFFERENCES IN VISUAL FUNCTION



Graphic 7. Differences in VFQ-25 response rates most pronounced in General Vision, Ocular Pain, and Driving subscales (p<0.05)(21)

HOW ISTENT *INJECT*® W MAY IMPROVE THE OCULAR SURFACE

Glaucoma and ocular surface disease are often associated, and a greater use of glaucoma medication is associated with reduced medication compliance and tolerability, said Prof Cédric Schweitzer MD, of the Bordeaux University Hospital, France. “Micro-invasive glaucoma surgery (MIGS) was developed in part to address these issues.”

Among the studies Prof Schweitzer cited was a 2002 paper by Pisella and colleagues published in the British Journal of Ophthalmology showing that many symptoms of signs and symptoms of ocular toxicity, including burning/stinging and foreign body sensation were more than twice as common with preserved eye drops than preservative-free, though rates were still substantial with preservative-free formulations. Adverse reactions were also found to be dose-dependent and reversible when switching to preservative-free medications (29).

A 2011 study examining histological findings on cultured human trabecular meshwork and ciliary epithelial cells confirmed the cytotoxic effects of both glaucoma medications and preservatives (30). One implication is that medication use may adversely affect the outcomes of filtration surgery, Prof Schweitzer said.

The clinical implications for compliance are also significant, Prof Schweitzer added. In a 2003 study examining health quality of life outcomes by

Nordmann and colleagues, **62.4% of glaucoma patients randomly selected complained of at least one side effect that led to poorer medication compliance. Symptoms included burning and blurry vision.** Based on a representative French sample, poor vision related QoL was associated with topical drug side effects that also impact patient satisfaction and compliance,” the study found (31).

To study the impact of the iStent technology implantation on IOP reduction and glaucoma medication burden in a real-life setting without selection bias, Prof Schweitzer and colleagues conducted a prospective registry study from 2012 to 2018. As with many similar studies a long-term reduction in IOP and medication use were observed among the 91 participants. Significantly, **the medication use decreased 72% at 4 years with nearly 44% medication-free while mean medication use fell to 1.0 from a preoperative mean of 2.3**, he said.

These findings are consistent with quality-of-life outcomes from a two-year pivotal trial quoted above, Prof Schweitzer said. **“The iStent technology approach could be an appropriate option for patients with existing ocular surface disease. It is an additive medication-sparing therapy that improves OSD symptoms and quality of life,”** he concluded.

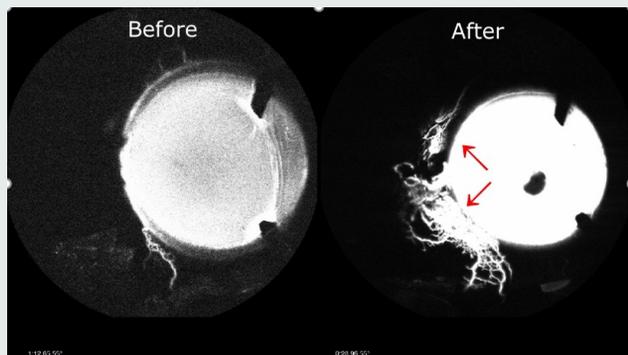
WHY ISTENT *INJECT*® W TRABECULAR MICRO-BYPASS? AND WHEN?

MR MASOOD DISCUSSES PATIENT SELECTION

For patients requiring treatment to reduce initial IOP of 25mmHg or less, trabecular micro-bypass using the iStent *inject*® W is the go-to-choice of Mr Imran Masood Bsc, MB, ChB, MRCS(Ed), FRCOphth, for many reasons.

Most important, **iStent Trabecular Micro-Bypass technology is the least traumatic and has the highest safety profile** – comparable to cataract surgery alone – of any MIGS procedure, said Mr Masood, of Birmingham and Midland Eye Centre, UK. It also targets the site of pathology, which is blocked trabecular meshwork. Recovery is rapid, there is no post-operative intervention required, and it is an excellent adjunct to cataract surgery, he added.

Recent studies by Alex Huang MD, PhD, clearly demonstrate restoration of natural physiological outflow (37), which may help prevent atrophy of Schlemm’s canal, Mr Masood said. This in turn may lead to improved **IOP reduction long-term through preservation of the natural outflow mechanism.** “This is a very powerful potential paradigm shift.”



Graphic 12. Aqueous Angiography Before and After Stenting (Alex Huang, MD, PhD)(37)

Natural outflow also has an IOP floor due to back-pressure from the episcleral blood veins. **“Therefore, hypotony-related complications are not common,”** Mr Masood noted.

iStent Trabecular Micro-Bypass technology helps reduce the need for IOP-reducing medications, which reduces progression risks associated with non-adherence, he added. For select patients, it is an alternative to combined trabeculectomy and phacoemulsification, which has lower success than trabeculectomy alone.

“Reduced OSD resulting from reduced use of topical IOP-reducing medications provides direct benefit to patient quality of life. Avoiding OSD may also improve the outcomes of filtration surgery should it become necessary.”

— Mr Masood

iStent *inject* is the first and only Trabecular Micro-Bypass device to show significant durable vision-related quality of life improvements in a pivotal trial. The results were consistent with his own observations.

After having cataract surgery combined with iStent *inject*, patients were happy they could see better from having the cataracts removed. “But it was more than that. The patients were talking about the impact the surgery was having on their quality of life.” **They reported more confidence, less anxiety about glaucoma-related sight loss, and greater eye comfort.**

A prospective study published in 2020 by Dr Justin A Schweitzer OD and colleagues, showed mean OSDI scores for 47 cataract and OAG patients receiving phacoemulsification and iStent or iStent *inject* fell from 40.1 ± 21.6 (severe) pre-operatively to 17.5 ± 15.3 (mild) at 3 months ($p < 0.0001$). While 73% of eyes had moderate or severe OSDI scores pre-operatively, 29% had such scores at 3 months, and the OSDI score was normal in 57% of eyes versus 9% pre-operatively. The number of glaucoma medications decreased from 1.5 ± 0.9 to 0.6 ± 0.8 mean medications, a 60% reduction ($p < 0.0001$), with all eyes maintaining or reducing medications versus pre-operatively and 55% of eyes becoming medication-free compared with 0% pre-operatively.

*“Implantation of trabecular micro-bypass stent(s) (iStent or iStent *inject*) with cataract surgery produced significant improvements in ocular surface health, alongside significant reductions in IOP and medications,” the study concluded (32).*

THE CASE FOR ISTENT *INJECT*® W PART 3 — SHORT- AND LONG-TERM SAFETY OUTCOMES

PROF HENGERER FINDS NO INTRAOPERATIVE, POST-OPERATIVE OR LONG-TERM ISTENT-RELATED ADVERSE EFFECTS

In his mixed cohort of 125 phaco-combined and standalone recipients of the iStent *inject*®, Germany’s Prof Hengerer found excellent safety outcomes through five years. He reported that among recipients:

- All eyes were successfully implanted with iStent *inject* with no intraoperative complications
- There were no reports of hypotony, peripheral anterior synechiae (PAS) or myopic shifts
- Five eyes, two combined and three standalone, underwent additional glaucoma procedures, either cyclophotocoagulation or additional MIGS, for disease progression unrelated to stent implantation

“And, this is very important, **no eyes underwent traditional glaucoma filtering surgery over the five-years follow up,**” Prof Hengerer said.

DR LINDSTROM SEES NO COMPLICATIONS RELATED TO ISTENT *INJECT* IMPLANTATION

Similarly, Dr Lindstrom saw no intra-operative adverse events in his prospective study of 57 patients on one medication receiving iStent *inject* as a standalone procedure, though this may be due in part to the fact that all the procedures were carried out by experienced glaucoma surgeons, according to the report. Three post-operative ocular adverse events occurred, though these were all deemed “definitely unrelated” to the study treatment. They were IOP elevation and loss of more than one line of best corrected vision at month 32 ultimately resolved by trabeculectomy; and two cases of loss of more than one line of vision due to cataract progression, both of which remained unresolved at month 48.

“The positive benefit-to-risk profile supports the consideration of iStent *inject* in providing a safe, long-term, effective treatment option for patients with mild to moderate glaucoma,” the study said.

META-ANALYSIS FINDS COMPLICATIONS NO HIGHER THAN CONTROLS

In Prof Healey’s meta-analysis involving 778 eyes in 13 studies of standalone iStent implants, adverse events reported in more than 5% of participants were progression of pre-existing cataract/ cataract surgery and loss of best-corrected visual acuity but these rates were no different to those reported in comparator medical therapy study arms.

While the iStent *inject* has a very strong safety record, the new iStent *inject W* should be even stronger said Prof José M. Martínez de la Casa MD, PhD, who heads the glaucoma department at Hospital Clínico San Carlos, Universidad Complutense, Madrid, Spain. “Now we have a new design for enhanced ease of use to improve the visibility of the implantation.”

MR MASOOD’S PERSONAL ISTENT *INJECT W* ALGORITHM

For cataract patients on 2 to 3 IOP-reducing medications, Mr Masood generally chooses:

- IOP <25mmHg – iStent *inject W*
- IOP 25-35mmHg – Ab interno canaloplasty
- IOP >35mmHg or patient on systemic carbonic anhydrase inhibitors – Gonioscopy-assisted transluminal trabeculectomy

“As the pressure goes up, I tend to go toward more invasive procedures,” even though they have more inflammation, bleeding, and complications, because they may lower IOP more, Mr Masood said.

Other selection criteria for iStent *inject W* include:

- Mild to moderate POAG, pseudoexfoliative or pigmentary glaucoma
- Cup-to-disc ratio ≤ 0.8
- Pre-operative IOP up to 30mmHg (medicated)
- Target post-operative IOP up to 15mmHg
- Phakic or pseudophakic with posterior chamber IOLs
- Difficulty taking medication
- Side-effects or complications of medications, such as dry eye, red eyes, toxic or allergic reactions
- Poor compliance taking medication
- Would benefit from reduced IOP and/or reduced medication
- Normal angle as determined by gonioscopy; Schaeffer grade 3-4
- Absence of peripheral anterior synechiae, rubeosis or other angle abnormalities that could impair proper placement of iStent

Mr Masood also uses trabecular bypass as a bridge to filtration surgery, removing cataract and implanting the iStent *inject W*, designed to reduce IOP and medication burden, improving the ocular surface while improving vision. Reduced OSD and inflammation improves the odds of success with trabeculectomy, which is done 9 to 12 months later.

CASE STUDY — STABILISING PROGRESSION

Long-term efficacy is another reason to choose iStent technology, Mr Masood said. Data from a study he conducted with colleagues of patients receiving phaco and the iStent *inject* show reduced need for eye drops in complex and moderate to advanced glaucoma patients, from a mean of 3.2 before surgery to 2.1 at 36 months, with reduction in mean IOP to 16.2mmHg from 24.2mmHg. Visual fields were also stable over the period (26).

Mr Masood illustrated the benefits of iStent technology with a complex case. A 76-year-old monocular patient with Marfan’s syndrome, a scleral-fixed IOL and significant visual field loss had a pre-operative IOP of 28mmHg with four medications. After implantation of two first generation iStent devices his pressure was stable at an acceptable level on three medications, and his visual fields were unchanged for 10 years. **“These devices are having a tremendous beneficial impact for our patients in terms of visual field preservation as well,”** he said.

CASE STUDIES – IOP LOWERING AND POST-FILTRATION SURGERY

PROF BECKERS PRESENTED TWO CASES IN WHICH AN ISTENT *INJECT* AND ISTENT *INJECT W* WERE SUCCESSFULLY PLACED.

Case 1 illustrates the benefit of reducing the use of medication to lower IOP.

A 75-year-old male, slightly myopic had POAG with nuclear cataract and a large glaucoma scotoma in the right eye and a smaller one in the left. He was intolerant to multiple medications in all classes, suffered from ocular surface disease and had tried later trabeculoplasty unsuccessfully. His pre-operative IOP was 20-21mmHg.

He received phaco plus iStent *inject* in the right eye in 2019, and the left eye in 2020. His IOP fell to 11 and 10mmHg with no medications at 1.5 years and 1 year after surgery in the right and left eyes respectively. Final visual acuity improved to 20/25 in the right and 20/20 in the left, Prof Beckers reported.

Case 2 was a more daunting, post-filtration surgery case, Prof Beckers said.

A 77-year-old male with very deep-set eyes had pigment dispersion syndrome glaucoma and cataract in both eyes, with a very large scotoma in the right eye. He had failed trabeculectomy in 2016 and 2017 and had unsuccessful micropulse trans-scleral laser therapy in 2017 and 2018. His pre-operative IOP was 18-20mmHg on 3 IOP-lowering medications.

He received phaco and iStent *inject W* in 2020. Six months after surgery his IOP fell to 8mmHg on 2 medications, and his visual acuity improved to 20/40 from 20/80 pre-operatively. "It was a spectacular outcome, and he was very happy, but of course we need more evidence on these kinds of patients," Prof Beckers said.

THE CASE FOR ISTENT *INJECT*[®] W PART 4 — IMPROVED DESIGN AND EASE OF USE

PROF MARTÍNEZ DE LA CASA ON IMPROVED PREDICTABILITY FROM ISTENT *INJECT W* ENHANCEMENTS

Long-term efficacy, safety, and predictability – improved with the iStent *inject W* model – are top reasons to choose the iStent *inject W* for IOP and medication reduction in patients with POAG, said Prof José M Martínez de la Casa MD, PhD.

Using **iStent *inject W* also does not compromise future glaucoma surgeries**, said Prof Martínez de la Casa, who, heads the glaucoma department at Hospital Clínico San Carlos, Universidad Complutense, Madrid, Spain. "This is a very important point."

In a study following 20 patients implanted with the iStent *inject* published in 2016 for a mean of about four years, Prof Martínez de la Casa and colleagues saw a mean IOP reduction of nearly 40% from unmedicated values along with a reduction in medication use to 0.75 from 1.3 (27). "Now we have a new device, the iStent *inject W*, and a new injector that improve the consistency of the procedure and the visibility of the implant after implantation," he said.

iStent *inject W* is shaped like an arrow and designed to be pushed through the wall of the trabecular meshwork with the pointed head residing in Schlemm's canal, the flange in the anterior chamber, and a narrower thorax held in place by the trabecular meshwork. **It is made of surgical grade, nonferromagnetic titanium, and is heparin coated to promote self-priming.** Two stents are preloaded into a single use inserter, allowing insertion about two to three clock hours apart during cataract surgery, or as a stand-alone procedure. **It combines elegantly with cataract extraction.**

The iStent *inject W* generation has a wider flange than the second generation iStent *inject*, which helps ease of use and predictable placement into the trabecular meshwork. The **new injector** also has a narrower tip for easier insertion, and an **enhanced retraction button for easier manipulation.**

Prof Beckers concluded that iStent *inject W* lowers IOP and reduces the need for IOP-lowering medications and is suitable for patients with cataract and stable glaucoma. More research and long-term outcomes are needed to assess its full potential for use after filtration surgery or in cases of secondary glaucoma.

THE CASE FOR ISTENT *INJECT*[®] W PART 5 – FAVOURABLE COST UTILITY

While complication rates are very low, Prof Beckers cautioned that IOP spikes and anterior chamber bleeding are sometimes seen shortly after surgery and recommended follow up at 1 day and 1 week after surgery. "Good gonioscopy skills are needed. If you don't have those, please refrain from this operation," she added.

As health services consume an ever-growing slice of national income, cutting treatment costs is critical. Several recent studies show that **iStent *inject*'s favourable efficacy and safety profile contributes to reduced need for post-operative medication and follow-up. This saves money and time for patients, their families, physicians and society at large** – making iStent *inject* a cost-effective treatment option for many patients with mild to moderate open-angle glaucoma.

A comparison of the costs of cataract surgery alone with combined cataract and iStent *inject* in France found the combined procedure improved patient quality of life as measured by Quality Adjusted Life Years (QALY) by 0.065 at a cost of €75 per patient over their lifetimes. That works out to €1,154 per QALY gained, making it a bargain at less than four percent of the ~€30,000 the UK's National Health Service considers a reasonable cost per QALY gained.

“iStent *inject* implantation in conjunction with cataract surgery offers a mechanism for IOP reduction that is more effective than cataract surgery alone while reducing the need for medication use and its associated side-effects. ... [And] can be considered cost-effective in patients with mild-to-moderate OAG by improving the patient's quality-of-life at very low incremental costs,” the French study concluded. (33)

A similar comparison in Spain found that combined iStent *inject* cataract surgery cost the Spanish National Health System an additional €1,002 than cataract surgery alone, for a cost per QALY gained of €13,077. When the cost of informal caregiver time was includ-

ed, the combined procedure actually reduced overall societal costs. “iStent *inject* translates ... provides good value for money in patients with mild-to-moderate OAG,” The Spanish study concluded. (35)

iStent *inject* may also be more cost-effective than procedures creating a subconjunctival aqueous channel in eligible mild to moderate OAG patients. One study found that substituting iStent *inject* combined with cataract surgery for 41 per cent of current Xen gel stents (Allergan) cataract combined surgeries would save the Spanish National Health System more than €3 million annually by reducing complications and follow up costs. (36)

Likewise, substituting iStent *inject* with or without cataract surgery for trabeculectomy would save the German statutory health insurance system about €300 per patient for inpatient iStent procedures and more than €1,800 for outpatient iStents over a three-year period. Overall, substituting iStent *inject* for 10 per cent of trabeculectomies would save German insurers about €17 million. (34) **Together these studies suggest a compelling economic case can be made for using iStent *inject* in suitable patients.**

ADDING ISTENT *INJECT*® W TO CATARACT SURGERY CAN IMPROVE PATIENT OUTCOMES AND SYSTEM EFFICIENCY

Adding iStent *inject* W at cataract surgery presents a unique opportunity to significantly improve not only clinical and quality-of-life outcomes for patients in need of IOP reduction, but also financial pressures for the patient as well as the efficiency of health services, according to Ms Laura Crawley BSC (Hons), MB, CHB (Hons), MRCP, FRCOphth, GMC.

“In the new era of MIGS, if you are inside the eye already carrying out cataract surgery in a patient needing pressure lowering treatment, please think about what else you might do at the same time to address the pressure,” said Ms Crawley, who is a consultant ophthalmic surgeon and honorary senior lecturer at the Imperial College Healthcare NHS Trust and Imperial College, London, UK.

Ms Crawley noted that the cost-utility of the iStent technology is becoming more evident now than even a few years ago. Long-term outcomes data, as reviewed in this supplement, can now justify the cost of Trabecular Micro-Bypass treatments.

Implanting the iStent *inject* W also fits well in the cataract surgery workflow. Ms Crawley suggested making an explicit plan for each patient who is having cataract surgery and is also on pressure-lowering drugs.

The disruptions and financial strains created by the COVID-19 pandemic make it even more important to consider procedures that smooth the demand for extra appointments in between routine visits, Ms Crawley said. “For very many of us our services were completely disrupted, and we were only able to see absolute sight-threatening emergencies.” As a result, large numbers of glaucoma patients had their treatment review delayed.

“If we had a better way of ensuring a non-patient-dependent control of pressure by using these devices, that facilitates better resource allocation in clinical time to see higher risk patients who need us,” Ms Crawley said. As such, Trabecular Micro-Bypass use can benefit the entire population a service manages. Implanting Trabecular Micro-Bypass devices also helps patients who have trouble adhering to medication regimes for a wide variety of reasons, even in cases where maximum medication involves taking just two combined medications once or twice a day.

“It really benefits the whole system if we as surgeons can consider a way of controlling pressure whilst we are already doing cataract surgery,” Ms Crawley said.

PRESERVE YOUR PATIENTS' QUALITY OF LIFE with iStent *inject*® W Trabecular Micro-Bypass

SOME GLAUCOMA FACTS


ONE-IN-FIVE
cataract patients
also needing
glaucoma
medication⁽⁵⁾


GLAUCOMA
is the **leading cause of
irreversible vision loss**⁽²⁾

74%
of diagnosed
glaucoma cases
are OAG^(3, 4)

GLAUCOMA
is the second leading
cause of blindness
worldwide ⁽²⁾

76
million people
worldwide in 2020
is affected by
glaucoma⁽¹⁾

How to treat OAG?



**HYPOTENSIVE
MEDICATIONS**
can lead to **ocular surface
disease and conjunctival
inflammation** and
**adherence is notoriously
problematic**⁽⁶⁻¹⁰⁾



**TRABECULECTOMY
AND TUBE SHUNT
IMPLANTATION**
expose patients to **safety
risks, including infection
and hypotony**⁽¹²⁻¹⁴⁾



**LASER
TRABECULOPLASTY**
may induce
inflammation in the
intermediate-term⁽¹¹⁾



iStent *inject*® W
Trabecular Micro-Bypass
restores **physiological
aqueous outflow**⁽¹⁵⁾

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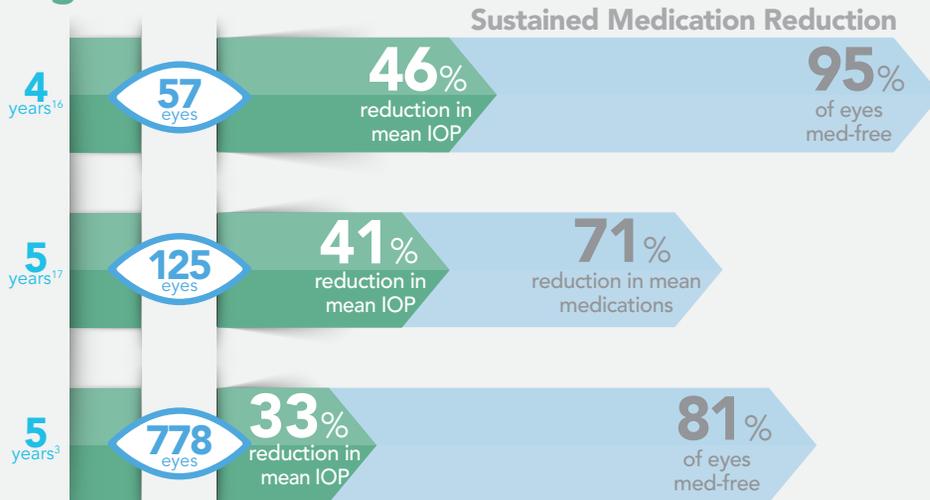
INDICATION FOR USE

The iStent *inject*® W is intended to reduce intraocular pressure safely and effectively in patients diagnosed with primary open-angle glaucoma, pseudo-exfoliative glaucoma or pigmentary glaucoma. The iStent *inject*® W can deliver two (2) stents on a single pass, through a single incision. The implant is designed to stent open a passage through the trabecular meshwork to allow for an increase in the facility of outflow and a subsequent reduction in intraocular pressure. The device is safe and effective when implanted in combination with cataract surgery or as stand-alone procedure in those subjects who require intraocular pressure reduction and/or would benefit from glaucoma medication reduction. The device may also be implanted in patients who continue to have elevated intraocular pressure despite prior treatment with glaucoma medications and conventional glaucoma surgery.

The **longest-term real world clinical** data of any Trabecular Micro-Bypass procedure **demonstrates significant advantages for your patients:**

iStent inject® W is the gold standard in **Trabecular Micro-Bypass surgery** continuing the legacy of excellence set throughout 20 years of iStent® devices.

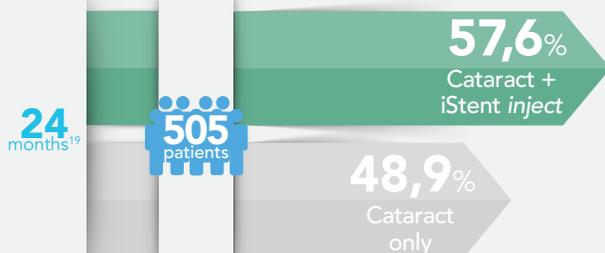
Long-term IOP Reduction



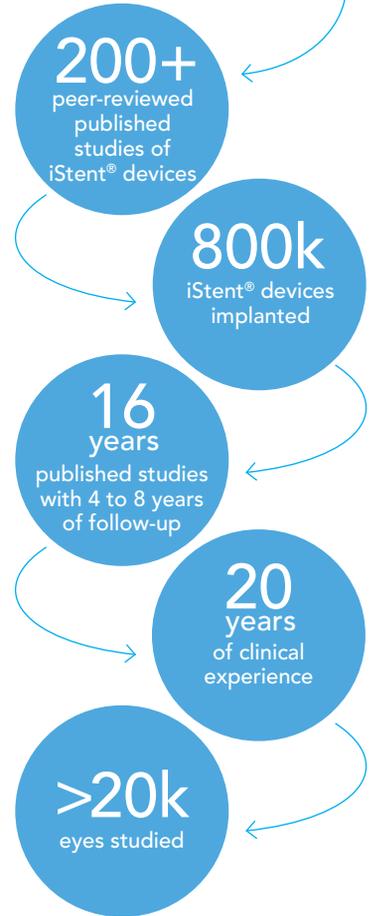
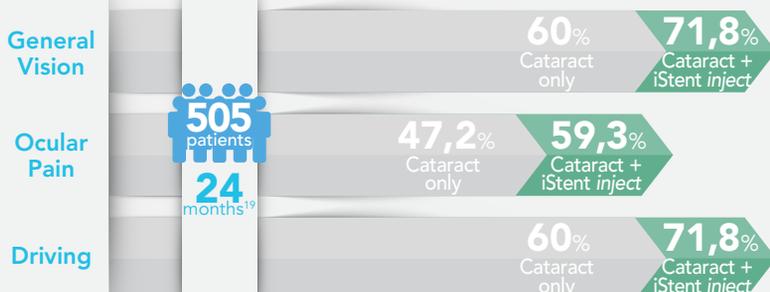
Improved OSD Symptoms



Significant Improvement in OSDI Score



Improved Quality of Life



Continue the iStent® legacy of excellence by making **iStent inject® W** your Trabecular Micro-Bypass device of choice.

iStent
inject® W



GLAUKOS¹⁵

CONCLUSION

A large and growing body of long-term research, including five-year outcomes data from completed and ongoing studies of iStent *inject*[®], show that the iStent[®] technology reliably reduces IOP and IOP-lowering medication need, with an excellent safety profile. For qualified OAG glaucoma patients, iStent *inject*[®] W may provide substantial clinical and lifestyle advantages, giving glaucoma and cataract surgeons a new tool to help prevent long-term vision loss while improving patient quality of life.

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