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Gel stent versus trabeculectomy: The randomized, multicenter, Gold-Standard Pathway Study (GPS) of effectiveness and safety at 12 months

Arsham Sheybani
Washington University School of Medicine in St. Louis

Vanessa Vera
Allergan

Davinder S Grover
Glaucoma Associates of Texas

Steven D Vold
Vold Vision

Frank Cotter
Vistar Eye Center

See next page for additional authors

Gel Stent Versus Trabeculectomy: The Randomized, Multicenter, Gold-Standard Pathway Study (GPS) of Effectiveness and Safety at 12 Months

ARSHAM SHEYBANI, VANESSA VERA, DAVINDER S. GROVER, STEVEN D. VOLD, FRANK COTTER, SAHAR BEDROOD, GAGAN SAWHNEY, SCOTT D. PIETTE, SUSAN SIMONYI, XUEMIN GU, MINI BALARAM, AND MARK J. GALLARDO

• PURPOSE: To compare effectiveness and safety of the gel stent to trabeculectomy in open-angle glaucoma (OAG).

• DESIGN: Prospective, randomized, multicenter, noninferiority study.

• METHODS: Patients with OAG and intraocular pressure (IOP) 15 to 44 mm Hg on topical IOP-lowering medication were randomized 2:1 to gel stent implantation or trabeculectomy. Primary end point (surgical success): percentage of patients at month 12 achieving ≥20% IOP reduction from baseline without medication increase, clinical hypotony, vision loss to counting fingers, or secondary surgical intervention (SSI) in a noninferiority test with 24% margins. Secondary end points (month 12) included mean IOP and medication count, postoperative intervention rate, visual recovery, and patient-reported outcomes (PROs). Safety end points included adverse events (AEs).

• RESULTS: At month 12, the gel stent was statistically noninferior to trabeculectomy (between-treatment difference [Δ], −6.1%; 95% CI, −22.9%, 10.8%); 62.1% and 68.2% achieved the primary end point, respectively (P=.487); mean IOP and medication count reductions from baseline were significant (P<.001); and the IOP change-related Δ (2.8 mm Hg) favored trabeculectomy (P=.024). The gel stent resulted in fewer eyes requiring in-office postoperative interventions (P=.024 after excluding laser suture lysis), faster visual recovery (P≤.048), and greater 6-month improvements in visual function problems (ie, PROs; P≤.022). The most common AEs were reduced visual acuity at any time (gel stent, 38.9%; trabeculectomy, 54.5%) and hypotony (IOP <6 mm Hg at any time) (gel stent, 23.2%; trabeculectomy, 50.0%).

• CONCLUSIONS: At month 12, the gel stent was statistically noninferior to trabeculectomy, per the percentage of patients achieving ≥20% IOP reduction from baseline without medication increase, clinical hypotony, vision loss to counting fingers, or SSI. Trabeculectomy achieved a statistically lower mean IOP, numerically lower failure rate, and numerically lower need for supplemental medications. The gel stent resulted in fewer postoperative interventions, better visual recovery, and fewer AEs. (Am J Ophthalmol 2023;252: 306–325. © 2023 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/))

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Washington University School of Medicine (A.S.), St Louis, Missouri, USA; Allergan, an AbbVie company (V.V.), Irvine, California, USA; Glaucoma Associates of Texas (D.S.G.), Dallas, Texas, USA; Vold Vision (S.D.V.), Fayetteville, Arkansas, USA; Vistar Eye Center (F.C.), Roanoke, Virginia, USA; Acuity Eye Group (S.B.), Arcadia, California, USA; Advanced Vision Care (S.B.), Los Angeles, California, USA; Georgia Eye Partners (G.S.), Atlanta, Georgia, USA; Mid Florida Eye Center (S.D.P.), Leesburg, Florida, USA; Allergan, an AbbVie company (S.S.), Singapore; AbbVie (X.G.), Madison, New Jersey, USA; Nethra Consulting LLC (M.B.), Princeton, New Jersey, USA; El Paso Eye Surgeons P.A. (M.J.G.), El Paso, Texas, USA

Inquiries to Arsham Sheybani, Washington University School of Medicine, 660 South Euclid Ave, Campus Box 8096, St Louis, MO 63110, USA; e-mail: sheybaniar@wustl.edu

GLAUCOMA CONTINUES TO BE THE LEADING CAUSE OF irreversible blindness in adults ≥50 years of age worldwide,[1] and intraocular pressure (IOP) is, as of this writing, the only modifiable factor that can be targeted to prevent (or delay) glaucoma progression.[2,3] While prostaglandin analogues are the first-line topical glaucoma treatment,[2,3] most patients eventually require polytherapy to control IOP,[4] which increases the likelihood of nonadherence/nonpersistence (reportedly ranging from 16% to 69%[5]). Of note, in a recent retrospective, single-center study, one-third of patients underwent glaucoma surgery because of intolerance to IOP-lowering medications.[6]

Many ophthalmologists still consider trabeculectomy as the gold standard glaucoma filtering procedure and one of the most effective IOP-lowering surgical options for the treatment of primary open-angle glaucoma. This traditional surgery has been extensively studied in clin-

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ical trials; however, it can be associated with significant complications.[7-19] Minimally invasive glaucoma surgery (MIGS) offers alternative surgical options with an improved safety profile, but is often associated with a lesser degree of IOP-lowering effect.

Modest IOP reduction can be achieved with canal-based MIGS, higher outflow capacity is possible with suprachoroidal MIGS, and filtration-like drainage can be achieved with subconjunctival MIGS.[20-22] However, there is a scarcity of data regarding patient-reported outcomes (PROs) after glaucoma surgeries.[23-29] Among the subconjunctival MIGS devices, the XEN45 Glaucoma Treatment System (gel stent; Allergan, an AbbVie company, North Chicago, Illinois) has been shown to lower IOP and medication use, offering an effective IOP-lowering alternative to traditional filtering procedures while mitigating adverse events (AEs).[30-33]

The gel stent is designed to divert outflow of aqueous humor to the subconjunctival space.[34,35] The implantation procedure has evolved over the years, leading to improvements in outcomes, and findings from various studies comparing the effectiveness and/or safety of the gel stent and trabeculectomy have been published.[7,36-45] Safety data from these studies demonstrated a possible favorable safety profile of the gel stent, compared with trabeculectomy. However, no prospective, randomized trials comparing these glaucoma filtering procedures have been published as of this writing. We report here the results of the Gold-Standard Pathway Study (GPS), the first prospective, randomized study to compare the effectiveness and safety of the gel stent with those of the gold standard trabeculectomy.

METHODS

• **STUDY DESIGN:** This prospective, randomized, parallel-group, open-label, multicenter study (ClinicalTrials.gov identifier: NCT03654885) was conducted between October 1, 2018, and May 13, 2021, at 35 centers in the United States, in compliance with the International Council for Harmonisation Good Clinical Practice Guideline, the Declaration of Helsinki, Health Insurance Portability and Accountability Act (HIPAA) compliance rules, and ISO 14155:2011 standard, as well as all applicable national and local laws/regulatory requirements. The study protocol was approved by an institutional review board before study start at each participating site, and all study participants provided written informed consent before undergoing any study-related procedures or examinations.

Study participants were randomized (2:1) to the gel stent or trabeculectomy arm at the site level, using the Medidata Rave Randomization and Trial Supply Management application. The sponsor's and clinical research organization's study team members, investigational site staff, and patients were unmasked after the randomization process.

• **STUDY POPULATION:** Eligible patients were ≥18 years of age and had open-angle glaucoma (OAG, including pseudoexfoliation and pigmentary glaucoma) with IOP ≥15 mm Hg and ≤44 mm Hg uncontrolled on current topical IOP-lowering therapy. Patients with failed ab-interno canal or ab-interno cycloablative procedures ≥3 months before enrollment were eligible. Additional key inclusion criteria were best corrected visual acuity (BCVA) of 20/100 Snellen or better; visual field mean deviation no worse than –18.0 dB (without dense paracentral scotomas, eg, >18 dB total deviation on ≥1 of the 4 paracentral points); and Shaffer grade ≥2 in the target area or open angle in eyes with prior failed angle surgery.

One eye per patient was eligible. If both eyes met the eligibility criteria, the eye with the worse visual field mean deviation at baseline was selected as the study eye. If both eyes had the same visual field mean deviation (up to 2 decimals), worse IOP determined the study eye.

Key exclusion criteria included active neovascular, uveitic, and angle-recession glaucoma, or any glaucoma associated with vascular disorders; prior transscleral cycloablative procedures, suprachoroidal CyPass Micro-Stent (Alcon), or conjunctival surgery; conjunctival scarring or other conjunctival pathologies in the target area; and history of complicated cataract surgery. A complete list of the exclusion criteria is available in Supplemental Table S1.

• **SURGICAL PROCEDURES:** One to 4 weeks before surgery, physicians were allowed to stop, reduce, or replace (with oral carbonic anhydrase inhibitors) patients' topical IOP-lowering medications and/or begin preoperative medications (eg, topical steroids) to prepare the ocular surface for surgery and improve the likelihood of treatment success overall. For both the gel stent implantation and trabeculectomy, anesthesia was left to the discretion of the investigator. Because there was consensus among investigators (during protocol development) that flexibility to adjust the mitomycin C (MMC) dose to a patient's needs and surgeon's preferences was needed, the dose and administration route were not prespecified in the protocol. Nonetheless, most surgeons incorporated a subconjunctival injection of 40 µg of MMC in both study surgical procedures.

Ab-interno implantation of the gel stent was performed following the surgical training provided by the manufacturer and standard of care at each center. A paracentesis was initially performed, and the anterior chamber was filled with a cohesive viscoelastic.[46] An inferotemporal clear cornea incision was then created with a keratome blade. The gel stent delivery system was placed across the eye, and the nonpigmented trabecular meshwork was engaged as close to 12 o'clock as possible. The needle was then advanced through the sclera and the implant deployed into the subconjunctival space, without conjunctival dissection.[46]

Trabeculectomy was performed in accordance with the standard of care at each center. A conjunctival flap was

made in the superior quadrant, and dissection of a partial thickness scleral flap was performed. The sclerostomy was created using the surgeon's standard practice, and peripheral iridectomy was optional. The scleral and conjunctival flaps were closed using sutures of the surgeon's preference.

Following surgery, the use of postoperative adjunctive antifibrotic therapy (eg, injection of steroids, 5-fluorouracil) was optional and at the treating physician's discretion. Also, to allow optimal clinical care by the treating physician, reintroduction of topical IOP-lowering medication(s) to reach target IOP was based on the patient's needs and medical history. This was not expected to impact the treatment arms differently as randomization was at site level and, at each site, the same investigator performed both surgical procedures and determined follow-up care.

• **STUDY VISITS AND ASSESSMENTS:** A mandatory baseline qualifying visit (baseline) and optional preoperative visit were scheduled ≤4 weeks before surgery day (day 0). Postoperative visits were scheduled at day 1 (hour 6-48), week 1 (day 3-10), week 2 (day 11-20), and months 1 (week 3-8), 3 (week 9-17), 6 (week 18-32), 9 (week 33-47), and 12 (week 48-60).

Demographics and patient/eye characteristics (including medical/ophthalmic history) were collected at baseline. IOP was assessed at baseline (medicated) and all postoperative visits using standard Goldmann applanation tonometry and a 2-person reading method (ie, 1 person adjusted the dial without viewing the numbers on the dial while the second person recorded the reading). Two consecutive measurements were taken, followed by a third if the first 2 differed by ≥3 mm Hg. The average or median IOP was used for analysis, depending on whether 2 or 3 measurements were taken, respectively.

Use of topical IOP-lowering medications (counted by individual class ingredients), BCVA (per the Snellen chart), and biomicroscopy findings were also recorded at all visits. Other assessments included visual field (evaluated at baseline, month 6, and month 12), ophthalmoscopy (performed at the baseline visit, day 1, week 1, and month 12), and pachymetry (carried out at the baseline visit and month 12). Perioperative use of adjunctive antifibrotic therapy was recorded. Postoperative interventions such as laser-based suture lysis and needling (with or without antifibrotic agents) were also captured.

PRO questionnaires evaluated patient quality of life in both treatment arms. The 2-domain, 18-item, glaucoma-related Symptom and Health Problem Checklist (SHPC-18) questionnaire,[47] developed and validated by the Collaborative Initial Glaucoma Treatment Study (CIGTS) group, measured the frequency and bothersomeness of local eye symptoms (first domain, 7 items) and visual function problems (second domain, 11 items) at baseline, day 1, weeks 1 and 2, and months 1, 3, and 6. Response to a postsurgical question on the extent to which patients were able to resume daily activities and routine ("Since your glaucoma surgery, would you consider that you have resumed your usual activities and daily routine?") was collected at week 2, month 1, and month 3 to better understand between-treatment differences (if any) in postoperative recovery. In addition, the Work Productivity and Activity Impairment (WPAI-GH) questionnaire assessed the effect of health problems (physical, emotional, or symptoms) on the patients' ability to work and perform regular activities at baseline, week 1, month 3, and month 12.[48] All questionnaires were self-administered before clinical evaluations. Details on the scoring of these PROs are summarized in Supplemental Table S2.

• **OUTCOME MEASURES:** Because IOP lowering alone does not fully reflect the outcomes of a filtering surgery, the primary end point was a composite of effectiveness and safety parameters defined as the proportion of patients at month 12 achieving ≥20% IOP reduction from baseline without increase in topical IOP-lowering medications, clinical hypotony (defined in the paragraph on safety outcomes), loss of vision to counting fingers, and/or secondary glaucoma surgical intervention (SSI, including trabeculectomy, placement of a glaucoma drainage device, etc).

Prespecified secondary effectiveness end points included mean IOP over time; mean number of topical IOP-lowering medications over time; changes in mean IOP and mean number of topical IOP-lowering medications from baseline at month 12; complete success, defined as IOP ≤18 mm Hg (excluding eyes with clinical hypotony) with ≥20% IOP lowering from medicated baseline without topical IOP-lowering medications at months 3, 6, 9, and 12; qualified success, defined as IOP ≤18 mm Hg (excluding eyes with clinical hypotony) with ≥20% IOP lowering from medicated baseline with topical IOP-lowering medications at months 3, 6, 9, and 12; proportion of eyes achieving IOP ≤18, ≤17, ≤16, ≤15, ≤14, ≤13, and ≤12 mm Hg at month 12; postoperative interventions; and needling rates and related variables (number of needlings per eye, antifibrotic use during needling, pre- and postneedling IOP, and outcomes).

Changes in visual acuity were assessed at prespecified visits. PROs were reported as described in Supplemental Table S2.

Safety outcomes were assessed throughout the study and included surgical complications and postoperative treatment-emergent AEs. Hypotony was defined as eyes with IOP <6 mm Hg at any time, whereas clinical hypotony was defined as IOP ≤6 mm Hg with vision reduction (≥2 lines) related to macular changes (macular folds), optic disc edema, and/or serous choroidal detachments. Changes in corneal thickness and visual field from baseline were also assessed at the prespecified visits.

• **STATISTICAL ANALYSES:** Statistical analyses were performed using SAS software version 9.2 or higher. The between-treatment difference (gel stent minus trabeculectomy) in the proportion of patients achieving the primary

end point (defined above) was tabulated with 95% CIs calculated using the normal approximation method, without imputation of missing data. With the planned sample size, the noninferiority test for the primary end point with the gel stent and trabeculectomy was the only formal hypothesis testing of the study. Noninferiority of the gel stent to trabeculectomy was claimed if the lower limit of the 95% CI was greater than –24%. All *P* values for other comparisons were provided for reference only, without adjustment for multiplicity.

The between-treatment difference in complete and qualified success was calculated as described above. All other secondary end points were summarized with descriptive statistics. For continuous secondary end points defined for 1 timepoint, the least squares mean (LSM) change from baseline and related between-treatment difference were estimated using the analysis of covariance model, with treatment as factor and baseline as covariate variable. For continuous secondary end points defined over time, the LSM change from baseline and related between-treatment difference were estimated using mixed-effects model for repeated measures, with treatment and time as factors, and treatment by time interaction and baseline as covariate variables.

Per the initial protocol, calculation of the sample size (285 patients) was based on an equivalence test of the gel stent to trabeculectomy with a 2-sided significance level of .05, 80% power, and 18% equivalence limit. In March 2020, however, COVID-19 considerably impacted enrollment and follow-up in clinical trials globally. Considering emerging information (at the time) from new studies of the gel stent[7,42,49-53] and the ab-externo MicroShunt (NCT01881425), a proactive approach was deemed necessary and a decision was made (ahead of database lock) to adopt a noninferiority test with a more reasonable margin of 24% as the primary analysis.

Based on historical data showing treatment success rates of ≥75% with the gel stent[30,31,54] (despite differences in the definition of success between studies) and a retrospective study showing comparable treatment success rates with the gel stent and trabeculectomy,[55] a conservative surgical success rate (primary end point defined in the Outcome Measures) of 70% was set as performance target for this study, and it was assumed (for the primary end point) that neither treatment was better or worse than the other. Considering the randomization ratio of 2:1, a 2-sided significance level of .05, an 80% power to demonstrate equivalence/noninferiority of the gel stent, and a 10% dropout rate for the first year, an estimated sample size of 102 patients with month 12 data (68 in the gel stent arm and 34 in the trabeculectomy arm) was required, and enrollment of 114 participants was planned.

The intent-to-treat (ITT) population, including all randomized, treated eyes, was used to analyze the demographics, baseline characteristics, effectiveness end points, and PROs. The safety population, consisting of all enrolled eyes that underwent surgery (whether completed or aborted) and had follow-up visits or evaluations, was used to analyze AEs, medical/ophthalmic history, and concomitant medications.

RESULTS

• **PATIENT DISPOSITION, DEMOGRAPHICS, AND BASELINE CHARACTERISTICS:** Of 158 eyes enrolled at 30 centers, 139 underwent gel stent implantation (n=95; 68.3%) or trabeculectomy (n=44; 31.7%), and 115/139 (82.7%) completed the study (Figure 1). In the gel stent and trabeculectomy arms, mean age was 69.5 vs 69.4 years and the major-

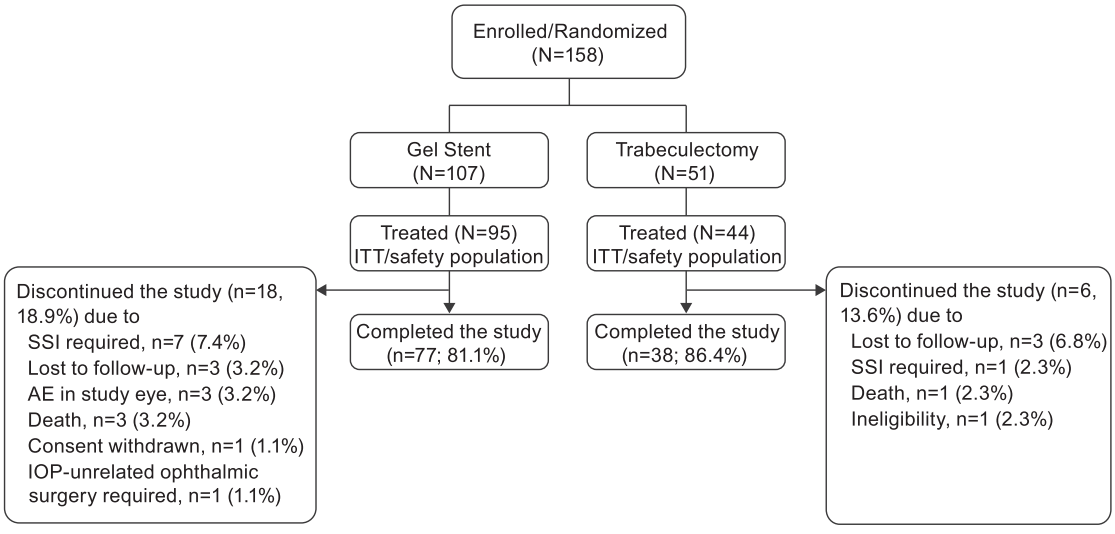

FIGURE 1. Patient disposition. AE = adverse event, IOP = intraocular pressure, ITT = intent-to-treat, SSI = secondary surgical intervention.

TABLE 1. Patient Demographics and Characteristics at Baseline

Patient-Level Data	Gel Stent (N=95)	Trabeculectomy (N=44)	*P* Value
Mean age (SD), y	69.5 (9.6)	69.4 (9.7)	.922
≥65 y, n (%)	64 (67.4)	29 (65.9)	.865
<65 y, n (%)	31 (32.6)	15 (34.1)	
Sex, n (%)			.998
Male	54 (56.8)	25 (56.8)	
Female	41 (43.2)	19 (43.2)	
Race, n (%)			.684
White	61 (64.2)	26 (59.1)	
Hispanic[a]	18 (18.9)	10 (22.7)	
Black/African American	14 (14.7)	8 (18.2)	
Asian	2 (2.1)	0	
Diagnosis, n (%)			.272
POAG	88 (92.6)	42 (95.5)	
Pseudoexfoliative glaucoma	4 (4.2)	0	
Pigmentary glaucoma	4 (4.2)	0	
Other	3 (3.2)	2 (4.5)	
Pseudophakic lens status	65 (68.4)	25 (56.8)	.183
Prior glaucoma procedures, n (%)	51 (53.7)	18 (40.9)	.161
Laser (LPI, ALT, SLT)	39 (41.1)	14 (31.8)	
Surgeries	24 (25.3)	12 (27.3)	
Cycloablation	2 (2.1)	1 (2.3)	
MIGS[b]	23 (24.2)	10 (22.7)	
Trabeculectomy	1 (1.1)	3 (6.8)	
Mean IOP (SD), mm Hg[c]	23.1 (5.8)	22.6 (5.7)	.586
Eyes with the following baseline IOP, n (%)			.614
<18 mm Hg	14 (14.7)	5 (11.4)	
≥18 and <21 mm Hg	27 (28.4)	16 (36.4)	
≥21 mm Hg	54 (56.8)	23 (52.3)	
Mean number of IOP-lowering medications (SD)	2.8 (1.2)	2.5 (1.3)	.289
Mean Humphrey visual field mean deviation (SD), dB	−7.4 (4.9)	−8.3 (5.2)	.343
Glaucoma severity classification, n (%)			.863
Normal (>−2.99 dB)	19 (20.0)	8 (18.2)	
Mild (−3.00 to −6.00 dB)	30 (31.6)	12 (27.3)	
Moderate (−6.01 to −12.00 dB)	26 (27.4)	12 (27.3)	
Advanced (−12.01 to −20.00 dB)	20 (21.1)	12 (27.3)	
Severe (≤−20.01 dB)	0	0	‘

ALT = argon laser trabeculoplasty, IOP = intraocular pressure, LPI = laser peripheral iridotomy, MIGS = minimally invasive surgery, POAG = primary open-angle glaucoma, SLT = selective laser trabeculoplasty.

[a] Hispanic patients have been previously presented as “American Indian or Alaska Native,” following the Clinical Data Interchange Standards Consortium (CDISC) control terminology tabulation model.

[b] Angle, suprachoroidal, or subconjunctival.

[c] Study eye.

ity of patients self-identified as White or Caucasian (64.2% vs 59.1%), had primary OAG (92.6% vs 95.5%), and were pseudophakic (68.4% vs 56.8%), respectively. Notably, the mean Zeiss-Humphrey visual field mean deviation (SD) was −7.4 (4.9) vs −8.3 (5.2) dB, respectively (*P*=.343). Demographics and baseline characteristics were balanced between treatment arms (*P*≥.161; Table 1).

• **PRIMARY EFFECTIVENESS END POINT:** At month 12, the gel stent was statistically noninferior to trabeculectomy (Figure 2); the between-treatment difference (gel stent minus trabeculectomy) was −6.1% (95% CI, –22.9%, 10.8%; *P*=.487), with 62.1% (gel stent) and 68.2% (trabeculectomy) of patients achieving the primary end point of ≥20% IOP reduction from baseline without increase in topical IOP-lowering medications, clinical hypotony, vision loss to counting fingers, or SSI (a composite of effectiveness and safety parameters).

• **SECONDARY EFFECTIVENESS END POINTS:** Mean (SD) IOP decreased from 23.1 (5.8) mm Hg on 2.8 (1.2) medications at baseline to 14.4 (4.1) mm Hg on 0.6 (1.1) medica-

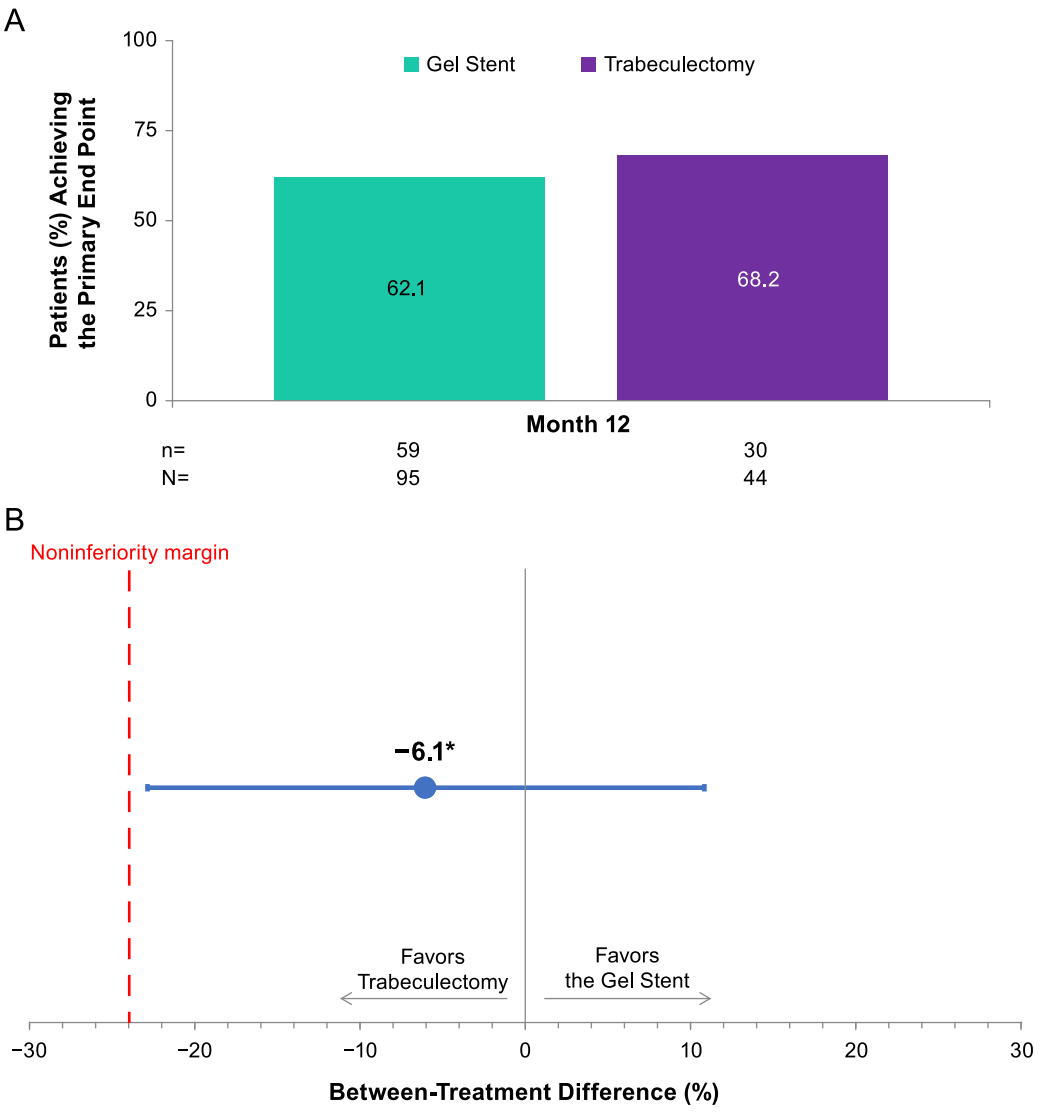

FIGURE 2. A. Proportion of patients achieving the primary end point of ≥20% IOP reduction from baseline without increase in topical IOP-lowering medication, clinical hypotony, vision loss to counting fingers, or secondary surgical intervention in both treatment arms. B. The between-treatment difference (gel stent minus trabeculectomy) is presented with the 95% CI and demonstrates statistical noninferiority of the gel stent to trabeculectomy. *P=.487. IOP = intraocular pressure.

tions at month 12 in the gel stent arm, and from 22.6 (5.7) mm Hg on 2.5 (1.3) medications to 11.8 (3.5) mm Hg on 0.3 (0.6) medications in the trabeculectomy arm (Figure 3). Mean reductions in IOP and topical IOP-lowering medication count from baseline were statistically significant in both treatment arms at all timepoints ($P<.001$ for all; Figure 3). The between-treatment difference in mean IOP reduction from baseline (2.8 mm Hg; 95% CI, 0.4, 5.2) was statistically significant at month 12 ($P=.024$, with a lower mean in the trabeculectomy arm), while the between-treatment difference in mean medication reduction from baseline (0.3; 95% CI, –0.0, 0.7) was not ($P=.068$).

At month 12, complete and qualified success rates (defined above) were 44.2% and 62.1% in the gel stent arm, compared with 59.1% and 72.7% in the trabeculectomy arm, respectively, without statistically significant differences between treatments ($P\geq.144$ for both success rates; Figure 4). In addition, the proportions of eyes achieving IOP ≤18, ≤17, ≤16, ≤15, ≤14, and ≤12 mm Hg at month 12 were not statistically significantly different in the gel stent and trabeculectomy arms ($P\geq.051$; Figure 5).

• **MEAN IOP AND MEDICATION COUNT IN THE SUBGROUP OF EYES WITH BASELINE IOP ≤18 MM HG:** Among patients whose baseline IOP was ≤18 mm Hg (n=33/144), 21 of 33 (63.6%) and 12 of 33 (36.4%) underwent gel stent implantation and trabeculectomy, respectively. At month 12 in those respective subgroups, mean (SD) IOP was 14.1 (2.4) and 12.8 (3.8) mm Hg, compared with 16.9 (1.0) and 17.4 (1.0) mm Hg at baseline; the reduction from base-

	Baseline		Month 1		Month 3		Month 6		Month 9		Month 12	
Eyes, n	95	44	94	43	89[a]	41[b]	81	41	81	41	78	38
Mean Meds	2.8	2.5	0.4	0.2	0.6	0.1	0.7	0.3	0.7	0.3	0.6	0.3
SD	1.2	1.3	1.0	0.6	1.1	0.4	1.2	0.8	1.3	0.6	1.1	0.6
Mean med change			−2.4	−2.3	−2.2	−2.4	−2.1	−2.1	−2.0	−2.2	−2.1	−2.2
SD			1.4	1.3	1.4	1.3	1.4	1.4	1.5	1.3	1.4	1.3

FIGURE 3. Mean and mean changes from baseline in IOP and topical IOP-lowering medication count over time. [a]n=91 (month 3), 82 (month 6), and 87 (month 12). [b]n=42 (month 3) and 41 (month 12). Both footnotes refer to the medication count analysis. $P<.001$ at all postoperative visits vs baseline. *$P\leq.024$ for the between-treatment differences (gel stent minus trabeculectomy) in mean IOP change from baseline (per least squares means analyses). †$P\leq.013$ for the between-treatment differences in mean medication change from baseline (per least squares means analyses). IOP = intraocular pressure, meds = medications.

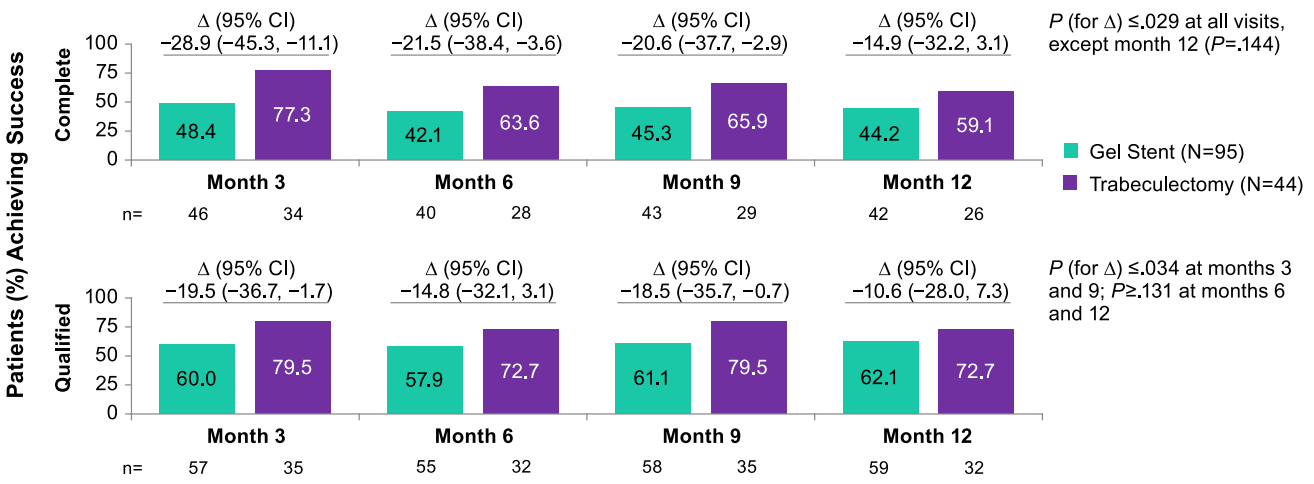

FIGURE 4. Proportions of patients achieving complete and qualified success over time. Complete success was defined as IOP ≤18 mm Hg (excluding eyes with hypotony) with ≥20% IOP lowering from medicated baseline without topical IOP-lowering medications. Qualified success was defined as IOP ≤18 mm Hg (excluding eyes with hypotony) with ≥20% IOP lowering from medicated baseline with topical medications. IOP = intraocular pressure, Δ = between-treatment difference (gel stent minus trabeculectomy).

line (≥2.9 mm Hg) was statistically significant in both subgroups ($P\leq.008$), whereas the between-treatment difference (1.8 mm Hg) was not (95% CI, −2.6, 6.2; $P=.421$). At month 12, the mean (SD) medication count was 0.6 (1.2) and 0.2 (0.4), compared with 2.9 (1.4) and 2.5 (1.2) at baseline, respectively; the reduction from baseline (≥2.1) was statistically significant in both subgroups ($P<.001$), whereas the between-treatment difference (0.4) was not (95% CI, −0.3, 1.0; $P=.238$).

• **KEY IOP-RELATED END POINTS IN EYES THAT WERE MEDICATION-FREE AT MONTH 12:** At month 12, 59 of 95

FIGURE 5. Proportion of patients achieving prespecified levels of IOP over time. All *P* values refer to between-treatment differences (gel stent minus trabeculectomy), calculated based on the least squares means for each treatment arm. IOP = intraocular pressure.

(62.1%) eyes were medication-free in the gel stent arm, compared with 31 of 44 (70.5%) in the trabeculectomy arm. In those respective subgroups, the mean (SD) medication count was 2.6 (1.2) and 2.4 (1.3) at baseline, and the change from baseline was −2.5 at month 12 in both subgroups (between-treatment difference, 0.0; 95% CI, −0.23, 0.20; *P*=.904). At month 12 in those respective subgroups, mean (SD) IOP was 13.8 (3.2) and 10.7 (3.3) mm Hg, compared with 22.6 (5.0) and 22.8 (5.3) mm Hg at baseline; the reduction from baseline (≥8.9 mm Hg) was statistically significant in both subgroups (*P*<.001), and the between-treatment difference (3.2 mm Hg) was statistically significant (95% CI, 0.7, 5.6; *P*=.012) as well, with a lower mean post-trabeculectomy.

• **OFFICE-BASED POSTOPERATIVE INTERVENTIONS:** During the study period, the proportion of patients/eyes that required a postoperative intervention in the office was statistically significantly lower with the gel stent (34.7%; n=33) than trabeculectomy (63.6%; n=28; *P*<.001). The needling rate was 23.2% with the gel stent and 18.2% with trabeculectomy (Table 2). Laser suture lysis was also required in 31.8% of eyes in the trabeculectomy arm and after excluding laser suture lysis from the analysis, the proportion of eyes with office-based procedures remained statistically significantly lower with the gel stent (34.7%) than trabeculectomy (40.9%; *P*=.024). Other office-based procedures performed during the study included 5-fluorouracil injections, bandage contact lens, and other procedures (Table 2).

Of the 30 patients/eyes (total of both treatment arms) that underwent needling during the study, most received only 1 such intervention (Table 3). The mean time to needling was 78.8 days in the gel stent arm and 53.3 days in the trabeculectomy arm, and the majority (76.7% overall) were performed with antimetabolites or antifibrotics (Table 3). Decreases in mean IOP from baseline were observed in both treatment arms following needling, and at least 85% of the needled patients achieved ≥20% IOP reduction from baseline at month 12 without increase in

TABLE 2. Office-Based and Operating Room–Based Postoperative Interventions in the Study Eyes

	Gel Stent (N=95)	Trabeculectomy (N=44)	*P* value
Office-based, n (%)	33 (34.7)	28 (63.6)	<.0001
Bandage contact lens	2 (2.1)[a]	8 (18.2)[b]	
5-Fluorouracil injection	15 (15.8)	8 (18.2)	
Laser suture lysis (LSL)	0	14 (31.8)	
Needling	22 (23.2)	8 (18.2)	
Other[c]	10 (10.5)	5 (11.4)	
Office-based excluding LSL, n (%)	33 (34.7)	18 (40.9)	.024
Operating room-based, n (%)	13 (13.7)	8 (18.2)	.163
Bleb revision[d]	5 (5.3)	2 (4.5)	
Secondary glaucoma surgical intervention	7 (7.4)	1 (2.3)	
Others	4 (4.2)	5 (11.4)	

[a]One patient had an overfiltering bleb associated with hypotony, and 1 had epithelial defects.

[b]Four patients had an overfiltering bleb associated with hypotony, 3 had bleb leaks at day 1 (n=1) and week 2 (n=2) with Seidel positive, and 1 had epithelial defects.

[c]Included air injection in the anterior chamber (n=2), gel stent removal (n=2), laser iridotomy (n=2), digital ocular compression (n=1), goniosynechialysis (n=1), laser iridoplasty (n=1), and paracentesis (n=1) in the gel stent arm, and digital ocular compression (n=2) and suture removal (n=3) in the trabeculectomy arm.

[d]Other than needling.

TABLE 3. Needling Procedure Performed During the Study Period and Related Variables

	Gel Stent (N=95)	Trabeculectomy (N=44)
Total patients needled, n (%)	22 (23.2)	8 (18.2)
Patients needled with antifibrotics/antimetabolites	16 (16.8)[a]	7 (15.9)
Mitomycin C	5 (31.3)	1 (14.3)
5-Fluorouracil	13 (81.3)	6 (85.7)
Mean (SD) number of needlings per eye	1.7 (1.0)	1.4 (0.7)
Range	1-4	1-3
Patients with the indicated number of needlings, n (%)		
1	13 (13.7)	6 (13.6)
2	4 (4.2)	1 (2.3)
≥3	5 (5.3)	1 (2.3)
Mean (SD) time to needling, days	78.8 (72.5)	53.3 (51.7)
Min, max	8, 274	8, 169
Mean IOP in needled patients, mm Hg (SD)		
Baseline	22.7 (5.2)	23.3 (7.3)
Preneedling	25.9 (10.7)	22.7 (3.9)
Postneedling	15.5 (7.5)	10.6 (7.2)
Month 12	16.2 (6.9)	12.2 (3.2)
Mean medication count in needled patients, n (SD)		
Baseline	3.0 (1.2)	2.8 (1.5)
Month 12	1.2 (1.7)	0.5 (0.9)
Eyes achieving >20% IOP reduction from baseline at month 12 without increase in medication count, n/N (%)[b]	14/16 (87.5)	6/7 (85.7)
Eyes not using any topical IOP-lowering medications at month 12, n/N (%)[c]	9/21 (42.9)	6/8 (75.0)

IOP = intraocular pressure.

[a]Two patients received both mitomycin C and 5-fluorouracil during needling.

[b]The difference between treatments, 1.8 (95% CI, −41.6, 44.1), was not statistically significant (*P*=1.0).

[c]The difference between treatments, −32.1 (95% CI, −66.8, 10.0), was not statistically significant (*P*=.215).

medication count (between-treatment difference, 1.8%; P=1.00) (Table 3).

• **INTRAOPERATIVE USE OF ADJUNCTIVE ANTIFIBROTIC THERAPY:** During implantation of the gel stent, 1 (1.1%) patient did not receive antifibrotic therapy while 94 (98.9%) patients received a subconjunctival injection of MMC. Of these 94 patients, 93 (98.9%) received a total dose of 40 µg and 1 (1.1%) received 20 µg. In the trabeculectomy arm, 1 (2.3%) patient did not receive antifibrotic therapy while 43 (97.7%) patients received MMC, including 37 (86.0%) patients in whom MMC (total dose, 40 µg) was administered via subconjunctival injection and 6 (14.0%) in whom MMC-soaked sponges were used.

• **VISUAL RECOVERY POSTSURGERY:** Return to baseline visual acuity was numerically faster and sustained over time in the gel stent arm, compared with the trabeculectomy arm ($P \leq .048$; Figure 6). At day 1 and week 1, BCVA with current glasses (Figure 6, A, top panel) was better in the gel stent arm, and this difference was statistically significant ($P \leq .004$). By month 3, BCVA with manifest refraction had returned to baseline in the gel stent arm (Figure 6, A, bottom panel), and this outcome was sustained until the month-12 visit, at which time the between-treatment difference was statistically significant (P=.021). Results from an analysis of the worst BCVA-line change from baseline across the 12-month follow-up further showed 1.5 times more patients with BCVA worsening in the trabeculectomy arm than the gel stent arm (Figure 6, B).

• **PATIENT-REPORTED OUTCOMES:** At baseline, the mean SHPC-18 frequency and bothersomeness scores for local eye symptoms and visual function problems were numerically higher in the gel stent arm than the trabeculectomy arm (Figure 7, A, C, E, and G). However, patients treated with the gel stent had numerically lower frequency and bothersomeness scores for both domains at all postoperative visits, compared with patients who underwent trabeculectomy (Figure 7, A, C, E, and G), suggesting numerically improved outcomes following gel stent implantation (Figure 7, B, D, G, and H). At 6 months (last prespecified timepoint for SHPC-18 assessments), statistically and clinically significant differences in LSM change from baseline scores favored the gel stent for both the frequency (P=.007; Figure 7, D) and bothersomeness of visual function problems (P=.022; Figure 7, H).

The LSM change from baseline scores for the frequency and bothersomeness of local eye symptoms showed numeric but not statistically significant benefits in favor of the gel stent. There were also statistically significant between-treatment differences in LSM change from baseline scores at earlier timepoints in the frequency of local eye symptoms (weeks 1 and 2; $P \leq .023$; Figure 7, B) and visual function problems (week 2, month 1, and month 3; $P \leq .030$; Figure 7, D), suggesting quicker reduction in frequency of eye symptoms and visual problems following gel stent implantation than trabeculectomy.

The questionnaire on postsurgical resumption of activities and daily routine showed that, at each visit during which patients were queried, the gel stent arm consistently had a numerically higher proportion of participants reporting complete resumption of their activities and daily routine, compared with the trabeculectomy arm; these proportions were 26.3% and 13.6% at week 2 (P=.125), 43.2% and 25.0% at month 1 (P=.059), and 41.1% and 31.8% at month 3 (P=.350), respectively.

Results from the WPAI-GH questionnaire showed that the patients' inability to work (work impairment) reached a maximum at week 1 in both treatment arms (Figure 8, A). The change from baseline was statistically significantly greater (worse) following trabeculectomy than gel stent implantation, as evidenced by the between-treatment difference at week 1 (−32.3%; 95% CI, −62.7, −1.9; P=.038). The patients' inability to perform daily activities (activity impairment) also reached a maximum at week 1 in both treatment arms (Figure 8, B), with statistically significant changes from baseline following both gel stent implantation (mean, 18.0%; SD, 38.3; P<.001) and trabeculectomy (mean, 22.1%; SD, 35.0; P=.002). At month 3, the change from baseline was statistically significantly greater (worse) following trabeculectomy than gel stent implantation, as evidenced by the between-treatment difference (mean, −14.3%; SD, 6.7; P=.033).

• **SAFETY:** Surgical complications were reported in 2 (2.1%) eyes in the gel stent arm and in 3 (6.8%) eyes in the trabeculectomy arm (Table 4). The most common surgical complication was anterior chamber bleeding (n=1, 1.1% with the gel stent; n=2, 4.5% post-trabeculectomy). Postoperatively in those respective treatment arms, 71 (74.7%) and 41 (93.2%) patients experienced at least 1 AE (Table 4), with visual acuity reduced by ≥2 lines (38.9% vs 54.5%), hypotony (23.2% vs 50.0%), and IOP increased ≥10 mm Hg from baseline (21.1% vs 11.4%) being the most common AEs (Table 4). Notably, the rate of clinical hypotony (reported at any time during the study) was 22.7% (n=10) in the trabeculectomy arm vs 1.1% (n=1) in the gel stent arm.

Five serious ocular AEs were reported in 4.2% (n=4) of patients in the gel stent arm, including 1 case of endophthalmitis (occurring 5 weeks after a 5-fluorouracil injection in the subconjunctival space [without needling], and 8 weeks after the initial surgery) that was treated with vitrectomy and resolved without sequelae at study end. The other serious AEs (n=1, 1.1% each) were device extrusion, IOP increased (resolved at study end), periorbital cellulitis (deemed not treatment-related by the investigator and ongoing at study end), and reduced visual acuity (consequence of the aforementioned endophthalmitis and resolved without sequelae at study end).

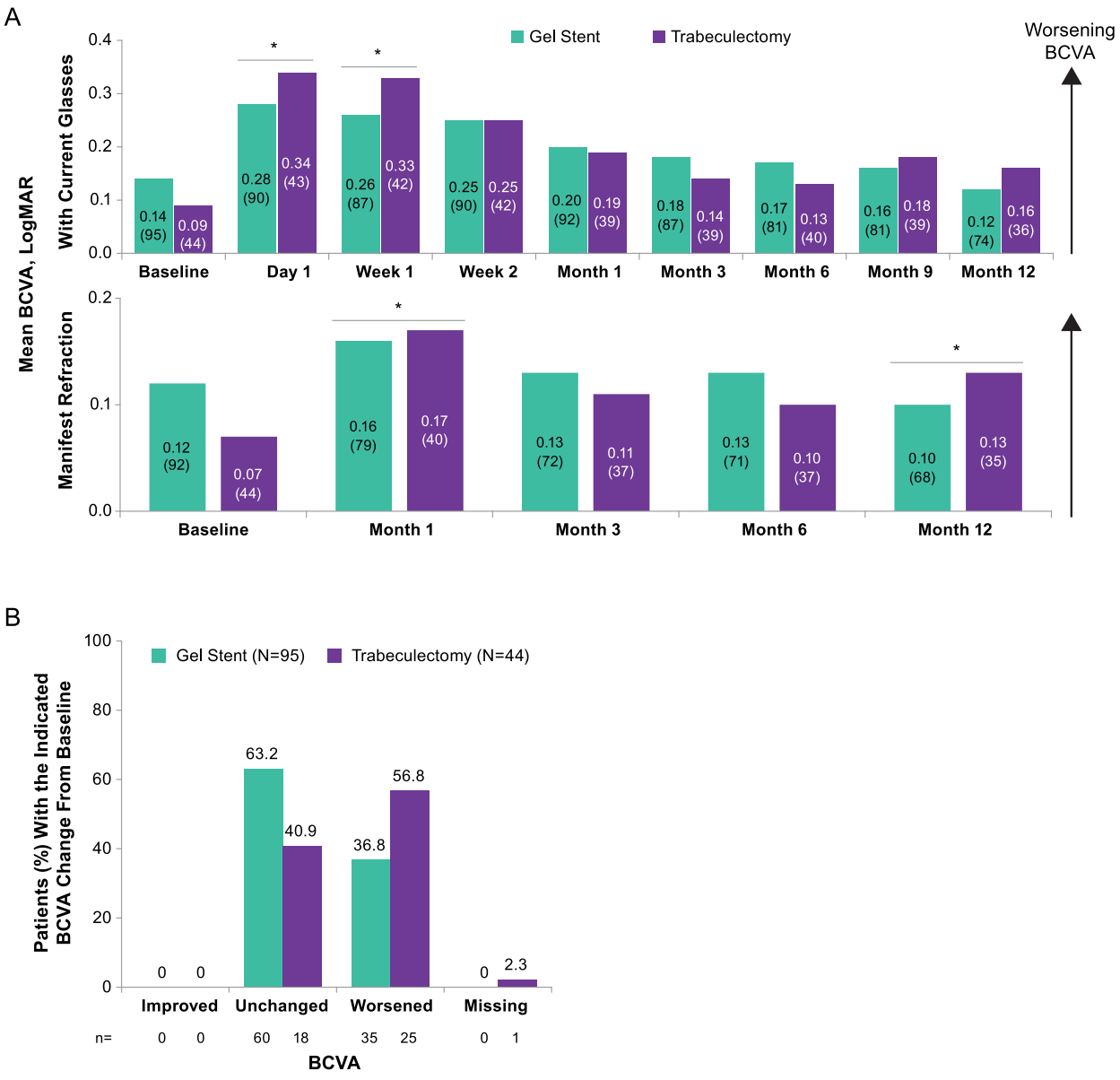

FIGURE 6. Visual recovery postsurgery in terms of (A) mean BCVA over time and (B) proportion of patients with improving, unchanged, or worsening BCVA at any time during the study. Numbers in parentheses represent patients with available data. *P≤.048 for the between-treatment differences (gel stent minus trabeculectomy), calculated based on the least squares means for each treatment arm. BCVA = best-corrected visual acuity.

Discontinuations due to AEs were reported in 3 (3.2%) patients in the gel stent arm, including 2 patients with a serious ocular AE. There were no serious ocular AEs or discontinuations due to AEs in the trabeculectomy arm.

Following gel stent implantation and trabeculectomy, subsequent surgical interventions were required in 13.7% (gel stent) and 18.2% (trabeculectomy) of eyes (P=.163). SSIs were required in 7.4% (gel stent) and 2.3% (trabeculectomy) of eyes, whereas 5.3% and 4.5% required bleb revision, and 4.2% and 11.4% required other procedures, respectively (Table 2).

The mean changes in central corneal thickness and visual field mean deviation from baseline to month 12 were not statistically significantly different, with between-treatment differences of 0.7 µm (95% CI, −3.3, 4.6) and −0.2 dB (95% CI, −1.0, 0.7), respectively.

DISCUSSION

In this first prospective, randomized, multicenter study of the gel stent vs trabeculectomy, the gel stent was statisti-

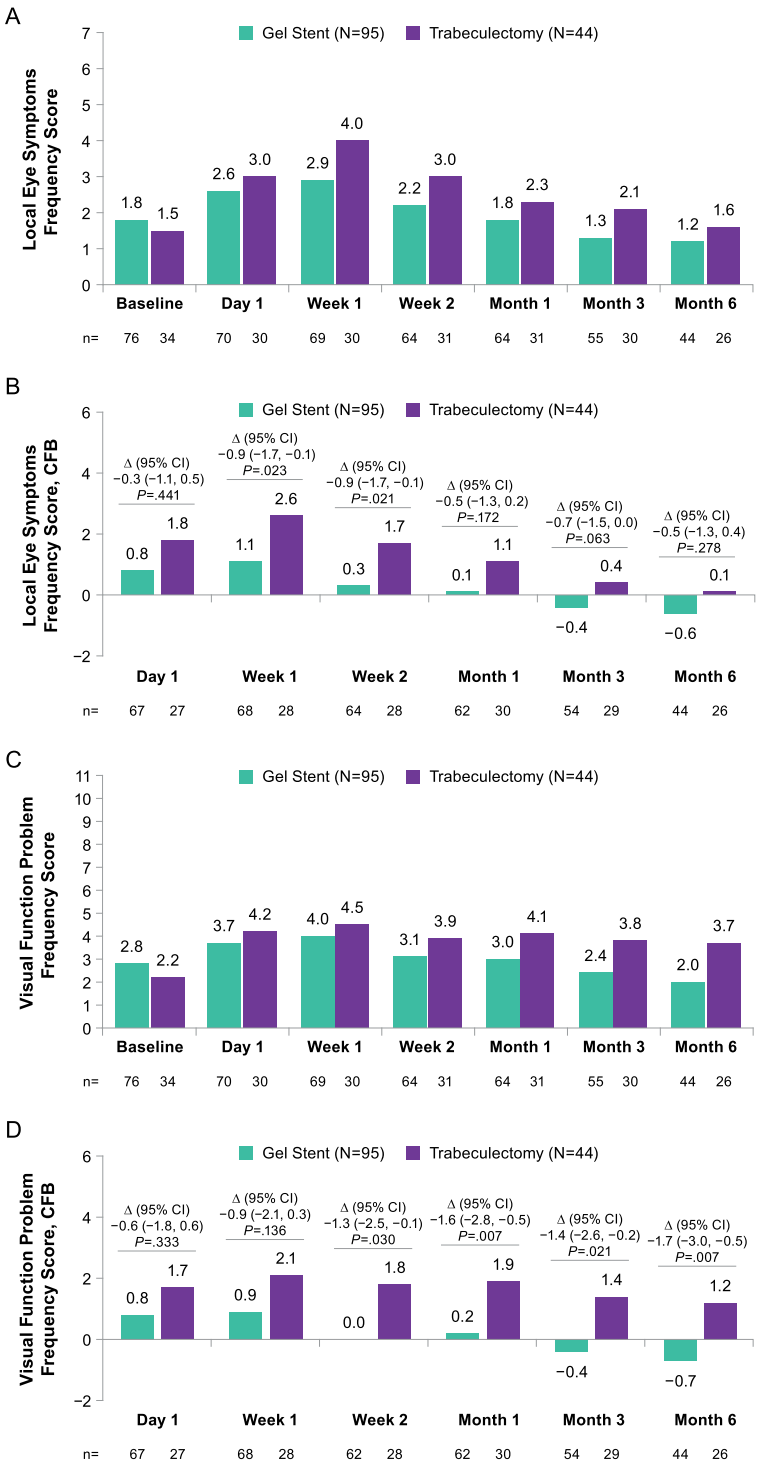

FIGURE 7. SHPC-18 scores and corresponding changes from baseline (CFB) in the frequency of local eye symptoms (A, B) and visual function problems (C, D), and the bothersomeness of local eye symptoms (E, F) and visual function problems (G, H). Higher scores indicated worse outcomes. Between-treatment differences (Δ; gel stent minus trabeculectomy) were calculated based on the least squares means for each treatment arm. *P* values relate to the between-treatment differences in CFB.

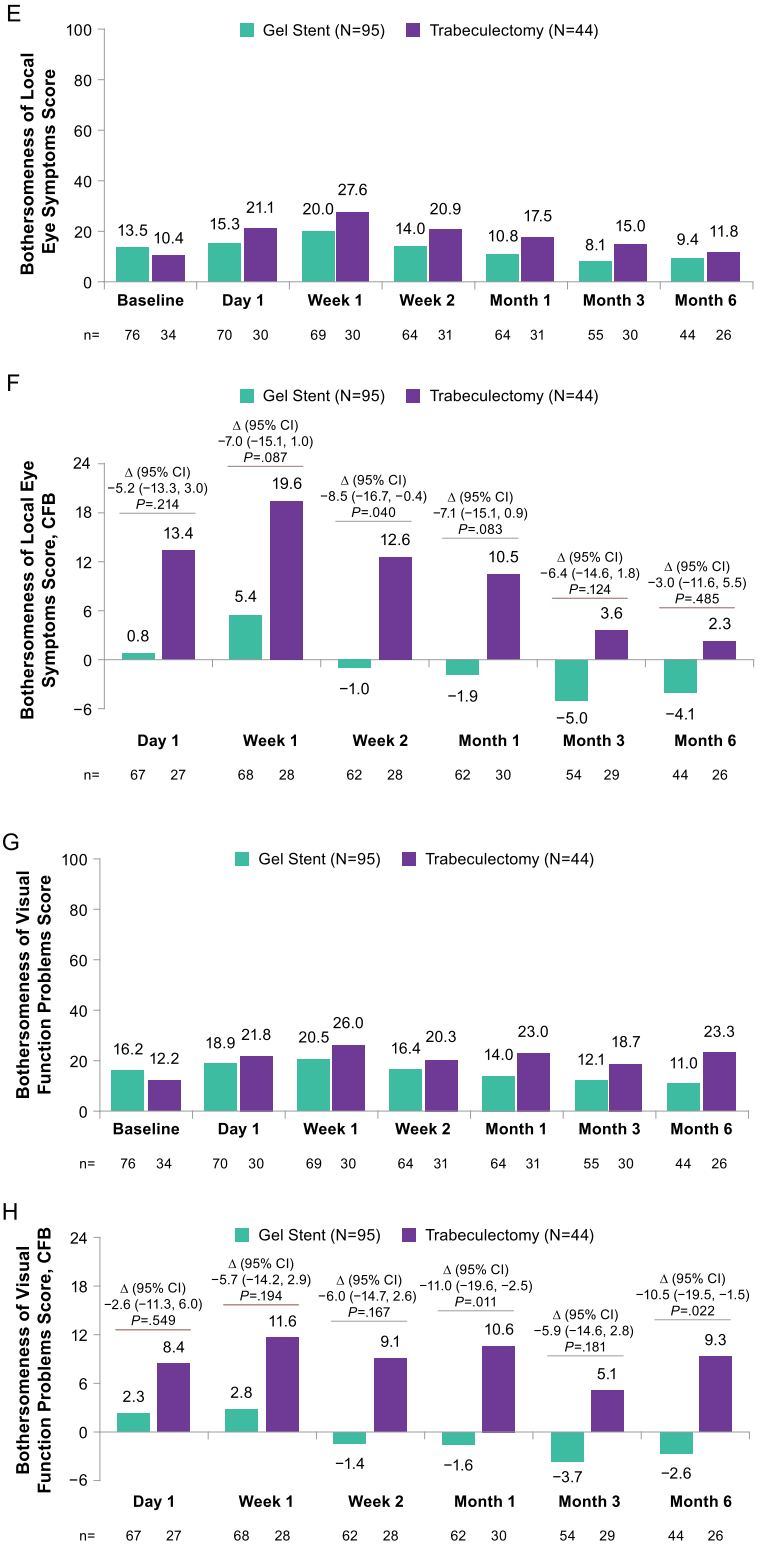

FIGURE 7. Continued

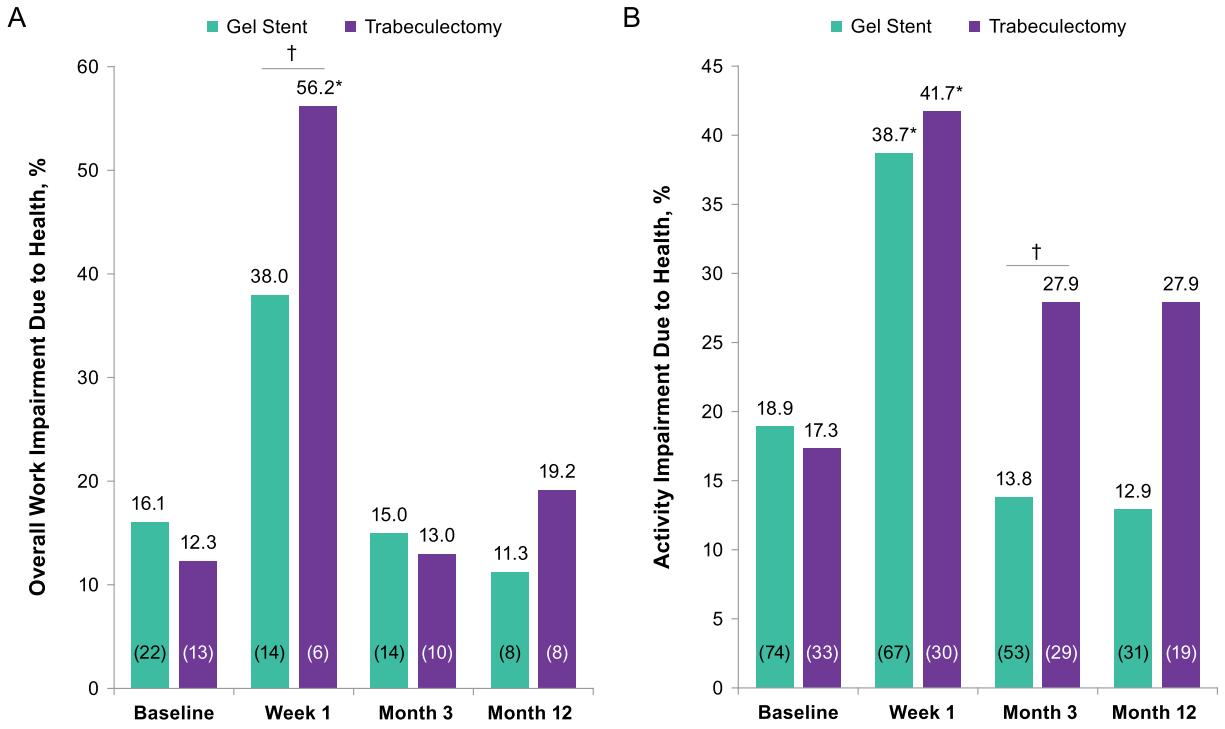

FIGURE 8. Mean percentage (A) overall work and (B) productivity impairment due to health, per the Work Productivity and Activity Impairment (WPAI-GH) Questionnaire.[a] Numbers in parentheses represent patients with available data. Calculations of means and mean changes from baseline included all patients with data at ≥1 visit and patients with data at baseline and the postoperative assessment timepoint, respectively. *P≤.014 vs baseline. †P≤.038 for the between-treatment difference in mean change from baseline. [a]The WPAI-GH Questionnaire assessed the effect of health problems (physical, emotional, or symptoms) on the patients' ability to work and perform regular activities.

cally noninferior to trabeculectomy, with 62.1% and 68.2% of eyes achieving the primary end point at month 12 (≥20% IOP reduction from baseline without increase in topical IOP-lowering medications, clinical hypotony, vision loss to counting fingers, or SSI), respectively. Statistically significant reductions in mean IOP and mean medication count from baseline were observed in both treatment arms at all visits. At month 12, mean IOP was statistically significantly lower in the trabeculectomy arm (11.8 mm Hg) than the gel stent arm (14.4 mm Hg), which could explain the slightly greater need (numerically speaking) for IOP-lowering medications in the gel stent arm. Notably, the mean IOP reported herein at 12 months following trabeculectomy (11.8 mm Hg) was consistent with findings from the pivotal Tube Versus Trabeculectomy (12.7 mm Hg[16,56]) and Primary Tube Versus Trabeculectomy (12.4 mm Hg[57]) studies.

At month 12 following implantation of the gel stent, findings of this study are consistent with those of other recently published prospective studies[31,33] in which the gel stent was implanted ab interno. Indeed, 62.1% of primary eyes achieved the aforementioned primary end point in this study. Similarly, Mansouri et al.[31] reported 62.1% of patients who achieved ≥20% IOP reduction from baseline at month 12 (primary end point). Reitsamer et al.[33] reported 65.7% of patients who achieved ≥20% IOP reduction from baseline at month 12 (secondary end point).

Mean reductions in IOP and medication counts from baseline observed herein at month 12 (−8.4 mm Hg and −1.9) are also in line with those reported in the other studies (−6.1 mm Hg and −1.4[31]; −6.5 mm Hg and −1.7[32]). Moreover, the proportions of primary eyes achieving low-teen IOP levels ≤15 mm Hg (55.8%) and ≤12 mm Hg (30.5%) in the current study were similar to those reported by Reitsamer et al. (60.7% and 27.5%, respectively).[32] It is also noteworthy that in a recently published meta-analysis of 56 studies (4410 eyes), the gel stent placed ab interno was found to lower IOP by ~35%, consistent with 36% following ab-interno implantation in this study, and to reduce the number of IOP-lowering medications by 1.9,[58] similar to the reduction of 2.1 reported herein.

In a retrospective, 4-center study comparing gel stent implantation with MMC (N=185) and trabeculectomy with MMC (N=169), Schlenker et al.[55] assessed the hazard ratio of failure (ie, 2 consecutive IOP readings <6 mm Hg with vision loss or >17 mm Hg without glaucoma medications ≥1 month postsurgery despite in-clinic interventions, including needling) as primary outcome in patients with uncontrolled glaucoma who had ≥1 month of follow-up data

TABLE 4. Surgical Complications and Relevant Postoperative AEs Reported in the Study Eyes

Surgical Complications, n (%)[a]	Gel Stent (N=95)	Trabeculectomy (N=44)
Anterior chamber bleeding	1 (1.1)	2 (4.5)
Conjunctival buttonhole	0	1 (2.3)
Iris damage	0	1 (2.3)
Other	1 (1.1)	1 (2.3)
Relevant postoperative AEs, n (%)		
Bleb fibrosis	4 (4.2)	0
Bleb leak	0	7 (15.9)
Cataract progression[b]	3 (3.2)	1 (2.3)
Choroidal effusion	2 (2.1)	4 (9.1)
Device extrusion	3 (3.2)	Not applicable
Glaucoma progression[c]	0	3 (6.8)
Hyphema	6 (6.3)	3 (6.8)
Hypotony (IOP <6 mm Hg at any time)	22 (23.2)	22 (50.0)
Clinical hypotony	1 (1.1)	10 (22.7)
IOP increased ≥10 mm Hg from baseline at any time	20 (21.1)	5 (11.4)
Iris adhesions	3 (3.2)	2 (4.5)
Visual acuity reduced (≥2 lines at any time)	37 (38.9)	24 (54.5)

AEs = treatment-emergent adverse events, IOP = intraocular pressure.

[a]Intraoperative complications of special interest are those that can occur during surgery, ie, anterior chamber bleeding, choroidal hemorrhage or effusion, conjunctival or scleral flap tearing, conjunctival perforation, detached Descemet membrane, device malfunction identified before implantation, flat anterior chamber with iridocorneal touch extending to the pupil, iris damage, lens contact, retrobulbar hemorrhage, shallow anterior chamber with peripheral iridocorneal touch, and vitreous bulge or loss.

[b]Per the investigator's slit lamp assessment and the following categories: lens clear; lens opacity present—not significant; and lens opacity present—visually significant.

[c]Based on visual field changes.

(up to 30 months). The authors concluded that there was no detectable difference in the risk of failure (or safety profiles) between treatments.[55]

In another retrospective study, Cappelli et al.[59] compared the outcome of gel stent implantation (N=34) and trabeculectomy (N=34) in patients with uncontrolled glaucoma who had ≥36 months of follow-up data. The authors concluded that the gel stent resulted in fewer hospitalization days ($P<.001$), a better safety profile, and less IOP reduction than trabeculectomy.[59] Findings from these[55,59] and additional retrospective studies showing data at ≥12 months[39,41,42,60] are consistent with the data presented herein. Other studies have reported similar IOP lowering with the gel stent and trabeculectomy.[7,38]

Numerically comparable proportions of patients/eyes required postoperative needling and 5-fluorouracil injection following gel stent implantation and trabeculectomy. However, the proportion of patients with an office-based postoperative intervention was statistically lower following gel stent implantation than trabeculectomy. Notably, the proportion of patients who required a 5-fluorouracil injection, laser suture lysis, and needling post-trabeculectomy was 21%, 29%, and 14% in the Primary Tube Versus Trabeculectomy study[57]; 22%, 49%, and 8% in the Tube Versus Trabeculectomy study[56]; and 18.2%, 31.8%, and 18.2% in the current study, respectively. It is also noteworthy that the proportion of patients requiring needling in the current study (23.2%) was in line with that reported at 1 year in other studies (32%-37%[30,31,33]) of the gel stent implanted ab interno.

Although reduced visual acuity was the most common AE in both treatment arms, the proportion of patients affected was 1.4 times higher following trabeculectomy than gel stent implantation. It is also worth noting that following gel stent implantation, return to baseline visual acuity occurred faster (likely because gel stent implantation was performed without conjunctival dissection), sustained worsening of BCVA was not observed at month 12, and fewer patients exhibited worsening in BCVA (≥2 lines) at any time during the study (Figure 6, A and B), compared with trabeculectomy.

Consistent with these findings, Schlenker et al.[44] reported 12.4% (gel stent) and 21.9% (trabeculectomy) of eyes with a vision loss >2 lines at last follow-up (median, 19.3 and 19.8 months, respectively) or reoperation ($P=.038$) in their retrospective study, adding that a higher proportion of eyes regained their preoperative visual acuity with the gel stent than trabeculectomy (adjusted hazard ratio, 1.46; 95% CI, 1.1, 2.0; $P=.025$). In 2 other retrospective studies, Schargus et al.[38] and Schlenker et al.[55]

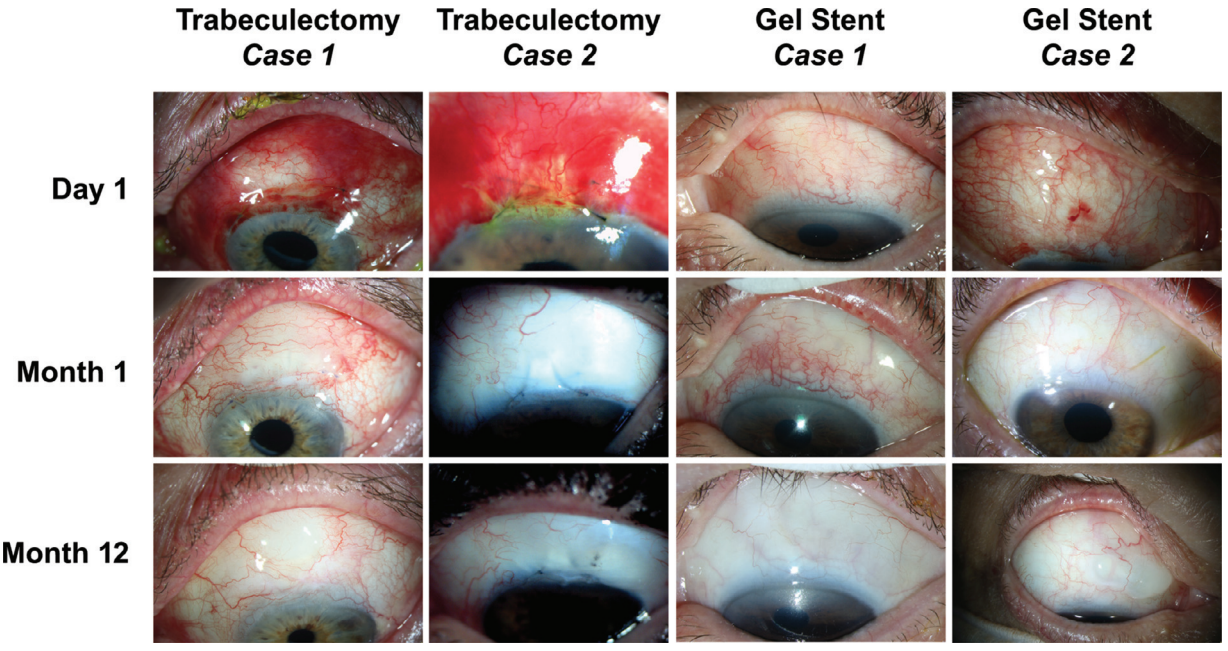

FIGURE 9. Slit lamp images showing bleb appearance on day 1, month 1, and month 12 following trabeculectomy and gel stent implantation.

found no statistically significant difference in visual acuity at month 12[38] and last follow-up (up to 30 months)[55] following gel stent implantation or trabeculectomy ($P \geq .11$).

From a patient perspective, the SHPC-18 showed statistically significant between-group differences in the change from baseline in frequency of local eye symptoms (week 1 and week 2) and visual function problems (week 2, months 1, 3, and 6), suggesting quicker and sustained reduction in frequency of local eye symptoms and visual problems following gel stent implantation than trabeculectomy. There were also statistically significant between-treatment differences in the change from baseline in bothersomeness in at least 1 domain; the mean scores and mean changes from baseline indicated a lower degree of bothersomeness in the gel stent arm than the trabeculectomy arm.

Together, these PROs suggest a better patient experience postoperatively following gel stent implantation, compared with trabeculectomy. This improved experience, along with the favorable visual recovery mentioned above, suggests an enhanced quality of life following gel stent implantation (which may be related to the bleb morphology [Figure 9], lack of sutures, or other factors). Notably, Kotecha et al.[61] demonstrated a correlation between better BCVA recovery and better quality of life in the Tube Versus Trabeculectomy study.

Regarding AEs recorded during the study, it is noteworthy that the proportion of patients with reported clinical hypotony was considerably higher with trabeculectomy than the gel stent, consistent with the gel stent having been designed using the principles of fluid dynamics to restrict outflow and reduce the risk of early postoperative hypotony.[62]

The rate of clinical hypotony observed herein following trabeculectomy also seems higher than that reported in other key studies of trabeculectomy.[55,56,63–66] This could be due (at least in part) to the fact that the studies by Gedde et al.,[56] Baker et al.,[63] Schlenker et al.,[55] Zahid et al.,[66] Edmunds et al.,[64] and Jampel et al.[65] reported hypotony maculopathy and/or serous choroidal detachment (for example) separately whereas they were grouped in the current study. Moreover, the lack of a standard definition of postoperative complications was mentioned as weakness/limitation of the pivotal Tube Versus Trabeculectomy study[56] and Collaborative Initial Glaucoma Treatment Study,[65,66] raising the possibility that complications grouped under clinical hypotony and analyzed as a prespecified safety end point herein may have been underestimated in the pivotal studies.[56,65,66] Nonetheless, rates of hypotony maculopathy of 18%[67] and 25%[68] have been recently reported following trabeculectomy, albeit in smaller studies.

It is also worth pointing that, consistent with implantation of the gel stent without conjunctival dissection, there were no reports of bleb leaks in this group, compared with 17.5% following trabeculectomy. Five serious ocular AEs were reported in the gel stent arm during the study, including 1 case of endophthalmitis with loss of vision at the time of diagnosis that was resolved without sequelae at study end. Only 1 serious AE (periorbital cellulitis; gel stent-unrelated) was ongoing at study end.

The fact that patients with failed MIGS (mostly ab-interno canal procedures) and ab-interno cycloablative procedures ≥3 months before enrollment were eligible for participation in the study should be noted as a potential

study limitation, as these procedures may have affected scarring following trabeculectomy and gel stent implantation, which in turn may have confounded the true magnitude of IOP reduction. However, the proportion of affected patients was highly similar in both treatment arms (as shown in Table 1), and this potentially confounding effect should have impacted both arms equally in this study. Although 98.6% (n=137/139) of all patients treated in this study received MMC during the surgical procedure, and the total dose was 40 μg in 94.9% (n=130/137), the MMC dose and administration route were not standardized in the protocol (to allow tailoring of the dose to a patient's needs and surgeon's preferences), and these variables may have affected outcomes.

In conclusion, this study demonstrated statistical noninferiority of the gel stent to trabeculectomy, based on the proportion of patients at month 12 achieving ≥20% IOP reduction from baseline without increase in topical IOP-lowering medications, clinical hypotony, vision loss to counting fingers, or SSI, and a noninferiority test with 24% margins. Both treatments produced statistically significant reductions in IOP and medications from baseline over time. At month 12, mean IOP was 14.4 mm Hg on 0.6 medications in the gel stent arm, and 11.8 mm Hg on 0.3 medications in the trabeculectomy arm. The change in mean IOP from baseline was statistically greater post-trabeculectomy while the change in mean IOP-lowering medications was only numerically larger. The failure rate was numerically lower post-trabeculectomy. The gel stent, however, resulted in fewer postoperative interventions, faster visual recovery with better visual function at 6 months, and fewer AEs, and should thus be considered as a surgical option in eyes requiring IOP in the mid- to low teens. In light of recently published studies reporting efficacy of the gel stent implanted ab interno at 3 and 4 years, prospective follow-up over a longer period should be performed.

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Data availability: AbbVie is committed to responsible data sharing regarding the clinical trials we sponsor. This includes access to anonymized, individual, and trial-level data (analysis data sets), as well as other information (eg, protocols, clinical study reports, or analysis plans), as long as the trials are not part of an ongoing or planned regulatory submission. This includes requests for clinical trial data for unlicensed products and indications.

These clinical trial data can be requested by any qualified researchers who engage in rigorous, independent scientific research, and will be provided following review and approval of a research proposal, Statistical Analysis Plan (SAP), and execution of a Data Sharing Agreement (DSA). Data requests can be submitted at any time after approval in the US and Europe and after acceptance of this manuscript for publication. The data will be accessible for 12 months, with possible extensions considered. For more information on the process, or to submit a request, visit the following link: https://www.abbvieclinicaltrials.com/hcp/data-sharing/.

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