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Guidelines for the Use of Trabecular Micro-bypass Glaucoma Stents (MBGS)

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1. Purpose and scope

The aim of this document is to provide guidance for ophthalmologists in appropriate patient selection and clinical indication for the use of trabecular micro-bypass glaucoma stents both with cataract surgery and as a cataract-independent procedure. This document does not describe the technical process of stent implantation or specific patient management techniques.

MIGS (Minimally or microinvasive glaucoma surgery) is an umbrella term that includes a number of different surgeries both with and without implants. These include those targeting the trabecular outflow (with or without trabecular micro-bypass glaucoma stents), creating suprachoroidal drainage and creating a bleb with subconjunctival drainage. The scope of this document is to provide guidance to trabecular micro-bypass glaucoma stents only.

2. What are Intraocular Micro-bypass Glaucoma Stents?

Intraocular micro-bypass glaucoma stents are a family of prostheses which are designed to be placed permanently in the eye to lower intraocular pressure (IOP). Two types of intraocular micro-bypass glaucoma stents have been available in Australia, trabecular-bypass glaucoma stents and suprachoroidal glaucoma stents. Each type targets one of two aqueous outflow pathways.

Trabecular micro-bypass glaucoma stents penetrate the trabecular meshwork and Schlemm's canal to provide direct aqueous access from the anterior chamber to the canal and collector channels.

Suprachoroidal micro-bypass glaucoma stents are placed between the sclera and iris root to create a controlled cyclodialysis to increase uveo-scleral aqueous flow from the anterior chamber. There are currently no available suprachoroidal stents following the recall of Cypass by its company in 2018 because of concerns about corneal endothelial loss. These will not be discussed further in this document.

3. Currently available Micro-bypass Glaucoma Stents

3.1 Trabecular micro-bypass glaucoma stents

Three Trabecular micro-bypass glaucoma stents are currently available in Australia:

- iStentTM (The term “iStent” will always refer to the original single stent in this document)
- iStent injectTM
- Hydrus MicrostentTM

The iStent, iStent inject and Hydrus Microstent are stents designed to cannulate the canal of Schlemm. The iStents are made of titanium. The original iStent has an outlet at a right-angle to the stent body and a sharp front end to perform the initial goniotomy. It is held in place by semi-circumferential rings along the body of the stent. These are generally decreasing in usage since the advent of iStent inject. However, it is important to note that many of the published studies are of the single iStent.

The iStent inject system contains two rivet-like stents with blunt arrowhead shaped front ends. They are designed to directly perforate the trabecular meshwork and penetrate the canal at right angles to the canal's course. Implantation force is provided by its spring-loaded introducer which contains a needle to incise the tissues. The two stents are designed to be placed

adjacent to collector channels, approximately 2-3 clock hours away from each other. The stents are preloaded on the needle within the introducer and are delivered one at a time upon activation of the actuator.

The Hydrus Microstent is made of a nickel-titanium alloy, Nitinol. It is larger than the iStent, occupying 3 clock hours of the canal. Prior to implantation, it sits inside a trocar which is used to incise the meshwork and canal. An actuator delivers the stent through the trocar upon rotation of a wheel on the introducer. Its outlet is in line with the stent, which also has 3 windows to facilitate trans-trabecular drainage. It is held in place by its size.

4. Guidelines for the Use of Trabecular Micro-bypass Glaucoma Stents

4.1. Trabecular Micro-bypass stents in Glaucoma Management

The addition of a trabecular micro-bypass stent to cataract surgery results in a greater percentage of eyes with sustained IOP reduction over time.^{1,2} The use of trabecular stents can be with or without cataract surgery. Cataract surgery and trabecular micro-bypass stents are independent procedures and the successful outcome of one does not depend on the other. Both can affect the intraocular pressure, and this has been the confounding factor; many of the available studies have compared cataract-stent surgery compared to cataract surgery alone. We would consider the evidence from stents combined with cataract surgery as additional evidence for the efficacy of the stent alone.

Findings from a relatively large number of randomised and non-randomised studies suggest that on average, micro-bypass glaucoma stents are at least as effective as topical medications or laser trabeculoplasty and safer than trabeculectomy or traditional glaucoma drainage devices such as the MoltenoTM and BaerveldtTM tubes.^{1,2} Efficacy in individual patients is dependent on a number of technical, physiological and patho-physiological factors not all of which are well understood. In light of current knowledge, the following generalisations can be made.

- being an incisional surgical procedure, micro-bypass glaucoma stent implantation brings with it specific and potentially serious risks which are not present with topical medical treatment and greater than with laser surgical treatment.
- compared with trabeculectomy and glaucoma drainage device implantation, complications reported to date are minimal but not non-existent. They include incorrect implantation, peripheral anterior synechiae and blocking of stents, anterior uveitis and stent displacement. There is no evidence that iStent, iStent inject and Hydrus has any effect on the corneal endothelium.
- the irido-corneal angle must be sufficiently open, or will be sufficiently open following cataract surgery, to enable implantation and to reduce the rate of occlusion of the stent by formation of peripheral anterior synechiae.
- all devices must be implanted correctly into the correct position to lower intraocular pressure. Successful penetration of Schlemm's canal by trabecular micro-bypass glaucoma stents is often heralded by blood reflux through the stent. If the stent is implanted into an incorrect position such as the ciliary body, it cannot work. It is therefore of utmost importance that accurate gonioscopic identification of the angle structures is performed before implantation.
- intraocular pressure lowering using trabecular micro-bypass glaucoma stents is dependent on functional distal conventional drainage pathways. At this stage, there is no proven clinical method to test this preoperatively although there is research interest in assessing aqueous veins preoperatively.
- reported average intraocular pressures at 1-2 years are in the teens most often with

concurrent topical medication use for all types of micro-bypass glaucoma stents. The Horizon study reported on the outcomes of the Hydrus stent³ and the US iStent Study Group reported on the iStent.⁴

- reported average topical medications are reduced by around 1 per patient.
- on average, the flow through the stents is insufficient to prevent an IOP rise in a strong steroid responder.
- outcomes beyond 4-5 years have not been reported.
- the nature of longer-term fibrosis or gliosis around the stents and its effect on intraocular pressure control has not been well described.

4.2 When to consider micro-bypass glaucoma stent implantation as a standalone/cataract independent procedure in glaucoma management

If intraocular pressure control can be established with adherence to well tolerated topical medications or with laser trabeculoplasty then stand-alone incisional glaucoma surgery should generally be deferred. This includes micro-bypass glaucoma stent implantation.

If intraocular pressure control cannot be established or maintained with conservative therapies, if they are likely to fail or if they are contraindicated, the surgeon should consider the relative risk and benefit of micro-bypass glaucoma stent implantation compared with a glaucoma filtering operation. The expected IOP lowering effect needs to be taken into account when considering a trabecular stent in this situation. The expectation is related to efficacy as described above. Another indication would be in a situation where external drainage surgeries are not possible or a highly likely to fail for example in conjunctiva cicatrising disease. Some efficacy has been seen when used after failed trabeculectomy.⁵

Safety and efficacy data suggest micro-bypass glaucoma stents should be considered as an escalation of therapy to lower IOP. In the glaucoma treatment algorithm, micro-bypass glaucoma stents would be indicated as an intermediary intervention between first line therapies (laser and medications) and glaucoma filtering surgery such as trabeculectomy.

4.3 When to consider micro-bypass glaucoma stent implantation as a combined operation with cataract surgery

A patient who has uncontrolled glaucoma on medical therapy and has a cataract requiring cataract surgery is a candidate for the combined procedure. Consideration should be given to the severity of glaucoma and the anticipation that the target pressure will be reached by this method of surgery.

A patient who has controlled glaucoma but is on multiple medications and is becoming intolerant, experiencing side effects, has poor adherence or compliance is also a candidate for combined surgery.

It is important to note that modern cataract surgery with phacoemulsification alone can sometimes decrease intraocular pressure.⁶ The effect can be long-lasting in a subpopulation, but is highly variable, and the effect is generally not sustained. Ocular hypertension, angle closure and pseudoexfoliation eyes are particularly known to experience a reduction in pressure with cataract surgery. Given the large variability, more research is required to elucidate who the best responders are to cataract surgery alone.

4.4 Patient and treatment selection

a). Choosing the Patient for Glaucoma Surgery

Patients should be considered for glaucoma surgery in the following circumstances.

- the patient is not at target pressure. If the target pressure is very low, then this will need further consideration as target pressures below episcleral pressure are not reachable with medications, laser or stents. The clinical evaluation will determine the appropriate surgery.
- the patient is receiving maximally tolerated medical therapy and has had laser trabeculoplasty or these treatments are contraindicated or likely to fail.
- the patient is likely to be disabled by their disease without further treatment.
- the benefit to the patient of incisional microinvasive glaucoma surgery outweighs the risks of the procedure.
- the patient is likely to adhere to pre, peri and post-operative medications, instructions, follow-up.
- the patient or their legal guardian is capable of consenting to the proposed procedure.

A combination of factors might lead to the decision, for example, the patient is having cataract surgery and is not adequately responsive to medications, is intolerant or non-adherent to medications.

b) Choosing between Cataract-independent Trabecular Micro-bypass Glaucoma Surgery and Trabeculectomy

Currently available data support the use of micro-bypass glaucoma stents in eyes with open-angle glaucoma. Their use in angle closure is the subject of research. We would generally advise against the use of micro-bypass glaucoma stents in active neovascularisation of the angle or active uveitis.

Individual patient factors play a critical role in treatment decisions and a discussion of these is outside the scope of this document. Guidance in choosing between micro-bypass glaucoma stents and trabeculectomy surgery can be gained by examining reported outcomes for the two procedures. The two critical outcomes are the degree and duration of intraocular pressure lowering, and the frequency and severity of complications.

The table below shows data from selected studies of initial trabeculectomy and stand-alone micro-bypass glaucoma stent implantation. The UK National Trabeculectomy Survey gives a pragmatic view of outcomes for trabeculectomy as actually performed in the community. The Collaborative Initial Treatment of Glaucoma Study CIGTS gives an alternative view of trabeculectomy performed as initial therapy for glaucoma. The micro-bypass glaucoma stent studies shown are all stand-alone. The iStent inject study recruited patients on a single medication in need of further IOP lowering. Patients in the iStent study had uncontrolled IOPs of 18-30mmHg on two medications for study entry. The Hydrus study recruited patient insufficiently controlled on a mean medical therapy of 2.5 eye drops.

Adverse event (AE) data has been presented so as to be as similar as possible across studies. Transient mild or moderately raised IOP, inflammation, discomfort or the need to perform a relatively minor additional procedure or therapy (e.g. additional laser/ suture removal or medications) have been omitted as AEs. Hyphaema rates are shown separately as almost none were reported to cause serious harm or persist for more than 4 weeks (apart from

recurrent hyphaemas in 3.6% of the UK Survey eyes). Cataract progression (cat) is also shown separately due to the differing age ranges, follow-up durations and rates of pre-existing cataract between the studies.

Notwithstanding this, the data suggests a higher rate of adverse events for trabeculectomy when compared with micro-bypass glaucoma stents. This is particularly important for the rare devastating late complications reported in CIGTS and the UK survey but not in any of the micro-bypass glaucoma stent studies (e.g. endophthalmitis, snuff out, hypotony maculopathy, cystoid macular oedema). The patient-related impact of trabeculectomy can be inferred from the 19% of CIGTS participants who were due to have a trabeculectomy in their fellow eye but refused the procedure.

The data also seem to suggest relatively little difference in IOP outcomes between trabeculectomy and micro-bypass glaucoma stent studies. However mean IOP outcomes do not capture the range of individual outcomes of surgery. For example, raw outcomes published by the UK National trabeculectomy Survey show a substantial number of patients with pre-operative IOPs >30mmHg and as high as the mid-50s mmHg. Half of the eyes in the survey had advanced glaucomatous visual field loss at the time of surgery in contrast to the less severe disease in the micro-bypass glaucoma stent studies. Furthermore some 22% of eyes in the Trabeculectomy survey had IOPs of 10mmHg or less at the last follow-up (albeit with 1.9% <6 mmHg). Similarly, the CIGTS had a higher mean initial IOP with a large standard deviation similar to the UK Survey.

In contrast the standard deviations of initial and postoperative IOPs for the micro-bypass glaucoma stent studies were generally small suggesting a relatively smaller range of IOPs both at baseline and follow-up. The exceptions are the Hydrus study which had a lower mean but similar standard deviation of IOP at baseline to the trabeculectomy studies. A larger set of published clinical studies of the efficacy and adverse effects of trabecular micro-bypass stents is listed in the bibliography.

Table: Examples of Efficacy, duration and Adverse events (AE) of published cataract-independent glaucoma surgery studies

Study/ Procedure	Mean Pre- op IOP (mmHg) \pm SD	1 -1.5 year	3-4 year	Early AE	Late AE (> 1 month)
UK National Trabeculectomy Survey ⁷	26.4 \pm 5.9	14.4 \pm 4.5		22% (+25% hyphaema)	22% (+20% cat)
CIGTS (Trabeculectomy) ^{8,9,10, 11}	27.6 \pm 5.7	14 \pm 4.3	14.4 \pm 4.3	44% (+18% hyphaema)	32% (+20% cat)
CIGTS (Trabeculectomy) ¹²				Refusal of same op on 2 nd eye	19%
Fea (2014) iStent inject ¹³	21.1 \pm 1.7 (25.2 \pm 1.4)*	13.0 \pm 2.3		1% (v. high IOP treated medically)	0%
Fea (2017) Hydrus ¹⁴	23.1 \pm 5.1	16.5 \pm 2.6			
Katz (2015) ² (2018) ¹⁵					At 18 months
1 iStent	19.8 \pm 1.3 (25.0 \pm 1.1)*	14.4 \pm 1.2	15.0 \pm 2.8 (17.4 \pm 0.9)	0%	0%
2 iStents	20.1 \pm 1.6 (25.0 \pm 1.7)*	12.8 \pm 1.4	15.7 \pm 1.0 (15.8 \pm 1,1)	0%	0% (+5% cat)
3 iStents	20.4 \pm 1.8 (25.1 \pm 1.9)*	12.2 \pm 1.5	14.8 \pm 1.3 (14.2 \pm 1.5)	0%	0% (+5% cat)

*IOP in brackets is washed out (medication-free)

c). Choosing between Trabecular Micro-bypass Glaucoma Surgery Stents

The table above and other published studies do not yet give clear guidance about which stent to use for a particular patient. At present, reported outcomes and adverse events appear relatively similar for all stents when compared with trabeculectomy.

d) General requirements for Trabecular Micro-bypass Glaucoma Surgery

- the treating ophthalmologist must always consider which treatment option is in the best interest of their patient;
- if other treatments have been previously attempted, their use and outcome (successful or otherwise) must be documented;
- all investigation results pertaining to the patient's condition (such as intraocular pressure measurements, glaucoma imaging and visual field testing) must be documented;
- the decision-making process that led to the decision to implant a micro-bypass glaucoma stent must be documented;
- the surgeon must be familiar with the risks and benefits of each stent being considered;
- the surgeon must be sufficiently technically skilled to implant the proposed stent safely and accurately;

4.5. Preventing and managing complications from Micro-bypass glaucoma stent implantation

Complications of micro-bypass glaucoma stent implantation include but are not limited to:

- infection (endophthalmitis)
- non-infectious inflammation
- failure to lower intraocular pressure (or raised pressure)
- cataract (traumatic and steroid-induced)
- physical damage to the irido-corneal angle or iris root or other parts of the eye.

To reduce the risk of adverse outcomes in the patient undergoing a micro-bypass glaucoma stent procedure, the surgeon's process must include the following:

- appropriate surgical and sterile techniques must be used to reduce the risk of surgical complications and endophthalmitis;
- preoperative gonioscopy and intraoperative gonioscopy needs to be accurate;
- patients must be monitored post-operatively for possible complications and appropriate follow-up arranged;
- patients must be informed of the symptoms of possible complications and how to seek timely treatment should these occur;
- micro-bypass glaucoma stent surgery must not be undertaken unless the treating surgeon is capable of managing the majority of possible complications which may ensue; and
- when complications are being treated, the ophthalmologist should remain in contact with the patient, even if this treatment is being given by a sub-specialist ophthalmologist.

4.6 Informed consent discussion

General guidelines involving appropriate consent should be adhered to, including adequacy of time, language issues and decision-making capacity of the patient. In addition:

- each patient should be informed of their diagnosis, all treatment options and the reason for choosing a micro-bypass glaucoma stent for their specific condition;
- each patient should be aware of the likelihood of success with micro-bypass glaucoma stent implantation in their specific condition, and be informed of alternatives if failure occurs;
- the known risks and complications of the procedure and peri-and post-operative medication should be explained. If written information about these risks is available, provide it to the patient;
- each patient must be guided through the consent process and be given the opportunity to discuss the proposed treatment with someone else of their choosing. Thereafter the ophthalmologist must be satisfied that patient freely signs the consent form prior to the procedure;
- if patients have specific risks pertaining to their individual situation, then these must be explained.

4.7 Documentation of care

It is recommended that the following are specifically documented when considering or performing a micro-bypass glaucoma stent procedure:

- document the clinical findings and investigation results that enabled a diagnosis to be

made;

- document any previously attempted treatments and their outcomes;
- document the gonioscopy findings in the eye considered for surgery, especially in the nasal angle and comparison with the fellow eye. Document any peripheral anterior synechiae in any area of the angle;
- document the decision-making process that led to trabecular micro-bypass glaucoma stent being considered;
- document the patient discussion of reasons for trabecular micro-bypass glaucoma stent implantation and possible risks, including risks specific to that patient;
- document any refusal of trabecular micro-bypass glaucoma stent, including the reasons the patient refused care;
- document the procedure, the details of the trabecular micro-bypass glaucoma stent used, including batch number and any adverse or unexpected perioperative events;
- provide the patient with a prosthesis card which includes the stent type, batch number, implantation date and surgeon;
- document any complications of the trabecular micro-bypass glaucoma stent implantation;
- provide follow-up instructions, symptoms of possible complications and how to seek timely treatment should these occur and document that these have been given;
- document efforts to monitor for and treat complications;
- document referrals to sub-specialists and keep a copy of the consultation letter in the patient's file; and
- document all communication to and from the patient, including phone calls.

4.8 Other Considerations

a) Cost-effectiveness of trabecular implants^{16,17}

The cost of implants needs to be considered compared to the cost of eyedrops:

- a projected Canadian study showed that a single iStent would show a cost benefit to 2-3 medications in 3 years which increases with time. This was against the original single iStent and not the iStent inject;¹⁶
- the Manchester iStent study looked at actual cost of combined surgery compared to the conservative treatment with eye drops. They showed that iStent was more cost-effective than brand name eyedrops but less cost-effective than generic eye drops;¹⁷
- an industry sponsored Columbian study used modelling to look at cost effectiveness and recently found greatly in favour of iStents compared to medical therapy.¹⁸

b) Potential conflicts of interests with industry associations

A final consideration is to keep in mind any potential conflict of interest with implants and industry associations. In particular, industry sponsored studies need to clearly demonstrate a distance from the study and study results.

5. Further reading

Edmunds, B., Thompson, J. R., Salmon, J. F., & Wormald, R. P. (2001). The National Survey of Trabeculectomy. II. Variations in operative technique and outcome. *Eye*, 15, 441-448

Edmunds, B., Thompson, J. R., Salmon, J. F., & Wormald, R. P. (2002). The national survey of trabeculectomy. III. early and late complications. *Eye*, 16(3),297-303.

Musch, D. C., Gillespie, B. W., Niziol, L. M., Lichter, P. R., Varma, R., & Group, C. S. (2011). Intraocular pressure control and long-term visual field loss in the Collaborative Initial Glaucoma Treatment Study. *Ophthalmology*, 118(9), 1766-1773. doi:10.1016/j.ophtha.2011.01.047

Zahid, S., Musch, D. C., Niziol, L. M., Lichter, P. R., & Collaborative Initial Glaucoma Treatment Study, G. (2013). Risk of endophthalmitis and other long-term complications of trabeculectomy in the Collaborative Initial Glaucoma Treatment Study (CIGTS). *Am J Ophthalmol*, 155(4), 674-680, 680 e671. doi:10.1016/j.ajo.2012.10.017

Jampel, H. D., Musch, D. C., Gillespie, B. W., Lichter, P. R., Wright, M. M., Guire, K. E., & Collaborative Initial Glaucoma Treatment Study, G. (2005). Perioperative complications of trabeculectomy in the collaborative initial glaucoma treatment study (CIGTS). *Am J Ophthalmol*, 140(1), 16-22. doi:10.1016/j.ajo.2005.02.013

Lichter, P. R., Musch, D. C., Gillespie, B. W., Guire, K. E., Janz, N. K., Wren, P. A., . . . Group, C. S. (2001). Interim clinical outcomes in the Collaborative Initial Glaucoma Treatment Study comparing initial treatment randomized to medications or surgery. *Ophthalmology*, 108(11), 1943-1953.

[Gupta D](#), [Musch DC](#), [Niziol LM](#), [Chen PP](#). (2016) Refusal of Trabeculectomy for the Fellow Eye in Collaborative Initial Glaucoma Treatment Study (CIGTS) Participants. *Am J Ophthalmol*. 2016 Jun;166:1-7

Fea, A. M., Belda, J. I., Rekas, M., Junemann, A., Chang, L., Pablo, L., Voskanyan, L., & Katz, L. J. (2014). Prospective unmasked randomized evaluation of the iStent inject ((R)) versus two ocular hypotensive agents in patients with primary open-angle glaucoma. *Clin Ophthalmol*, 8, 875-882. doi:10.2147/opth.s59932

Katz, L. J., Erb, C., Carceller, G. A., Fea, A. M., Voskanyan, L., Wells, J. M., & Giamporcaro, J. E. (2015). Prospective, randomized study of one, two, or three trabecular bypass stents in open-angle glaucoma subjects on topical hypotensive medication. *Clin Ophthalmol*, 9, 2313-2320. doi:10.2147/OPTH.S96695

Katz, L. J., Erb, C., Carceller, G. A., Fea, A. M., Voskanyan, L., & Giamporcaro, J. E., Hornbeak G. M. (2018). Long-term titrated IOP control with one, two, or three trabecular micro-bypass stents in open-angle glaucoma subjects on topical hypotensive medication: 42-month outcomes. *Clin Ophthalmol*, 12, 255-262.

Fea, A. M., Ahmed, II, Lavia, C., Mittica, P., Consolandi, G., Motolese, I., Pignata, G., Motolese, E., Rolle, T., & Frezzotti, P. (2017). Hydrus microstent compared to selective laser trabeculoplasty in primary open angle glaucoma: one year results. *Clin Exp Ophthalmol*, 45(2), 120-127. doi:10.1111/ceo.12805

Ahmed, II, Katz, L. J., Chang, D. F., Donnenfeld, E. D., Solomon, K. D., Voskanyan, L., & Samuelson, T. W. (2014). Prospective evaluation of microinvasive glaucoma surgery with trabecular microbypass stents and prostaglandin in open-angle glaucoma. *J Cataract Refract Surg*, 40(8), 1295-1300. doi:10.1016/j.jcrs.2014.07.004

Berdahl, J., Voskanyan, L., Myers, J. S., Hornbeak, D. M., Giamporcaro, J. E., Katz, L. J., & Samuelson, T. W. (2017). Implantation of two second-generation trabecular micro-bypass stents and topical travoprost in open-angle glaucoma not controlled on two preoperative medications: 18-month follow-up. *Clin Exp Ophthalmol*. doi:10.1111/ceo.12958

Chang, D. F., Donnenfeld, E. D., Katz, L. J., Voskanyan, L., Ahmed, II, Samuelson, T. W., Giamporcaro, J. E., Hornbeak, D. M., & Solomon, K. D. (2017). Efficacy of two trabecular micro-bypass stents combined with topical travoprost in open-angle glaucoma not controlled on two preoperative medications: 3-year follow-up. *Clin Ophthalmol*, 11, 523- 528. doi:10.2147/ophth.s121041

Donnenfeld, E. D., Solomon, K. D., Voskanyan, L., Chang, D. F., Samuelson, T. W., Ahmed, II, & Katz, L. J. (2015). A prospective 3-year follow-up trial of implantation of two trabecular microbypass stents in open-angle glaucoma. *Clin Ophthalmol*, 9, 2057-2065. doi:10.2147/ophth.s91732

Ferguson, T. J., Berdahl, J. P., Schweitzer, J. A., & Sudhagoni, R. (2016). Evaluation of a Trabecular Micro-Bypass Stent in Pseudophakic Patients With Open-Angle Glaucoma. *J Glaucoma*, 25(11), 896-900. doi:10.1097/ijg.0000000000000529

Gandolfi, S. A., Ungaro, N., Ghirardini, S., Tardini, M. G., & Mora, P. (2016). Comparison of Surgical Outcomes between Canaloplasty and Schlemm's Canal Scaffold at 24 Months' Follow-Up. *J Ophthalmol*, 2016, 3410469. doi:10.1155/2016/3410469

Katz, L. J., Erb, C., Carceller, G. A., Fea, A. M., Voskanyan, L., Wells, J. M., & Giamporcaro, J. E. (2015). Prospective, randomized study of one, two, or three trabecular bypass stents in open-angle glaucoma subjects on topical hypotensive medication. *Clin Ophthalmol*, 9, 2313-2320. doi:10.2147/ophth.s96695

Klamann, M. K., Gonnermann, J., Pahlitzsch, M., Maier, A. K., Jousen, A. M., Torun, N., & Bertelmann, E. (2015). iStent inject in phakic open angle glaucoma. *Graefes Arch Clin Exp Ophthalmol*, 253(6), 941-947. doi:10.1007/s00417-015-3014-2

Lindstrom, R., Lewis, R., Hornbeak, D. M., Voskanyan, L., Giamporcaro, J. E., Hovanesian, J., & Sarkisian, S. (2016). Outcomes Following Implantation of Two Second-Generation Trabecular Micro-Bypass Stents in Patients with Open-Angle Glaucoma on One Medication: 18-Month Follow-Up. *Adv Ther*, 33(11), 2082-2090. doi:10.1007/s12325-016-0420-8

Pahlitzsch, M., Klamann, M. K., Pahlitzsch, M. L., Gonnermann, J., Torun, N., & Bertelmann, E. (2017). Is there a change in the quality of life comparing the micro-invasive glaucoma surgery (MIGS) and the filtration technique trabeculectomy in glaucoma patients? *Graefes Arch Clin Exp Ophthalmol*, 255(2), 351-357. doi:10.1007/s00417-016-3550-4

Vold, S. D., Voskanyan, L., Tetz, M., Auffarth, G., Masood, I., Au, L., Ahmed, II, & Saheb, H. (2016). Newly Diagnosed Primary Open-Angle Glaucoma Randomized to 2 Trabecular Bypass Stents or Prostaglandin: Outcomes Through 36 Months. *Ophthalmol Ther*, 5(2), 161-172. doi:10.1007/s40123-016-0065-3

Voskanyan, L., Garcia-Feijoo, J., Belda, J. I., Fea, A., Junemann, A., & Baudouin, C. (2014). Prospective, unmasked evaluation of the iStent(R) inject system for open-angle glaucoma: synergy trial. *Adv Ther*, 31(2), 189-201. doi:10.1007/s12325-014-0095-y

Burr J, Azuara-Blanco A, Avenell A et al. Medical versus surgical interventions for open-angle glaucoma. *Cochrane Database of Systematic Reviews* 2012, Issue 9. Art. No.: CD004399

6. References

1. Fea AM, Belda JI, Rekas M et al. Prospective unmasked randomized evaluation of the iStent inject ((R)) versus two ocular hypotensive agents in patients with primary open-angle glaucoma. *Clin Ophthalmol*. 2014;8:875-882.
2. Katz LJ, Erb C, Carceller GA et al. Prospective, randomized study of one, two, or three trabecular bypass stents in open-angle glaucoma subjects on topical hypotensive medication. *Clin Ophthalmol*. 2015;9:2313-2320.
3. Samuelson TW, Chang DF, Marquis R et al. A Schlemm Canal Microstent for Intraocular Pressure Reduction in Primary Open-Angle Glaucoma and Cataract: The HORIZON Study. *Ophthalmology*. 2018
4. Samuelson TW, Katz LJ, Wells JM, Duh YJ, Giamporcaro JE. Randomized evaluation of the trabecular micro-bypass stent with phacoemulsification in patients with glaucoma and cataract. *Ophthalmology*. 2011;118:459-467.
5. Davids AM, Pahlitzsch M, Boeker A et al. iStent inject as a reasonable alternative procedure following failed trabeculectomy. *Eur J Ophthalmol*. 2018;1120672117747010.
6. Mansberger SL, Gordon MO, Jampel H et al. Reduction in intraocular pressure after cataract extraction: the Ocular Hypertension Treatment Study. *Ophthalmology*. 2012;119:1826-1831.
7. Edmunds B, Thompson JR, Salmon JF, Wormald RP. The National Survey of Trabeculectomy. II. Variations in operative technique and outcome. *Eye (Lond)*. 2001;15:441-448.
8. Musch DC, Gillespie BW, Niziol LM, Lichter PR, Varma R, CIGTS SG. Intraocular pressure control and long-term visual field loss in the Collaborative Initial Glaucoma Treatment Study. *Ophthalmology*. 2011;118:1766-1773.
9. Zahid S, Musch DC, Niziol LM, Lichter PR, Collaborative IGTS. Risk of endophthalmitis and other long-term complications of trabeculectomy in the Collaborative Initial Glaucoma Treatment Study (CIGTS). *Am J Ophthalmol*. 2013;155:674-680, 680.e1.
10. Jampel HD, Musch DC, Gillespie BW et al. Perioperative complications of trabeculectomy in the collaborative initial glaucoma treatment study (CIGTS). *Am J Ophthalmol*. 2005;140:16-22.
11. Lichter PR, Musch DC, Gillespie BW et al. Interim clinical outcomes in the Collaborative Initial Glaucoma Treatment Study comparing initial treatment randomized to medications or surgery. *Ophthalmology*. 2001;108:1943-1953.
12. Gupta D, Musch DC, Niziol LM, Chen PP. Refusal of Trabeculectomy for the Fellow Eye in Collaborative Initial Glaucoma Treatment Study (CIGTS) Participants. *Am J Ophthalmol*. 2016;166:1-7.
13. Ahmed IIK, Fea A, Au L et al. A prospective randomized trial comparing Hydrus and iStent micro-invasive glaucoma surgery implants for standalone treatment of open-angle glaucoma: The COMPARE Study. *Ophthalmology*. 2019
14. Fea AM, Ahmed II, Lavia C et al. Hydrus microstent compared to selective laser trabeculoplasty in primary open angle glaucoma: one year results. *Clin Exp Ophthalmol*. 2017;45:120-127.
15. Katz LJ, Erb C, Carceller Guillamet A et al. Long-term titrated IOP control with one, two, or three trabecular micro-bypass stents in open-angle glaucoma subjects on topical hypotensive medication: 42-month outcomes. *Clin Ophthalmol*. 2018;12:255-262.
16. Iordanous Y, Kent JS, Hutnik CM, Malvankar-Mehta MS. Projected cost comparison of Trabectome, iStent, and endoscopic cyclophotocoagulation versus glaucoma medication in the Ontario Health Insurance Plan. *J Glaucoma*. 2014;23:e112-8.
17. Tan SZ, Au L. Manchester iStent study: 3-year results and cost analysis. *Eye (Lond)*. 2016;30:1365-1370.
18. Ordóñez JE, Ordóñez A, Osorio UM. Cost-effectiveness analysis of iStent trabecular micro-bypass stent for patients with open-angle glaucoma in Colombia. *Curr Med Res Opin*. 2018;1-12.

7. Record of amendments to this document

Page	Details of Amendment	Date amended
Entire document	Reviewed	
Entire document	Reviewed	