Safety and effectiveness of the PRESERFLO® Microshunt in primary open-angle glaucoma: results from a 2-year multicenter study

Beckers, Henny J M; Aptel, Florent; Webers, Carroll A B; Bluwol, Elisa; Martínez-de-la-Casa, José M; García-Feijoó, Julián; Lachkar, Yves; Méndez-Hernández, Carmen D; Riss, Isabelle; Shao, Hui; Pinchuk, Leonard; Angeles, Raymund; Sadruddin, Omar; Shaarawy, Tarek

How to cite

BECKERS, Henny J M et al. Safety and effectiveness of the PRESERFLO® Microshunt in primary open-angle glaucoma: results from a 2-year multicenter study. In: Ophthalmology. Glaucoma, 2021. doi: 10.1016/j.ogla.2021.07.008

This publication URL: https://archive-ouverte.unige.ch/unige:154474

Publication DOI: 10.1016/j.ogla.2021.07.008

AMERICAN ACADEMY OF OPHTHALMOLOGY®

In partnership with the AMERICAN GLAUCOMA SOCIETY

Safety and Effectiveness of the PRESERFLO® MicroShunt in Primary Open-Angle Glaucoma

Results from a 2-Year Multicenter Study

Henny J.M. Beckers, MD, PhD,[1] Florent Aptel, MD, PhD,[2] Carroll A.B. Webers, MD, PhD,[1] Elisa Bluwol, MD,[3] José M. Martínez-de-la-Casa, MD, PhD,[4] Julián García-Feijoó, MD, PhD,[4] Yves Lachkar, MD,[3] Carmen D. Méndez-Hernández, MD,[4] Isabelle Riss, MD,[5] Hui Shao, PhD,[6] Leonard Pinchuk, PhD, DSc,[7] Raymund Angeles, MD,[6] Omar Sadruddin, MD, MBA,[6] Tarek M. Shaarawy, MD, FRCOphth[8]

Purpose: To assess the safety and effectiveness of the PRESERFLO® MicroShunt (formerly InnFocus MicroShunt) in patients with primary open-angle glaucoma (POAG).

Design: The MicroShunt, a controlled ab externo glaucoma filtration surgery device, was investigated in a 2-year, multicenter, single-arm study.

Participants: Eligible patients were aged 18−85 years with POAG inadequately controlled on maximal tolerated medical therapy with intraocular pressure (IOP) ≥18 and ≤35 mmHg or when glaucoma progression warranted surgery.

Methods: The MicroShunt was implanted as a stand-alone procedure with adjunctive use of topical mitomycin C (MMC; 0.2−0.4 mg/ml) for 2−3 minutes.

Main Outcome Measures: The primary effectiveness outcome was IOP reduction and success (not requiring reoperation or pressure failures [IOP > 21 mmHg and < 20% reduction in IOP]) at year 1. Additional end points at year 2 included IOP reduction, success, glaucoma medications, adverse events (AEs), and reoperations. Results are reported in the overall population and subgroups of patients receiving 0.2 or 0.4 mg/ml MMC.

Results: In 81 patients, mean (± standard deviation [SD]) IOP decreased from 21.7 ± 3.4 mmHg at baseline to 14.5 ± 4.6 mmHg at year 1 and 14.1 ± 3.2 mmHg at year 2 ($P < 0.0001$). Overall success (with and without supplemental glaucoma medication use) at year 1 was 74.1%. Mean (± SD) number of medications decreased from 2.1 ± 1.3 at baseline to 0.5 ± 0.9 at year 2 ($P < 0.0001$), and 73.8% of patients were medication free. Most common nonserious AEs were increased IOP requiring medication or selective laser trabeculoplasty (25.9%) and mild-to-moderate keratitis (11.1%). There were 6 (7.4%) reoperations and 5 (6.2%) needlings by year 2. In an analysis (post hoc) according to MMC concentration, overall success was 78.1% (0.2 mg/ml) and 74.4% (0.4 mg/ml; $P = 0.710$). In the 0.2 and 0.4 mg/ml MMC groups, 51.9% and 90.3% of patients were medication free, respectively ($P = 0.001$). There was a trend toward lower IOP and higher medication reduction in the 0.4 mg/ml MMC subgroup.

Conclusions: In this study, mean IOP and glaucoma medication reductions were significant and sustained over 2 years postsurgery. No long-term, sight-threatening AEs were reported. Further studies may confirm potential risk/benefits of higher MMC concentration. *Ophthalmology Glaucoma 2021;■:1−15 © 2021 by the American Academy of Ophthalmology. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).*

Supplemental material available at www.ophthalmologyglaucoma.org.

Primary open-angle glaucoma (POAG) is the most common form of glaucoma.[1] Intraocular pressure (IOP) is the only well-established modifiable risk factor,[1] and often, the initial IOP-lowering approach for the management of glaucoma is medical therapy.[1] However, patient adherence to medication can be suboptimal.[2] Laser and incisional surgical approaches, including trabeculectomy and tube shunt surgery, can provide long-term IOP reduction for patients with glaucoma.[3−5] Both trabeculectomy and tube shunt surgery are invasive procedures and associated with the requirement for substantial postoperative management;[3,4] therefore, minimally invasive glaucoma surgery (MIGS) has been developed to potentially provide a safer, easier, and less-invasive alternative to traditional incisional surgery.[6] Most canal-based or suprachoroidal-based MIGS devices have been associated with only modest IOP

https://doi.org/10.1016/j.ogla.2021.07.008
ISSN 2589-4196/21

reductions and are often indicated for patients who require cataract surgery[6] and the IOP-lowering effect of the device itself may be confounded by the effects of cataract surgery.[7] Furthermore, such MIGS devices are often implanted in patients with mild-to-moderate glaucoma.[8] Alternatively, MIGS devices that result in the formation of a bleb have been associated with substantial IOP reductions; for these devices, postsurgical management of the bleb, such as early needling with or without the concomitant injection of mitomycin C (MMC) to mitigate fibrosis, tends to play a vital role in surgical success.[9,10] Long-term IOP data for the majority of new devices/techniques are still unavailable.[8]

The PRESERFLO MicroShunt (MicroShunt, formerly known as the InnFocus MicroShunt) received Conformité Européenne marking in 2012 and Health Canada and Therapeutic Goods Administration of Australia approval in 2021 for uncontrolled POAG on maximum tolerated glaucoma medications or when glaucoma progression warrants surgery;[11–13] the MicroShunt has not yet received Food and Drug Administration approval. The MicroShunt is an 8.5-mm–long (70-μm lumen and 350-μm outer diameter) controlled ab externo glaucoma filtration surgery device composed of poly(styrene-*block*-isobutylene-*block*-styrene), a highly biocompatible and bioinert material.[14] The MicroShunt is inserted via an ab externo procedure. After implantation, the proximal tip of the device sits in the anterior chamber, parallel to the iris, and the distal tip sits underneath the conjunctiva and Tenon's capsule, approximately 6 mm behind the limbus, allowing flow of aqueous humor through the lumen to form a posterior bleb.[14,15]

In a prospective, single-arm study conducted at a single site in the Dominican Republic, 23 patients with POAG received the MicroShunt alone or in combination with cataract surgery.[15,16] Published results showed IOP and glaucoma medication lowering after MicroShunt implantation.[15] Mean IOP ± standard deviation (SD) was reduced from 23.8 ± 5.3 mmHg at baseline (n = 23) to 10.7 ± 3.5 mmHg at year 3 (n = 22; representing a −55% change), and mean ± SD number of glaucoma medications per patient was reduced from 2.4 ± 0.9 (n = 23) to 0.7 ± 1.1 (n = 22), with 64% of patients medication free at year 3. The success rate (IOP ≤ 14 mmHg and ≥ 20% IOP reduction with or without use of supplemental medication) was 95% at year 3. There were few device-related intraoperative and postoperative adverse events (AEs) after MicroShunt implantation; the most common AEs were device touching iris (n = 3, 13%), transient hypotony (n = 3, 13%), shallow or flat anterior chamber (n = 3, 13%), and transient choroidal effusion (n = 2, 9%). Of note, there were no reports of device migration or erosion, bleb leaks, bleb infection, persistent corneal edema, endophthalmitis, or chronic hypotony and only 1 patient required a reoperation by year 3.

The study reported was the first study to be conducted across multiple European centers and by multiple surgeons. The aim of this study and analysis was to assess the safety and effectiveness of MicroShunt implantation as a standalone procedure in patients with POAG. The final 2-year results from this study are presented.

Methods

Study Design

This was a prospective, single-arm, multicenter study assessing the safety and effectiveness of the MicroShunt in patients with mild-to-severe POAG (ClinicalTrials.gov Identifier: NCT02177123). The study was conducted across 6 European sites, including 3 sites in France and 1 site each in The Netherlands, Spain, and Switzerland. A qualifying assessment was carried out preoperatively, and further tests were conducted postoperatively on day 1, day 7, week 4, month 3, month 6, month 9, year 1, and year 2. The study was conducted in accordance with the Declaration of Helsinki and the requirements for medical device investigations as presented in EN/ISO 14155 (2011), Clinical Investigation of Medical Devices for Human Subjects − Good Clinical Practice, Annex X of the European Medical Devices Directive 93/42/EEC, as amended by Directive 2007/47/EEC, MEDDEV 2.7/4, and applicable local regulatory requirements. Institutional Review Board approval was obtained for each site, and patients provided written informed consent before their enrollment in the study.

Patients

Eligible patients were aged 18–85 years with POAG inadequately controlled on maximal tolerated medical therapy with IOP ≥ 18 and ≤ 35 mmHg or when glaucoma progression warranted surgery. Only 1 eye per patient was enrolled in the study. Treatment success and safety analyses were based on data from the eye specified during enrollment. As part of standard-of-care treatment, patients were permitted to undergo MicroShunt implantation in the non-study eye; however, this did not affect the analyses reported for the study eye. Key exclusion criteria included vision level of no light perception; known allergy to MMC; previous incisional surgery, excluding uncomplicated cataract surgery at least 6 months before enrollment; laser surgery within 90 days of enrollment; and need for glaucoma surgery combined with other ocular procedures or anticipated need for additional ocular surgery in the study eye during the investigational period.

Procedure and Assessments

The MicroShunt was provided by InnFocus Inc., in a sterile package with a 3-mm scleral marker, a 1-mm triangular-bladed knife, 3 LASIK Shield sponges (EYETEC), a marker pen, and a 25-gauge needle. The MicroShunt was implanted as a stand-alone procedure via an ab externo approach. Before implantation, topical or sub-Tenon's anesthesia was applied to the study eye. The MicroShunt was removed from sterile packaging onto a sterile field and rinsed using a balanced salt solution. Corneal traction was performed at the surgeon's discretion. A fornix-based conjunctival flap was created by peritomy between 2 rectus muscles followed by a posterior sub-Tenon's delamination, approximately 8-mm deep and 90°–120° wide. Hemostasis was controlled with bipolar diathermy or other means at the discretion of the surgeon. Three MMC-soaked LASIK Shield sponges were placed under the subconjunctival flap (2 sponges posteriorly and 1 more anteriorly) for 2–3 minutes; on removal of the sponges, the flap was rinsed with a balanced saline solution. The concentration and exposure time of MMC varied between sites; 3 sites used MMC 0.2 mg/ml (2 sites for 2 minutes and 1 site for 3 minutes), 2 sites used 0.4 mg/ml (1 site each for 2 or 3 minutes), and 1 site used 0.28 mg/ml for 2 minutes.

A location 3 mm from the limbus was marked with an inked scleral marker, and a 1-mm–wide, 1- to 2-mm–long, shallow scleral pocket was formed 3 mm posteriorly and toward the limbus

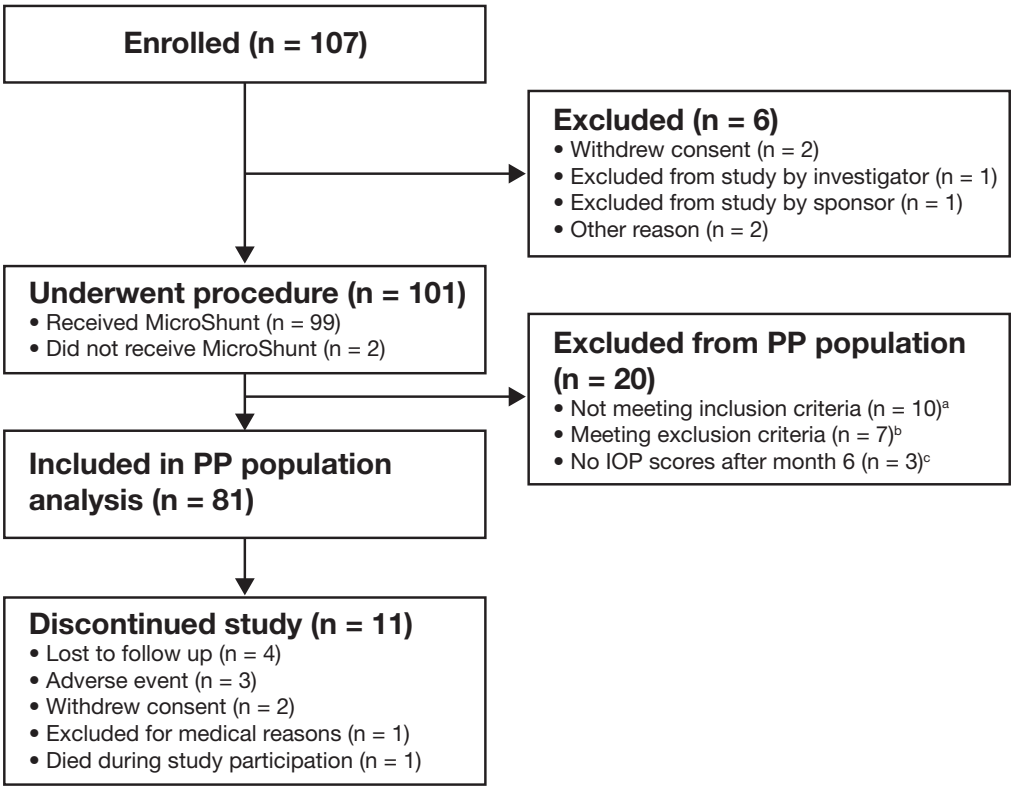

Figure 1. Patient disposition. [a]Reasons for not meeting inclusion criteria included patients with an intraocular pressure (IOP) < 18 or > 35 mmHg at baseline (n = 7) and a type of glaucoma other than primary open-angle glaucoma (n = 3). [b]Reasons for meeting exclusion criteria included prior laser surgery in the last 90 days (n = 3), previous incisional surgery in the last 6 months (n = 2), and use of ocular hypotensive medications in the fellow eye (n = 2). [c]The patients who did not receive the MicroShunt (n = 2) were included in the patients who had no IOP score after month 6 (n = 3). PP = per-protocol.

with a stab incision of the 1-mm triangular-bladed knife. A needle tract was formed by passing a 25-gauge needle through the scleral pocket, under the limbus and into the anterior chamber, approximately bisecting the cornea and iris, and then retracting the needle. With the use of forceps, the MicroShunt was threaded through the needle tract, and the 1.1-mm−wide fins of the device were wedged into the 1-mm−wide scleral pocket. Flow of aqueous humor from the anterior chamber through the lumen and out the distal end of the device was confirmed before tucking the device beneath the conjunctiva and Tenon's capsule. The conjunctiva and Tenon's capsule were repositioned using 10-0 nylon or 8-0 or 9-0 Vicryl sutures at the surgeon's discretion. The surgical site was examined for bleb leaks, and the corneal traction suture, if used, was removed.

Intraocular pressure was measured using Goldmann applanation tonometry. Slit-lamp biomicroscopy was used to evaluate any changes in ocular status and the safety of the MicroShunt. Visual acuity (VA) (measured by Snellen or Monoyer chart and converted to logarithm of the minimum angle of resolution) and any potential complications were evaluated at follow-up intervals.

End Points

The primary effectiveness end point of this 2-year study was IOP reduction after 1 year of follow-up, with the determination of success at year 1. Success was defined by patients who were not pressure or surgical failures. Surgical failures were defined by patients requiring additional glaucoma surgery in the operating room (e.g., bleb revisions, new device implantation, trabeculectomy, repositioning the MicroShunt). Bleb needlings were reported but not considered failures. Pressure failures were defined by patients out of the target IOP range (between ≥ 6 and < 21, < 18, or < 15 mmHg) or with less than 20% reduction from baseline on 2 consecutive scheduled follow-up visits after 3 months and did not achieve 20% reduction below baseline in the last visit in which the success rate was reported. Complete success was reported as without the use of supplemental glaucoma medications and without 2 consecutive pressure failures. Qualified success was reported as requiring supplemental medication to control IOP but without 2 consecutive pressure failures. Overall success is the sum of both qualified and complete success. The secondary effectiveness end points were success at year 2 and the number of glaucoma medications per patient. The primary safety end point was the incidence of all device- or procedure-related AEs in the study eye during the study. Additional safety end points were VA change from baseline and the incidence of glaucoma reoperations.

Statistical Methods

Statistical analyses were performed with SAS System Version 9.2 (SAS Institute Inc.) or higher on locked databases. A sample size of 85 was calculated as being required to demonstrate a surgical success > 50% at year 1. Calculations were performed using a 1-group chi-square test with a 5% alpha level and 80% power (nQuery software). The sample size was increased to 100 to allow for patients exiting the study before the year-1 visit. The intention-to-treat (ITT) population was defined as all enrolled patients who attended the procedure visit to receive the MicroShunt. Data for the per-protocol (PP) population, defined as patients who had at least 1 IOP measurement collected at or after month 6 and had no major

protocol deviations (i.e., deviations from the inclusion or exclusion criteria) are reported herein. The PP population is included in all effectiveness and safety end points; safety data for the ITT population are also reported.

Quantitative end points are reported in terms of mean and SD or median and interquartile range, and qualitative end points are reported in terms of number and percentage of each modality. Descriptive summaries are based on observed cases, with the exception of the calculation of success rates, where missing IOP measurements were replaced with the last observed IOP measurement. The number of glaucoma medications at each visit was calculated on the basis of medication start/end dates, visit date, and study exit date. Adverse event summaries were based on AEs that began on or before year 2 (or day 730 if dates were missing). The MicroShunt surgery date was used if the AE start date was missing; this date was then used to derive the resolution day. Summary statistics for resolution day were missing if the corresponding patient had a missing end date (i.e., the AE was ongoing at study exit). Device- and procedure-related AEs are presented together to avoid double-counting and categorized as early (before or on month 1) and late (after month 1), as suggested in the World Glaucoma Association guidelines.[17] Of note, serious AEs (SAEs) are reported separately. Data collected after reoperation (surgical failures) were excluded from the effectiveness and safety analyses.

Post Hoc Analyses

Data were analyzed in the subgroups of patients with 0.2 or 0.4 mg/ml MMC; all statistical, comparative analysis of the varied concentration of MMC was conducted retrospectively. Six patients received an intermediate concentration of MMC of 0.28 mg/ml; because of the small sample size, data from these patients were not included in the majority of the subanalyses, with the exception of safety.

In addition, statistical methods for generating *P* values were performed post hoc. *P* values were not adjusted by baseline covariates or for multiplicity. The majority of *P* values were calculated on the basis of 2 sample *t* tests (IOP measurements, number of glaucoma medications, and VA change from baseline). *P* values for success were calculated using a chi-square test. *P* values for the procedure or device-related AEs, according to MMC concentration, were calculated using the Fisher exact test.

Results

Study Patients

Patients were enrolled over a 1-year period and followed for 2 years; the first and last patient visits were in April 2014 and November 2017, respectively. A total of 107 patients were enrolled in the study, and of these, 101 attended MicroShunt procedure visit (ITT population). Overall, 81 patients did not experience any major protocol deviations and had at least 1 IOP measurement collected after month 6; these patients comprised the PP population (Fig 1). A total of 11 patients in the PP population discontinued the study, and 1 patient received a second MicroShunt before year 2 (Fig 1).

Patient demographics and baseline characteristics for the PP and ITT populations are shown in Table 1 and Table S2 (available at www.ophthalmologyglaucoma.org), respectively.

Effectiveness

In the overall population, mean IOP ± SD was reduced from 21.7 ± 3.4 mmHg at baseline (N = 81) to 14.5 ± 4.6 mmHg at year 1 (n = 67; −7.7 ± 4.6 mmHg; −31.4%; $P < 0.0001$) and 14.1 ± 3.2 mmHg at year 2 (n = 60; −7.8 ± 4.1 mmHg; −34.1%; $P < 0.0001$) (Fig 2; for year 1 data, Fig S3, available at www.ophthalmologyglaucoma.org).

At year 1, overall success (defined as an absence of 2 consecutive pressure failures; outside target range or < 20% reduction from baseline, with and without supplemental glaucoma medication use) was 74.1%, with 78.3% of these patients being complete success (i.e., supplemental glaucoma medications not required to maintain controlled levels of IOP) and 21.7% being qualified success (i.e., requiring supplemental glaucoma medications to maintain controlled levels of IOP). The same overall success rate (74.1%) was observed at year 2, of which 80.0% were complete and 20.0% were qualified success (Table S3, available at www.ophthalmologyglaucoma.org). Fourteen patients (17.3%) were classified as pressure failures at year 2. The success probabilities are shown in Figure 4.

The mean ± SD number of glaucoma medications per patient decreased from 2.1 ± 1.3 (N = 81) at baseline to 0.5 ± 0.9 at year 2 (n = 61; $P < 0.0001$) (Fig 5). The percentage of medication-free patients (regardless of IOP level) at year 2 was 73.8%. The types and number of postoperative glaucoma medications varied between sites (Fig S6, available at www.ophthalmologyglaucoma.org).

Safety

In the ITT population, device- or procedure-related nonserious AEs and SAEs were reported in 57 (56.4%) and 7 (6.9%) patients, respectively; the most common (≥3%) nonserious AEs and all SAEs that occurred by year 2, categorized by early (on or before month 1) and late (after month 1) events, are shown in Table S4 (available at www.ophthalmologyglaucoma.org). In the PP population, device- or procedure-related nonserious AEs and SAEs were reported in 49 (60.5%) and 6 (7.4%) patients, respectively. The most common (≥3%) nonserious AEs and all SAEs that

Table 1. Patient Demographics and Baseline Characteristics (Per-Protocol Population)

Demographics and Baseline Characteristics	Overall Population (N = 81)
Age, yrs (mean ± SD)	64.4 ± 12.2
Range	28–85
Male, n (%)	36 (44.4)
Lens status, n (%)	
Phakic	55 (67.9)
Pseudophakic	26 (32.1)
Medicated IOP, mmHg (mean ± SD)	21.7 ± 3.4
Range	18–33
IOP ≥ 18 and ≤ 21 mmHg, n (%)	45 (55.6)
IOP > 21 mmHg, n (%)	36 (44.4)
Medicated IOP, mmHg (median [IQR])	20.0 (4.5)
No. of glaucoma medications (mean ± SD)	2.0 ± 1.3
Range	0–5
No. of glaucoma medications (median [IQR])	2.0 (2.0)
VA, logMAR (mean ± SD)	0.12 ± 0.17
Range	−0.1–1.0
VA, logMAR (median [IQR])	0.10 (0.15)

IOP = intraocular pressure; IQR = interquartile range; logMAR = logarithm of the minimum angle of resolution; SD = standard deviation; VA = visual acuity.

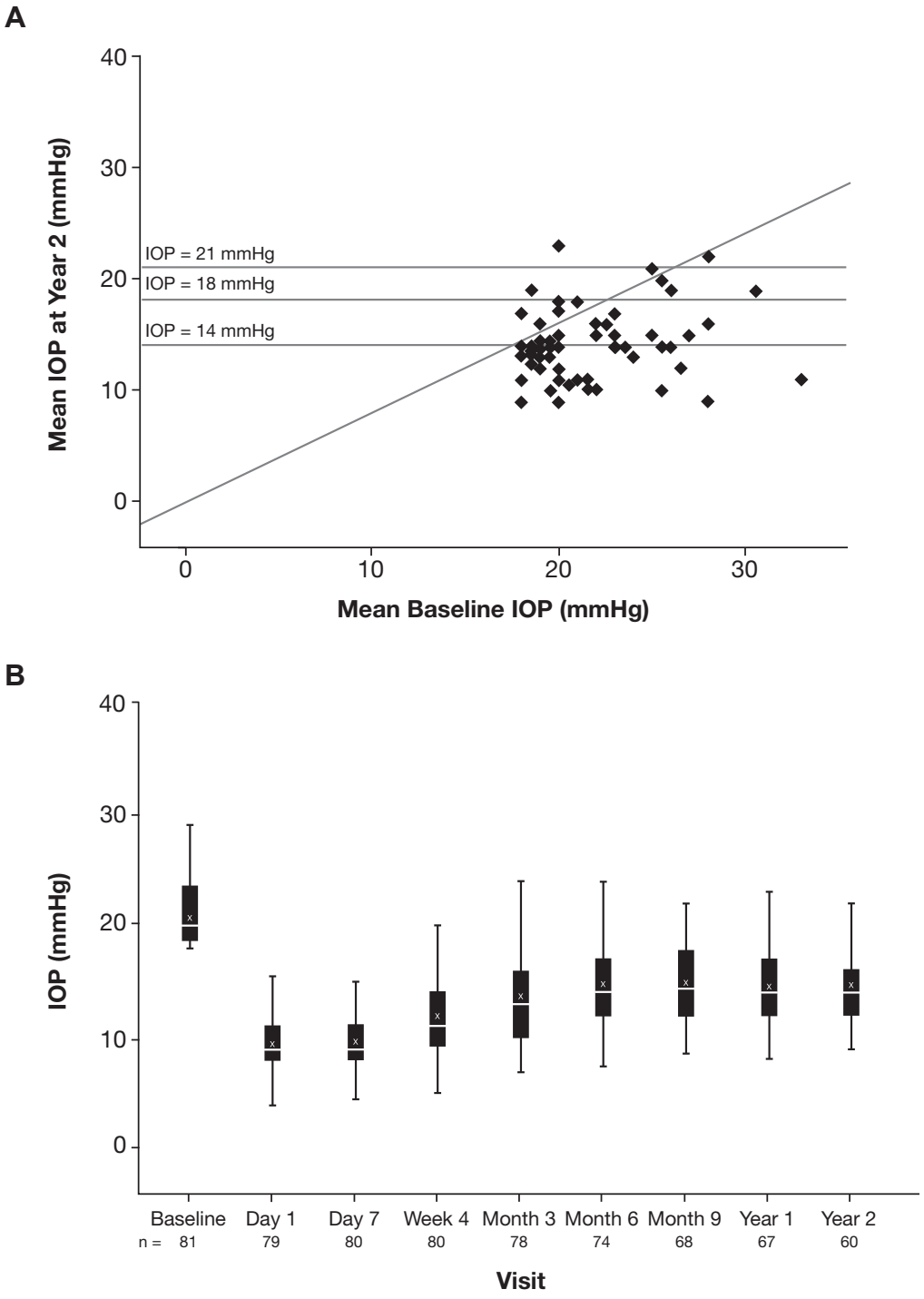

Figure 2. (**A**) Postoperative intraocular pressure (IOP) levels compared with preoperative IOP at 2 years of follow-up. The diagonal line represents a 20% reduction in mean IOP. (**B**) Mean and median medicated IOP over 2 years of follow-up (per-protocol population). The upper and lower borders of the box indicate the 75th and 25th percentiles, respectively. The whiskers indicate the maximum and minimum values. The horizontal line and white symbol within each box indicate the median and mean, respectively.

occurred by year 2, categorized by early and late events, are shown in Table 5. All SAEs resolved within 46 days, apart from 1 event requiring unplanned surgical reintervention. In the PP population, mean ± SD VA logarithm of the minimum angle of resolution scores changed from 0.12 ± 0.17 (N = 81) at baseline to 0.10 ± 0.14 at year 2 (n = 58). In the PP population, 8 patients (9.9%) underwent a bleb revision alone by year 2. Needling or postsurgical injection of the bleb with 5-fluorouracil was required in 5 patients. In total, 6 patients required a reoperation. These are further described in the MMC subgroup analysis.

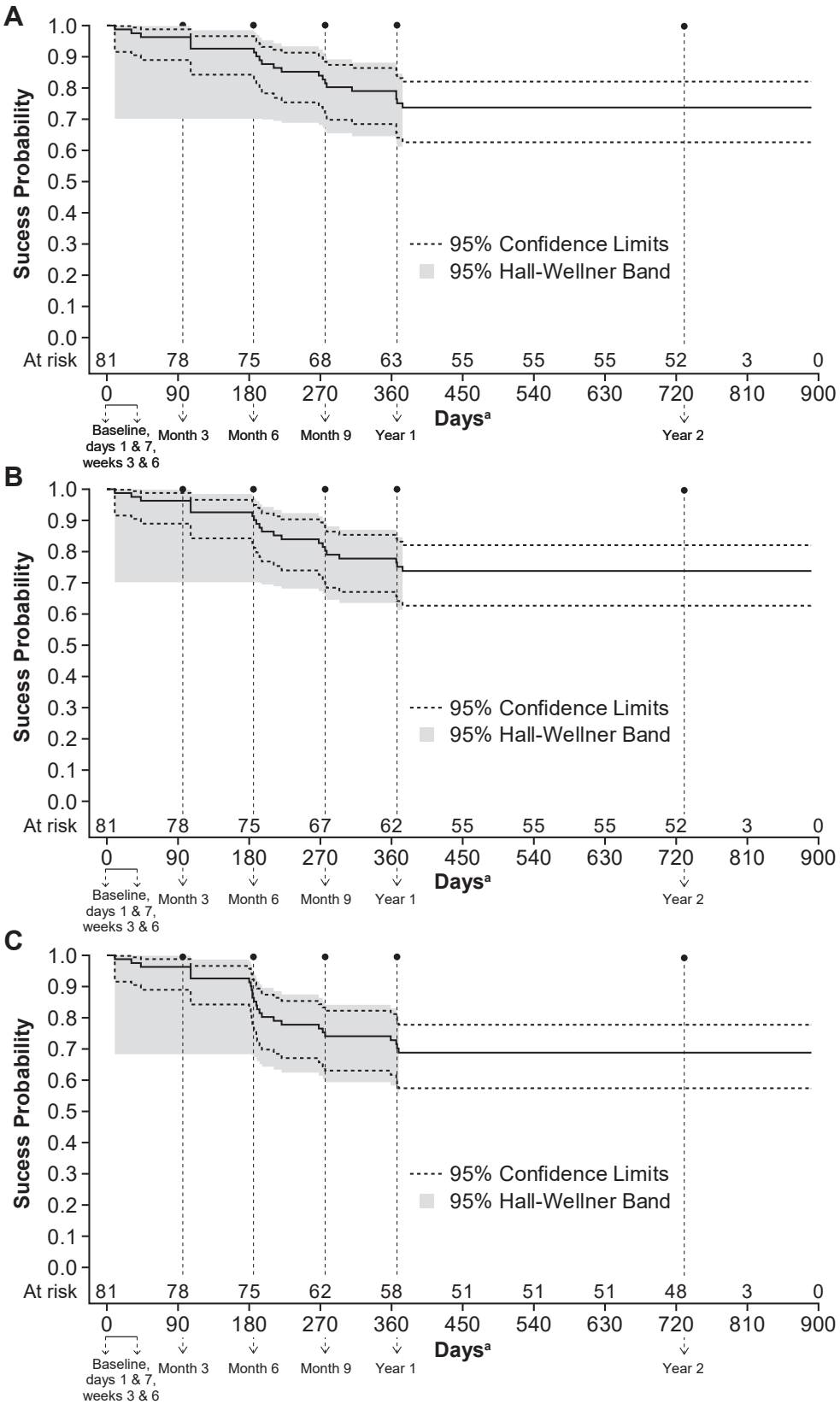

Figure 4. Success probabilities for the overall population according to intraocular pressure (IOP) target range over 2 years of follow-up (per-protocol population): (**A**) IOP $\geq$ 6 and $<$ 21 mmHg, (**B**) IOP $\geq$ 6 and $<$ 18 mmHg, (**C**) IOP $\geq$ 6 and $<$ 15 mmHg. [a]Success was assessed in all patients (N = 81); 44 patients had their year 2 visit after day 730.

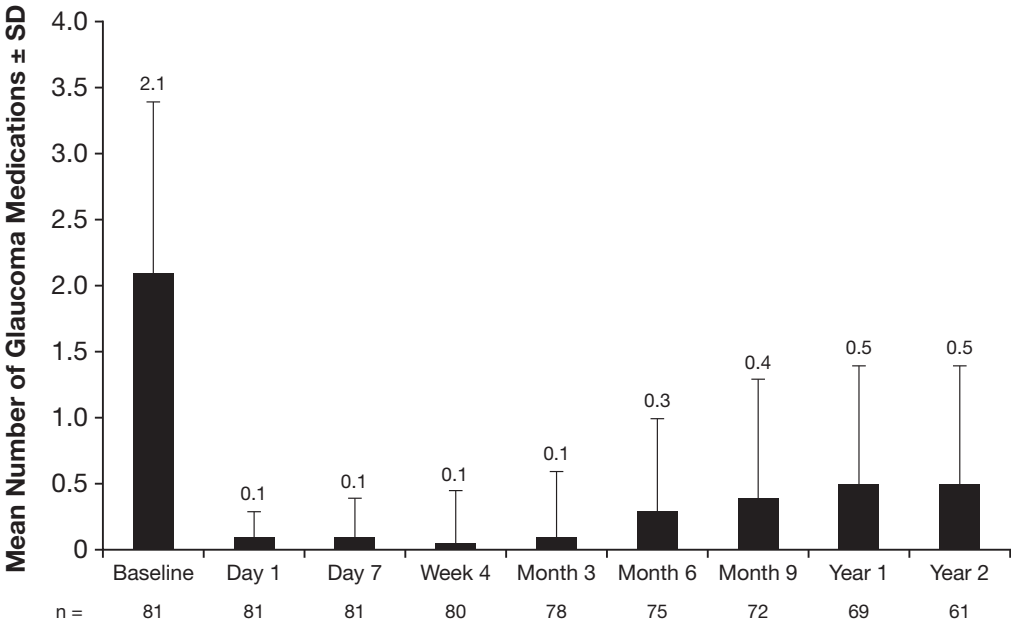

Figure 5. Mean (± SD) number of glaucoma medications per patient over 2 years of follow-up. SD = standard deviation.

Key Findings from Post Hoc Analyses: MMC Subgroup Analysis

The surgery was performed using 0.2 mg/ml MMC in 32 patients and 0.4 mg/ml MMC in 43 patients. Patient demographics and disease characteristics were balanced between groups (Table 6).

In the 0.2 mg/ml MMC subgroup, mean IOP reduced from 20.9 ± 2.5 mmHg at baseline (n = 32) to 15.3 ± 5.9 mmHg at year 1 (n = 29; −7.0 ± 4.0 mmHg; −25.6%) and 14.4 ± 3.3 mmHg at year 2 (n = 27; −6.7 ± 2.8 mmHg; −30.6%). In the 0.4 mg/ml MMC group, mean IOP was reduced from 21.9 ± 3.7 mmHg at baseline (n = 43) to 13.7 ± 3.4 mmHg at year 1 (n = 35; −8.2 ± 4.9 mmHg; −35.7%) and 13.5 ± 3.1 mmHg at year 2 (n = 30; −8.8 ± 4.9 mmHg; −37.6%). There was a significant difference in IOP at month 6 between the 0.2 mg/ml and 0.4 mg/ml MMC groups ($P = 0.038$), but the difference was not significant at any other visit (Fig 7).

At year 1, the overall success rates (with and without supplemental glaucoma medication use) in the 0.2 mg/ml and 0.4 mg/ml MMC groups were 78.1% and 74.4%, respectively ($P = 0.710$). In patients with overall success, the qualified success rates (target pressure range between ≥ 6 and < 21 mmHg) in the 0.2 mg/ml and 0.4 mg/ml MMC groups were 36.0% and 12.5%, respectively; the complete success rate was 64.0% in the 0.2 mg/ml MMC group compared with 87.5% in the 0.4 mg/ml MMC group. A similar trend was observed at year 2. Of the 14 patients classed as treatment failures, 7 patients were in the 0.2 mg/ml MMC group (21.9%) and 7 patients were in the 0.4 mg/ml MMC group (16.3%). The success probabilities are shown in Figures 8 and 9 (Table S7, available at www.ophthalmologyglaucoma.org).

In the 0.2 mg/ml MMC group, the mean number of glaucoma medications was reduced from 2.2 ± 1.3 at baseline (n = 32) to 0.9 ± 1.1 at year 2 (n = 27) (51.9% medication free). In the 0.4 mg/ml MMC group, the number of glaucoma medications was reduced from 2.0 ± 1.3 at baseline (n = 43) to 0.1 ± 0.4 at year 2 (n = 31) (90.3% medication free). A significant difference in the number of glaucoma medications (Fig 10) and percentage of medication-free patients at month 6 onward was observed between the 0.2 mg/ml and 0.4 mg/ml MMC groups ($P < 0.05$) (Fig 10).

In the 0.2 mg/ml MMC group, mean VA changed from 0.12 ± 0.15 (n = 32) at baseline to 0.12 ± 0.16 at year 2 (n = 25). In the 0.4 mg/ml MMC group, mean VA changed from 0.12 ± 0.13 (n = 43) at baseline to 0.08 ± 0.12 at year 2 (n = 30). Although there was a trend for maintenance or slight improvement of VA in the 0.4 mg/ml MMC group over 2 years, there were no statistically significant differences between the groups in VA at any visit.

Device- or procedure-related nonserious AEs were reported in 11 (34.4%) and 32 (74.4%) patients in the 0.2 mg/ml and 0.4 mg/ml MMC subgroups, respectively. Serious adverse events were reported in 2 (6.3%) and 4 (9.3%) patients in the 0.2 mg/ml and 0.4 mg/ml MMC subgroups, respectively. In the 0.4 mg/ml MMC subgroup, the majority (56%) of nonserious AEs occurred before month 1, compared with 16% in the 0.2 mg/ml MMC subgroup ($P < 0.001$). The most common (≥3%) nonserious AEs and all SAEs that occurred by year 2, categorized by early and late events, are shown in Table 8.

Of the 8 patients undergoing a bleb revision, 5 were in the 0.4 mg/ml MMC group and 3 were in the 0.28 mg/ml MMC group. Reoperations included bleb revision in combination with the implantation of a new glaucoma surgical implant (2 patients in the 0.2 mg/ml MMC group), trabeculectomy (1 patient in the 0.2 mg/ml MMC group), implantation of a second MicroShunt because it was not possible to correctly position the first device (1 patient in the 0.4 mg/ml MMC group), flap resuture (1 patient in the 0.4 mg/ml MMC group), and sclerectomy for increased IOP (1 patient in the 0.4 mg/ml MMC group).

Discussion

In this study, MicroShunt implantation in 81 patients with POAG resulted in significant reductions in IOP and use of glaucoma medications that were maintained over 2 years.

Table 5. Summary of Procedure- or Device-Related Nonserious AEs (Occurring in ≥ 3 % of Patients) and All SAEs in the Study Eye on or before 2 Years of Follow-up (Per-Protocol Population)

AEs (Procedure or Device Related), n (%)	Overall Population (N = 81)	
*Timing of AE**	*Early (on or before Month 1)*	*Late (after Month 1)*
Patients with any nonserious AE	32 (39.5)	33 (40.7)
Increased IOP	3 (3.7)[†]	20 (24.7)[†]
Transient hypotony (< 6 mmHg)	9 (11.1)	0 (0.0)
Keratitis[‡]	5 (6.2)	4 (4.9)
Leakage of wound site based on Seidel test	3 (3.7)	0 (0.0)
Pain	3 (3.7)	1 (1.2)
Flat anterior chamber	2 (2.5)	0 (0.0)
Hyphema	2 (2.5)	0 (0.0)
Diplopia	0 (0.0)	1 (1.2)
Corneal abrasion during surgery	1 (1.2)	0 (0.0)
Complication of device insertion	2 (2.5)	0 (0.0)
Cataract	0 (0.0)	1 (1.2)
Device touching cornea	0 (0.0)	1 (1.2)
Patients with any SAE	3 (3.7)	3 (3.7)
Event requiring unplanned glaucoma-related surgical reintervention	0 (0.0)	2 (2.5)
Keratitis[§]	1 (1.2)	0 (0.0)
Conjunctival dehiscence	1 (1.2)	0 (0.0)
Corneal ulcer[‖]	1 (1.2)	0 (0.0)
Increased IOP	0 (0.0)	1 (1.2)[¶]
Leakage of wound site based on Seidel test	1 (1.2)	0 (0.0)

AE = adverse event; IOP = intraocular pressure; SAE = serious adverse event.
*Patients who experienced multiple AEs are captured in both early and late categories depending on the AE start date.
[†]After the event of increased IOP, 9 patients received medication, 5 underwent surgical procedure, 3 received medication and surgical procedure, 2 underwent postsurgical injection of 5-fluorouracil, 2 underwent needling, 2 did not receive any intervention, and 1 received medication and needling. Some patients required multiple actions for increased IOP.
[‡]One patient had an IOP increase of ≥ 10 mmHg compared with baseline because of an encapsulated bleb.
[§]Keratitis is listed as an AE and an SAE depending on the severity of the reaction. The patient with an SAE of keratitis required hospitalization and medication. Keratitis as an AE is a mild-to-moderate reaction resolved with medication.
[‖]Corneal ulcer was defined as an epithelial erosion and was recorded as an SAE because of sponsor coding.
[¶]After the SAE of increased IOP, 1 patient received medication and underwent a surgical procedure.

Overall success (with and without supplemental glaucoma medication use) was 74.1% at years 1 and 2.

Previously reported data from the first single-center study conducted by Batlle et al[15] also showed sustained reductions in IOP after MicroShunt implantation, although IOP was reduced in the preliminary study to a greater extent at year 2 (mean IOP at baseline: 23.8 mmHg; year 2: 11.9 mmHg) compared with the current study (mean IOP at baseline: 21.7 mmHg; year 2; 14.1 mmHg). This difference in effectiveness may be explained by the exclusive use of the higher MMC concentration (0.4 mg/ml) with an application time of 3 minutes and some patients who underwent

Table 6. Patient Demographics and Baseline Characteristics for the Mitomycin C Subgroup Analysis (Per-Protocol Population)

Demographics and Baseline Characteristics	0.2 mg/ml MMC (n = 32)	0.4 mg/ml MMC (n = 43)	*P* Value
Age, yrs (mean ± SD)	64.0 ± 12.4	64.4 ± 12.5	0.884
Male, n (%)	13 (40.6)	22 (51.2)	0.366
Lens status, n (%)			
Phakic	24 (75.0)	28 (65.1)	0.359
Pseudophakic	8 (25.0)	15 (34.9)	
Medicated IOP, mmHg (mean ± SD)	20.9 ± 2.5	21.9 ± 3.7	0.195
IOP ≥ 18 and ≤ 21 mmHg, n (%)	22 (68.8)	23 (53.5)	
IOP > 21 mmHg, n (%)	10 (31.3)	20 (46.5)	
Medicated IOP, mmHg (median [IQR])	20.0 (3.0)	20.0 (6.0)	NA
No. of glaucoma medications (mean ± SD)	2.2 ± 1.3	2.0 ± 1.3	0.497
No. of glaucoma medications (median [IQR])	2.0 (2.0)	2.0 (2.0)	NA
VA, logMAR (mean ± SD)	0.12 ± 0.15	0.12 ± 0.13	0.984
VA, logMAR (median [IQR])	0.10 (0.10)	0.10 (0.15)	NA

IOP = intraocular pressure; IQR = interquartile range; logMAR = logarithm of the minimum angle of resolution; MMC = mitomycin C; NA, not applicable; SD = standard deviation; VA = visual acuity.

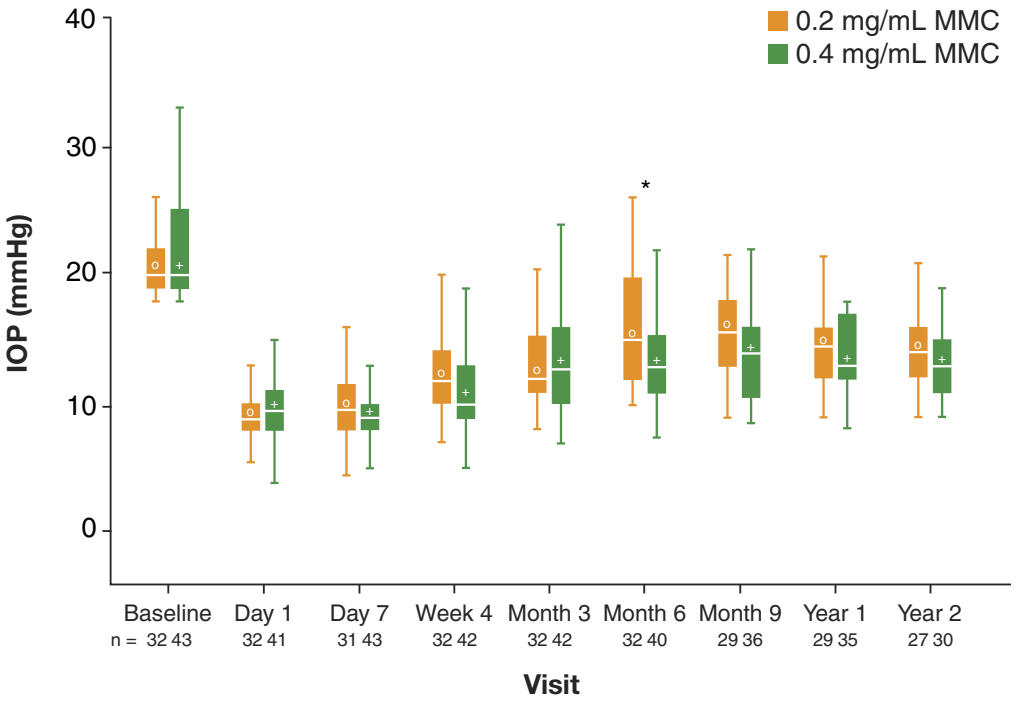

Figure 7. Mean and median medicated intraocular pressure (IOP) over 2 years of follow-up (per-protocol population). Asterisk denotes statistical significance between the 0.2 mg/ml and 0.4 mg/ml mitomycin C (MMC) groups at month 6 ($P = 0.038$). The upper and lower borders of the box indicate the 75th and 25th percentiles, respectively. The whiskers indicate the maximum and minimum values. The horizontal line and white symbol within each box indicate the median and mean, respectively.

combination surgery with phacoemulsification in the preliminary study.[15] Although the study by Batlle et al[15] was conducted at a single site in the Dominican Republic with a relatively homogeneous population consisting of patients predominantly of Afro-Caribbean descent, the present study assessed a stand-alone surgery for all patients that was conducted across multiple European sites and by multiple surgeons using various MMC concentrations and application times between the sites. The differences in demographics, varying surgical technique, and postoperative management practices among the sites may have influenced the results. The variations in results from multiple sites reported in this study reinforce that a one-size-fits-all approach may not be suitable, and although filtration surgery is a good option for many patients, there is still a requirement to customize treatment plans on an individual patient basis. Glaucoma medications received by patients before surgery might have differed between the studies, which may have been a confounding factor. Furthermore, there was a lower baseline IOP in this European study (21.7 ± 3.4 mmHg) compared with the baseline IOP in the study by Batlle et al[15] (23.8 ± 5.3 mmHg). At year 2 in this European study, there was a trend toward greater IOP reductions compared with year 1; this may be explained by the exclusion of patients from analysis if they were pressure/surgical failures before year 2 or prescribing glaucoma medications for patients not achieving optimal IOP control. This study also showed that the MicroShunt is well tolerated in patients with POAG, supporting the previously observed safety profile.[15] Yet, more patients experienced AEs in this study (60.5%) compared with the study by Batlle et al[15] (30.4%); again, the varying clinical practice across multiple centers and larger patient population in the current study may have contributed to the higher incidence of AEs compared with the previous single-site study.[15]

Postoperative IOP was similar between the 0.2 mg/ml and 0.4 mg/ml subgroups at year 1 and year 2; however, there was a trend toward greater IOP reduction with 0.4 mg/ml MMC compared with 0.2 mg/ml MMC postoperatively after month 6. Notably, in this study at month 6 onward, there was a significant difference between groups in medication reduction, and 90.3% of patients in the 0.4 mg/ml MMC group were medication free at year 2 compared with only half of the patients in the 0.2 mg/ml MMC group. The significantly higher medication use from month 6 onward in patients with 0.2 mg/ml MMC may have been caused by fibroses of the bleb reducing aqueous outflow in these patients. Alternatively, different prescribing practices among sites may have contributed to the higher use of medications in patients receiving 0.2 mg/ml. An MMC concentration of 0.4 mg/ml may have been considered more appropriate than 0.2 mg/ml MMC in the eyes of patients with more severe disease by some surgeons included in the study. However, it should be noted that this study was not powered to assess the effects of different MMC concentrations, and all comparisons between the MMC groups were conducted post hoc. Therefore, further research to determine whether the choice of MMC concentrations used by surgeons is

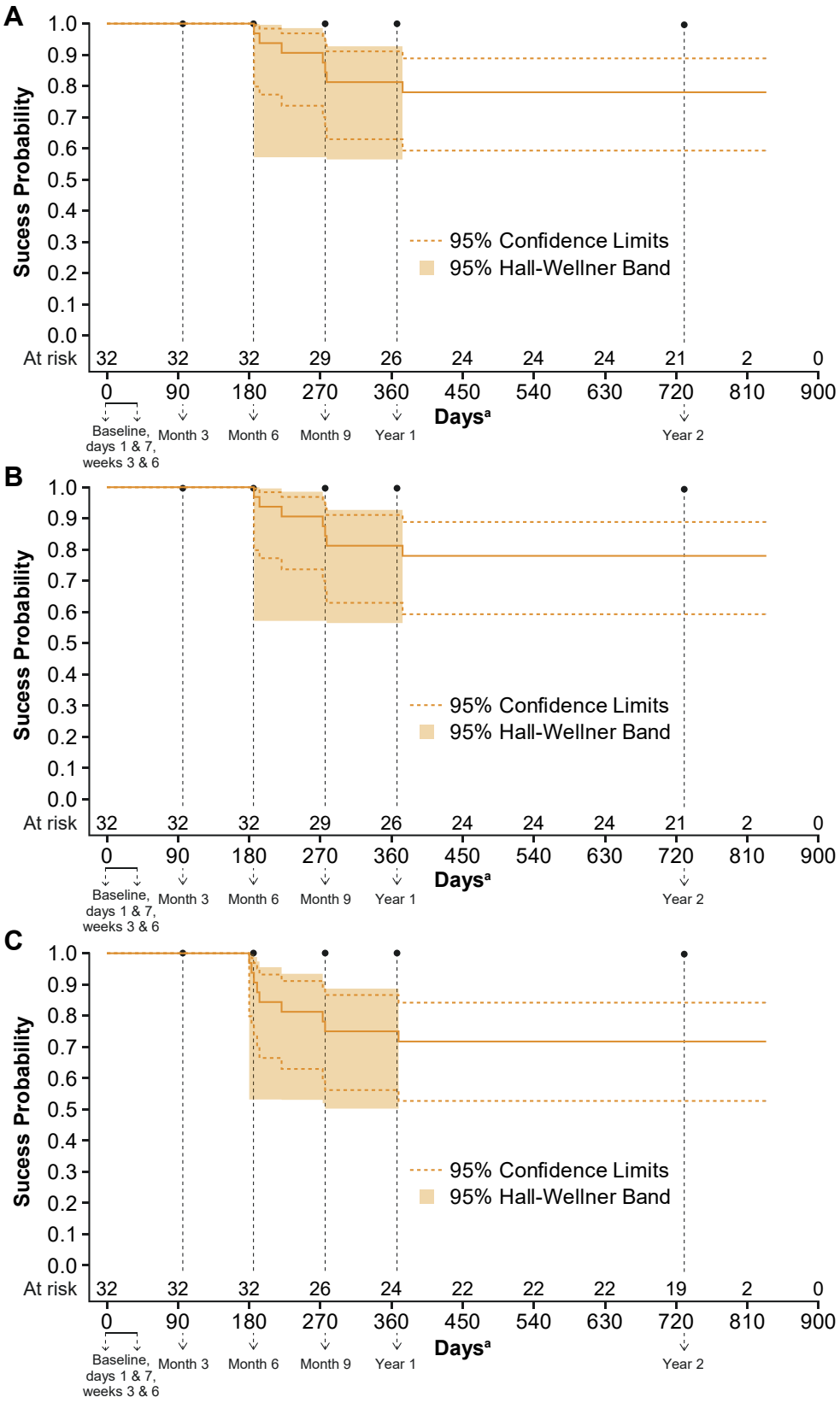

Figure 8. Success probabilities for the 0.2 mg/ml mitomycin C (MMC) concentration and intraocular pressure (IOP) target range over 2 years of follow-up (per-protocol population): (**A**) IOP ≥ 6 and < 21 mmHg, (**B**) IOP ≥ 6 and < 18 mmHg, (**C**) IOP ≥ 6 and < 15 mmHg. [a]Success was assessed in all patients (N = 81); 44 patients had their year 2 visit after day 730.

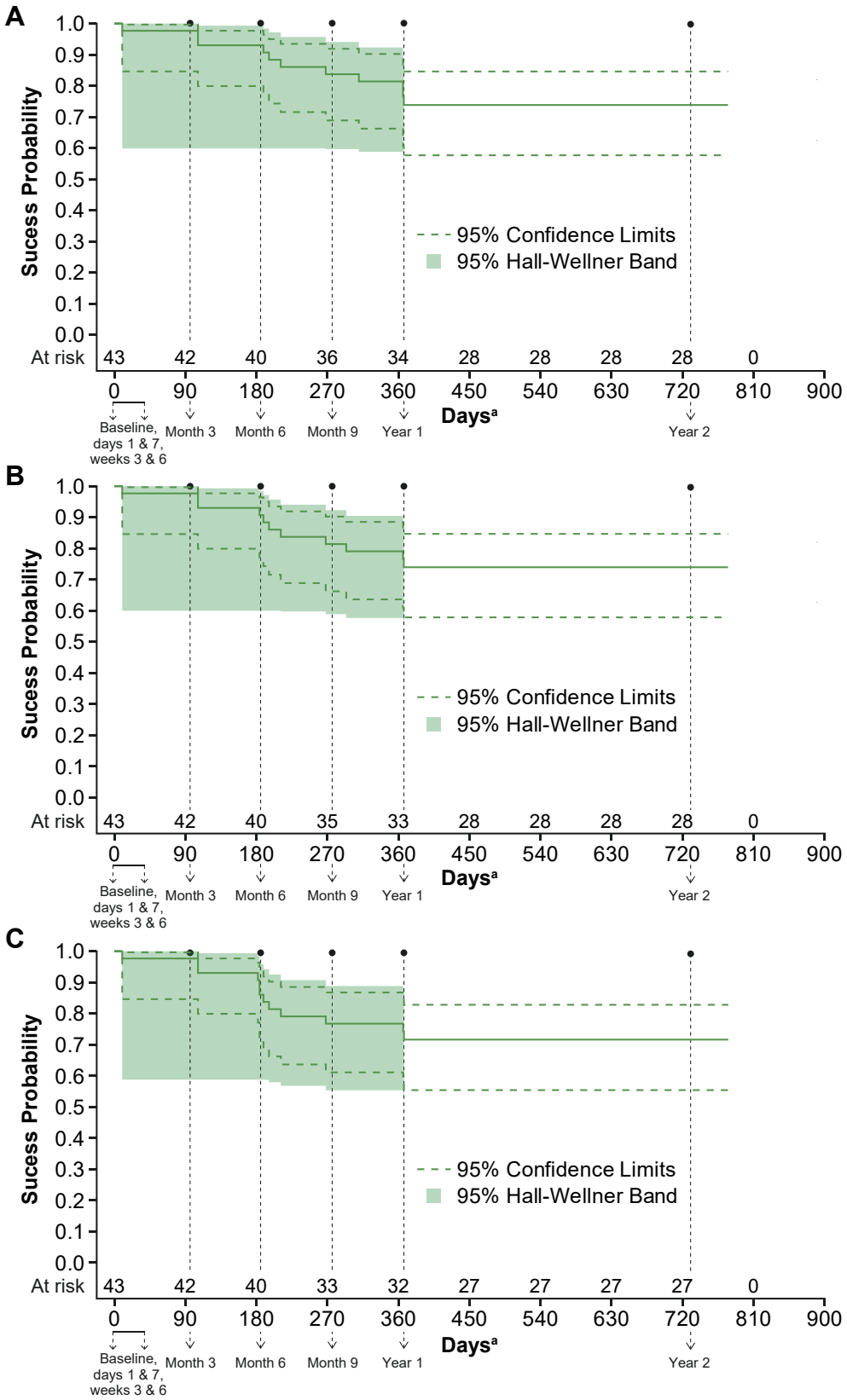

Figure 9. Success probabilities for the 0.4 mg/ml mitomycin C (MMC) concentration and intraocular pressure (IOP) target range over 2 years of follow-up (per-protocol population): (**A**) IOP $\geq$ 6 and $<$ 21 mmHg, (**B**) IOP $\geq$ 6 and $<$ 18 mmHg, (**C**) IOP $\geq$ 6 and $<$ 15 mmHg. [a]Success was assessed in all patients (N = 81); 44 patients had their year 2 visit after day 730.

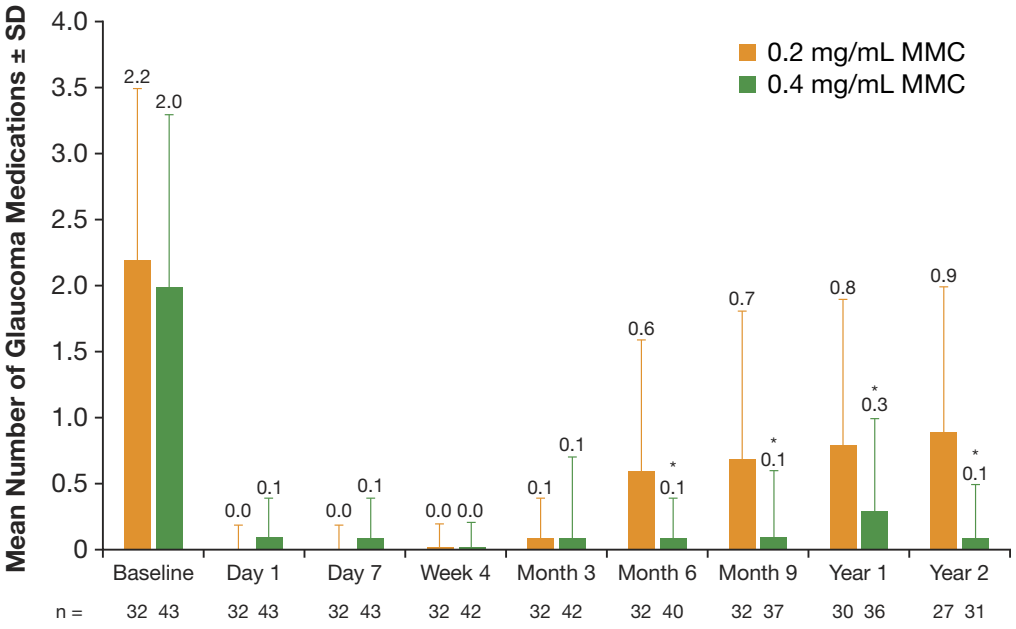

Figure 10. The mean number of glaucoma medications ± standard deviation (SD) over time in the 0.2 mg/ml and 0.4 mg/ml mitomycin C (MMC) subgroups. Asterisk denotes statistical significance between the 0.2 mg/ml and 0.4 mg/ml MMC groups at month 6 ($P = 0.003$), month 9 ($P = 0.003$), year 1 ($P = 0.012$), and year 2 ($P < 0.001$).

dependent on case severity or individual preferences are warranted.

Sanders et al[18] found that for procedures such as trabeculectomy, which is performed under the anterior Tenon's capsule, 0.2 mg/ml MMC was as efficacious as higher MMC doses (0.4 mg/ml) with regard to IOP reduction 1 year postsurgery. A rationale for this equivalence may be that the presence of fewer fibroblasts could allow for effective neutralization and saturation with 0.2 mg/ml MMC, implying that a dose of 0.4 mg/ml MMC may be unnecessary. In other glaucoma filtration procedures, a dose-response relationship has been observed with MMC, but this has not been consistently reported.[19] Our findings suggest that, contrary to other procedures, MMC dose may play an important role in MicroShunt surgery outcomes and reflect the possibility that more MMC is required in the mid-posterior part of the eye where the MicroShunt drains, the Tenon's capsule is thicker, and more fibroblast may reside.[20] However, some AEs, such as transient hypotony, occurred more frequently in the 0.4 mg/ml MMC group compared with the 0.2 mg/ml MMC group; therefore, the adverse effects of a higher MMC concentration need to be explored further.

Current bleb-based surgical approaches for glaucoma management that are performed with adjunctive use of MMC include XEN implantation and trabeculectomy.[4,9] The Primary Tube Versus Trabeculectomy study reported that in 242 eyes with uncontrolled glaucoma, baseline IOP was reduced from 23.9 ± 5.7 mmHg (mean ± SD) to 12.4 ± 4.4 mmHg at year 1 in the trabeculectomy group and from 23.3 ± 4.9 to 13.8 ± 4.1 mmHg in the tube shunt group. Further, the number of medications were reduced from 3.2 ± 1.1 to 0.9 ± 1.4 in the trabeculectomy group and 3.1 ± 1.1 to 2.1 ± 1.4 in the tube shunt group.[4] Postoperative intervention rates were high in both the trabeculectomy (n = 74; 63%) and tube shunt (n = 75; 60%) groups.[4] Early postoperative complications, such as wound leak and encapsulated bleb, were higher after trabeculectomy compared with tube shunt surgery.[4] In addition, 14% of patients required bleb needling after trabeculectomy.[4] In contrast, in our study, there was a low rate of postoperative interventions observed after MicroShunt implantation; however, randomized prospective clinical trial results comparing the outcomes of MicroShunt surgery with the outcomes after trabeculectomy or tube shunt implantation have not yet been published.

Likewise, substantial postoperative interventions to maintain IOP reductions have been required after more novel bleb-forming procedures. In a prospective, multicenter study of 65 patients with open-angle glaucoma, the mean IOP change from baseline (25.1 ± 3.7 mmHg) to year 1 (15.9 ± 5.2 mmHg) was −9.1 mmHg after XEN implantation, yet during the 1-year follow-up period, needling was required in 21 patients (32.3%).[9] In a retrospective study comparing trabeculectomy with XEN implantation, the number of needling procedures was significantly higher in the XEN group (n = 13; 20%) compared with the trabeculectomy group (n = 3; 5.4%) ($P = 0.0182$).[10] In contrast, in our study, there were a small number of needlings or postsurgical injections of the bleb (n = 5; 6.2%), and only 7.4% of patients required a reoperation by year 2. The number of bleb revisions alone (n = 8; 9.9%) in the current study was comparable to, or lower than,

Table 8. Summary of Procedure- or Device-Related Nonserious AEs (Occurring in ≥ 3% of Patients) and All SAEs in the Study Eye on or before 2 Years of Follow-up (Per-Protocol Population)

AEs (Procedure or Device Related), n (%)	0.2 mg/ml MMC (N = 32)		0.4 mg/ml MMC (N = 43)		*P* Value	
*Timing of AE:**	*Early (on or before month 1)*	*Late (after month 1)*	*Early (on or before month 1)*	*Late (after month 1)*	*Early (on or before month 1)*	*Late (after month 1)*
Patients with any nonserious AE	5 (15.6)	11 (34.4)	24 (55.8)	18 (41.9)	<0.001	0.633
Increased IOP[†]	2 (6.3)	9 (28.1)	0 (0)	10 (23.3)[‡]		
Transient hypotony (< 6 mmHg)	0 (0.0)	0 (0.0)	7 (16.3)	0 (0.0)		
Keratitis[§]	0 (0.0)	1 (3.1)	5 (11.6)	3 (7.0)		
Leakage of wound site based on Seidel test	0 (0.0)	0 (0.0)	3 (7.0)	0 (0.0)		
Pain	1 (3.1)	0 (0.0)	2 (4.7)	1 (2.3)		
Flat anterior chamber	0 (0.0)	0 (0.0)	2 (4.7)	0 (0.0)		
Hyphema	1 (3.1)	0 (0.0)	1 (2.3)	0 (0.0)		
Diplopia	0 (0.0)	1 (3.1)	0 (0.0)	0 (0.0)		
Corneal abrasion during surgery	1 (3.1)	0 (0.0)	0 (0.0)	0 (0.0)		
Complication of device insertion	1 (3.1)	0 (0.0)	1 (2.3)	0 (0.0)		
Cataract	0 (0.0)	1 (3.1)	0 (0.0)	0 (0.0)		
Device touching cornea	0 (0.0)	1 (3.1)	0 (0.0)	0 (0.0)		
Patients with any SAE	1 (3.1)	1 (3.1)	2 (4.7)	2 (4.7)	1.000	1.000
Event requiring unplanned glaucoma-related surgical reintervention	0 (0.0)	1 (3.1)	0 (0.0)	1 (2.3)		
Keratitis[§]	1 (3.1)	0 (0.0)	0 (0.0)	0 (0.0)		
Conjunctival dehiscence	0 (0.0)	0 (0.0)	1 (2.3)	0 (0.0)		
Corneal ulcer[‖]	0 (0.0)	0 (0.0)	1 (2.3)	0 (0.0)		
Increased IOP	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.3)[¶]		
Leakage of wound site based on Seidel test	0 (0.0)	0 (0.0)	1 (2.3)	0 (0.0)		

AE = adverse event; IOP = intraocular pressure; MMC = mitomycin C; SAE = serious adverse event.
In total, 6 patients received 0.28 mg/ml of MMC; these patients were not included in the 0.2 or 0.4 mg/ml MMC analyses. *P* values were based on Fisher exact test and not adjusted for baseline glaucoma medications or multiplicity.
*Patients who experienced multiple AEs are captured in both early and late categories depending on the AE start date.
[†]After the event of increased IOP, 9 patients received medication, 5 underwent surgical procedure, 3 received medication and surgical procedure, 2 underwent postsurgical injection of 5-fluorouracil, 2 underwent needling, 2 did not receive any intervention, and 1 received medication and needling. Some patients required multiple actions for increased IOP.
[‡]One patient had an IOP increase of ≥ 10 mmHg compared with baseline because of an encapsulated bleb.
[§]Keratitis is listed as an AE and SAE depending on the severity of the reaction. The patient with an SAE of keratitis required hospitalization and medication. Keratitis as an AE is a mild-to-moderate reaction resolved with medication.
[‖]Corneal ulcer was defined as an epithelial erosion and was recorded as an SAE because of sponsor coding.
[¶]After the SAE of increased IOP, 1 patient received medication and underwent a surgical procedure.

published data for other bleb-forming surgeries, such as trabeculectomy (n = 5; 4.7%)[3] and XEN implantation (n = 80; 34.0%).[21] In the 8 patients who underwent a bleb revision, needling of the bleb may have been sufficient to maintain the IOP-lowering effects of the MicroShunt, as seen after failed trabeculectomies.[22] However, the choice between bleb needling or revision, and glaucoma reoperation (trabeculectomy or tube shunt surgery), was at the surgeon's discretion, and because MicroShunt implantation was a new technique, optimal postsurgical management was still being determined throughout the study. Comparative, prospective, randomized studies between MicroShunt and XEN implantation have not been conducted to date.

The current study has its limitations. The analysis presented outcomes from procedures performed by 10 surgeons across 6 sites. The study was conducted after MicroShunt approval in the European Union, but at the time of the study, MicroShunt implantation was a new technique, and the investigators' experience with the device was limited. Subsequently, optimal implantation technique and postsurgical management were learned by the surgeons throughout the study. Furthermore, differences were apparent between surgeons and sites relating to concentration and time of application of MMC, glaucoma medication prescription, and postoperative management practices. A longer follow-up period is required to examine the IOP- and medication-lowering effects of MicroShunt implantation over time and assess the effect of this treatment on pertinent factors, such as corneal endothelial cell density. Although this study suggests that a higher concentration of MMC (0.4 mg/ml) may result in better efficacy outcomes after MicroShunt implantation compared with a lower concentration of MMC (0.2 mg/ml), this study was not powered to assess the effects of different MMC concentrations, and all comparisons between the MMC groups were conducted post hoc. Further, variation among surgeons, sites, and in the placement and exposure time of MMC may have confounded the results. Therefore, additional prospective studies may be useful to determine the effects of different MMC concentrations and optimal MMC delivery method and placement.

In conclusion, in this study, IOP and number of glaucoma medications were reduced and maintained below 15 mmHg for up to 2 years postsurgery. Variability within the results may be a result of differences in clinical practice between multiple centers and individual surgeons' surgical techniques and learning curves. No long-term, sight-threatening AEs were reported, and only a small number of patients required needlings/postsurgical injections of the bleb to maintain desirable IOP levels after MicroShunt implantation. A clinical study is ongoing that aims to compare the safety and efficacy of the MicroShunt with trabeculectomy.[23]

Acknowledgments. Medical writing support, including preparation of manuscript drafts for critical revision and approval by the authors in accordance with GPP3, was provided by Bethany Broughton, MSc, Helios Medical Communications, which was funded by Santen Inc. The study was sponsored by InnFocus Inc., a Santen Pharmaceutical Co. Ltd. company. The authors thank Santen for support in the development of this manuscript and Tuan Nguyen for statistical support and data analysis.

Footnotes and Disclosures

Originally received: April 1, 2021.
Final revision: July 16, 2021.
Accepted: July 21, 2021.
Available online: ■■■. Manuscript no. D-21-00094

[1] University Eye Clinic, Maastricht University Medical Center, Maastricht, the Netherlands.

[2] CHU de Grenoble-Alpes, Grenoble, France.

[3] Hôpital Paris Saint Joseph, Paris, France.

[4] Departamento de Oftalmologia Universidad Complutense, Hospital Clínico San Carlos, OFTARED, Madrid, Spain.

[5] Pôle Ophtalmologique de la Clinique Mutualiste, Bordeaux, France.

[6] Santen Inc., Emeryville, California.

[7] InnFocus Inc., a Santen Company, Miami, Florida.

[8] Hôpitaux Universitaires de Genève, Geneva, Switzerland.

Disclosure(s):

All authors have completed and submitted the ICMJE disclosures form.

The author(s) have made the following disclosure(s): H.B.: Consultant − Research support − InnFocus Inc. (a Santen Pharmaceutical Co. Ltd. company), Consultant-Santen, Consultant-Glaukos.

F.A.: financial support − Allergan, Glaukos, Santen.

C.W.: support in the form of 'other' − Santen.

J.G.F.: Financial support − Allergan, Glaukos, Santen.

Y.L.: financial disclosures − Allergan, Alcon, Bausch & Lomb, Théa.

I.R.: Research support − Santen.

L.P.: Employee − InnFocus Inc., a Santen Pharmaceutical Co. Ltd. company.

R.A., H.S. and O.S.: Research Scientist − Santen Inc.

T.S.: Research funding support − Santen.

The sponsor (InnFocus Inc., a Santen Pharmaceutical Co. Ltd. Company) participated in the design and conduct of the study, data collection, and management. This analysis was also sponsored by Santen Inc., which participated in the data analysis, interpretation of the data, preparation, review, and approval of the manuscript.

Clinical trial registration number NCT02177123.

Meeting Presentations

Beckers H, Aptel F, Webers C, et al. Two-year results of a multicentre study assessing the MicroShunt in patients with primary open-angle glaucoma: 0.4 mg/ml Mitomycin C outcomes. ePoster presented at the 37th Congress of the European Society of Cataract & Refractive Surgeons (ESCRS), Paris, France, 2019 (FP-297894).

Aptel F, Beckers H, Webers C, et al. Two-year results of the MicroShunt Glaucoma Drainage System in patients with primary open-angle glaucoma. Poster presented at the Annual Academy of Ophthalmology (AAO), Chicago, IL, USA, 2018 (PO109).

Beckers H, Webers C, Aptel F, et al. 12-month results of a multicentre open-label study of the InnFocus MicroShunt Glaucoma Drainage System in patients with primary open-angle glaucoma (POAG). Poster presented at the 9th International Congress on Glaucoma Surgery (ICGS), Montréal, Canada, 2018 (P2199).

Riss I, Aptel F, Beckers H, et al. Interim 1-year outcomes following MicroShunt Glaucoma Drainage System implantation: multicentre Phase 4 study. Paper presented at the World Ophthalmology Congress (WOC); Barcelona, Spain, 2018.

Beckers H, Kujovic-Aleksov S, Webers C. Interim single-centre 12-month results from an open-label study of the InnFocus MicroShunt Glaucoma Drainage System in patients with primary open-angle glaucoma. Poster presented at the 13th European Glaucoma Surgery (EGS) Congress, Florence, Italy, 2018 (P4.037).

Aptel F, Bluwol E, Graber M, et al. Interim 12-month results from two centres of an open-label study of the InnFocus MicroShunt Glaucoma Drainage System in patients with primary open-angle glaucoma. Poster presented at the 13th European Glaucoma Surgery (EGS) Congress, Florence, Italy, 2018 (P4.032).

Shaarawy T, Aptel F, Beckers H, et al. 12-month interim results of a multicenter open-label study of the MicroShunt Drainage System in POAG patients. Paper presented at the Association of Research in Vision and Ophthalmology (ARVO) Annual Meeting, Honolulu, HI, USA, 2018 (3457).

HUMAN SUBJECTS: Human subjects were included in this study. The study was conducted in accordance with the Declaration of Helsinki. Institutional review board approval was obtained for each site, and patients provided written informed consent prior to their enrollment in the study. All participants provided informed consent.

No animal subjects were used in this study.

Author Contributions:

Conception and design: Pinchuk

Data collection: Beckers, Aptel, Webers, Bluwol, Martínez-de-la-Casa, García-Feijoó, Lachkar, Méndez-Hernández, Riss, Shaarawy

Analysis and interpretation: Beckers, Aptel, Webers, Bluwol, Martínez-de-la-Casa, García-Feijoó, Lachkar, Méndez-Hernández, Riss, Shao, Pinchuk, Angeles, Sadruddin, Shaarawy

Obtained funding: N/A

Overall responsibility: Beckers, Aptel, Webers, Bluwol, Martínez-de-la-Casa, García-Feijoó, Lachkar, Méndez-Hernández, Riss, Shao, Pinchuk, Angeles, Sadruddin, Shaarawy

Abbreviations and Acronyms:
AE = adverse event; **IOP** = intraocular pressure; **ITT** = intention-to-treat; **MIGS** = minimally invasive glaucoma surgery; **MMC** = mitomycin C; **POAG** = primary open-angle glaucoma; **PP** = per-protocol; **SAE** = serious adverse event; **SD** = standard deviation; **VA** = visual acuity.

Keywords:
Clinical trial, Glaucoma filtration surgery, MIGS, Primary open-angle glaucoma.

Correspondence:
Henny J. M. Beckers, MD, PhD, University Eye Clinic, Maastricht University Medical Center, P. Debyelaan 25, 6229 HX Maastricht, the Netherlands. E-mail: henny.beckers@mumc.nl.

References

1. El Hajj Moussa WG, Farhat RG, Nehme JC, et al. Comparison of efficacy and ocular surface disease index score between bimatoprost, latanoprost, travoprost, and tafluprost in glaucoma patients. *J Ophthalmol*. 2018;2018:1319628.
2. Jones JP, Fong DS, Fang EN, et al. Characterization of glaucoma medication adherence in Kaiser Permanente Southern California. *J Glaucoma*. 2016;25:22−26.
3. Gedde SJ, Herndon LW, Brandt JD, et al. Postoperative complications in the Tube Versus Trabeculectomy (TVT) study during five years of follow-up. *Am J Ophthalmol*. 2012;153:804−814.
4. Gedde SJ, Feuer WJ, Shi W, et al. Treatment outcomes in the Primary Tube Versus Trabeculectomy study after 1 year of follow-up. *Ophthalmology*. 2018;125:650−663.
5. Gazzard G, Konstantakopoulou E, Garway-Heath D, et al. Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial. *Lancet*. 2019;393:1505−1516.
6. Richter GM, Coleman AL. Minimally invasive glaucoma surgery: current status and future prospects. *Clin Ophthalmol*. 2016;10:189−206.
7. Poley B, Lindstrom R, Samuelson T, Schulze RJ. Intraocular pressure reduction after phacoemulsification with intraocular lens implantation in glaucomatous and nonglaucomatous eyes: evaluation of a causal relationship between the natural lens and open-angle glaucoma. *J Cataract Refract Surg*. 2009;35:1945−1955.
8. Pillunat LE, Erb C, Jünemann AG, Kimmich F. Micro-invasive glaucoma surgery (MIGS): a review of surgical procedures using stents. *Clin Ophthalmol*. 2017;11:1583−1600.
9. Grover DS, Flynn WJ, Bashford KP, et al. Performance and safety of a new ab interno gelatin stent in refractory glaucoma at 12 months. *Am J Ophthalmol*. 2017;183:25−36.
10. Marcos Parra MT, Salinas López JA, López Grau NS, et al. XEN implant device versus trabeculectomy, either alone or in combination with phacoemulsification, in open-angle glaucoma patients. *Graefes Arch Clin Exp Ophthalmol*. 2019;257:1741−1750.
11. Glaukos Announces Australia's TGA Regulatory Approval for PRESERFLO™ MicroShunt. 2021. http://investors.glaukos.com/investors/press-releases/press-release-details/2021/Glaukos-Announces-Australias-TGA-Regulatory-Approval-for-PRESERFLO-MicroShunt/default.aspx; Accessed July 9, 2021
12. Santen Announces Health Canada Approval of PRESERFLOTM MicroShunt. 2021. https://www.santenusa.com/pdfs/preserflo-microshunt-canada-approval.pdf; Accessed July 12, 2021
13. Pinchuk L, Riss I, Batlle JF, et al. The use of poly(styrene-*block*-isobutylene-*block*-styrene) as a microshunt to treat glaucoma. *Regen Biomater*. 2016;3:137−142.
14. Pinchuk L, Riss I, Batlle JF, et al. The development of a microshunt made from poly(styrene-*block*-isobutylene-*block*-styrene) to treat glaucoma. *J Biomed Mater Res B Appl Biomater*. 2017;105:211−221.
15. Batlle JF, Fantes F, Riss I, et al. Three-year follow-up of a novel aqueous humor microshunt. *J Glaucoma*. 2016;25:e58−e65.
16. ClinicalTrials.gov. NCT00772330. Clinical study of the safety and performance of the Miami InnFocus Drainage Implant to relieve glaucoma symptoms. 2017. https://clinicaltrials.gov/ct2/show/NCT00772330; Accessed August 6, 2020.
17. World Glaucoma Association. In: Shaarawy T, ed. *Guidelines on Design and Reporting of Glaucoma Surgical Trials*. Amsterdam: Kugler; 2009.
18. Sanders SP, Cantor LB, Dobler AA, Hoop JS. Mitomycin C in higher risk trabeculectomy: a prospective comparison of 0.2- to 0.4-mg/cc doses. *J Glaucoma*. 1999;8:193−198.
19. Al Habash A, Aljasim LA, Owaidhah O, Edward DP. A review of the efficacy of Mitomycin C in glaucoma filtration surgery. *Clin Ophthalmol*. 2015;9:1945−1951.
20. Kakizaki H, Takahashi Y, Nakano T, et al. Anatomy of tenons capsule. *Clin Exp Ophthalmol*. 2012;40:611−616.
21. Widder RA, Dietlein TS, Dinslage S, et al. The XEN45 Gel Stent as a minimally invasive procedure in glaucoma surgery: success rates, risk profile, and rates of re-surgery after 261 surgeries. *Graefes Arch Clin Exp Ophthalmol*. 2018;256:765−771.
22. Fagerli M, Løfors KT, Elsås T. Needling revision of failed filtering blebs after trabeculectomy: a retrospective study. *Acta Ophthalmol Scand*. 2003;81:577−582.
23. ClinicalTrials.gov. NCT01881425. InnFocus MicroShunt versus trabeculectomy study (IMS). 2018. http://www.clinicaltrials.gov/ct2/show/NCT01881425; Accessed August 6, 2020