Published in final edited form as:

Ophthalmology. 2018 May ; 125(5): 774–781. doi:10.1016/j.ophtha.2017.10.037.

The Primary Tube Versus Trabeculectomy (PTVT) Study: Methodology of a Multicenter Randomized Clinical Trial Comparing Tube Shunt Surgery and Trabeculectomy with Mitomycin C

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Abstract

Purpose: To describe the methodology of the Primary Tube Versus Trabeculectomy (PTVT) Study.

Design: Multicenter randomized clinical trial.

Participants: Patients with medically uncontrolled glaucoma and no prior incisional ocular surgery.

Methods: Patients will be enrolled at 16 Clinical Centers and randomly assigned to treatment with a tube shunt (350-mm^2 Baerveldt glaucoma implant) or trabeculectomy with mitomycin C (0.4 mg/ml for 2 minutes).

Main Outcome Measures: The primary outcome measure is the rate of surgical failure, defined as intraocular pressure (IOP) > 21 mm Hg or reduced < 20% from baseline, IOP ≤ 5 mm Hg, reoperation for glaucoma, or loss of light perception vision. Secondary outcome measures include IOP, glaucoma medical therapy, visual acuity, visual fields, and surgical complications.

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This article contains additional online-only material. The following should appear online-only: Appendix.

Conclusions: Practice patterns vary in the surgical management of glaucoma, and opinions differ among surgeons regarding the preferred primary operation for glaucoma. The PTVT Study will provide valuable information comparing the two most commonly performed glaucoma surgical procedures.

PRECIS

The Primary Tube Versus Trabeculectomy (PTVT) Study is a multicenter randomized clinical trial comparing the safety and efficacy of tube shunt surgery and trabeculectomy with mitomycin C in eyes without previous ocular surgery.

Glaucoma surgery is generally indicated when additional intraocular pressure (IOP) reduction is needed despite the use of maximum tolerated medical therapy and appropriate laser treatment. Trabeculectomy and tube shunt implantation are the most commonly performed incisional glaucoma procedures worldwide. Trabeculectomy has historically been the initial glaucoma operation of choice, and tube shunts have been reserved for refractory glaucomas at high risk of filtration failure. However, a growing concern about bleb-related complications associated with trabeculectomy and a greater appreciation for the efficacy of tube shunts has prompted an expanded use of shunts as an alternative to trabeculectomy.

Medicare claims data show a 72% decrease in the number of trabeculectomy procedures and a concurrent 410% increase in tube shunt implantation between 1994 and 2012.[1] Anonymous surveys of the American Glaucoma Society membership have also demonstrated a shift in glaucoma surgical practice patterns.[2–5] The use of trabeculectomy to manage medically uncontrolled glaucoma in several clinical settings has declined, while selection of tube shunts has risen. These surveys also indicate differing opinions regarding the preferred primary operation for glaucoma.[4,5]

The Primary Tube Versus Trabeculectomy (PTVT) Study is a multicenter randomized clinical trial comparing the safety and efficacy of tube shunt implantation and trabeculectomy with mitomycin C (MMC) in eyes without prior ocular surgery. The goal of this investigator-initiated trial is to provide information that will assist in surgical decision-making in similar patient groups. This paper describes the methodology of the PTVT Study.

METHODS

Patients with medically uncontrolled glaucoma who have not previously undergone incisional ocular surgery will be randomized in a 1:1 ratio to placement of a 350-mm^2 Baerveldt glaucoma implant or trabeculectomy with MMC. A synopsis of the PTVT Study is provided in Table 1. The Institutional Review Board at each Clinical Center will approve the study protocol before beginning recruitment. An effort will be made to enroll every eligible patient in the study. Written informed consent will be obtained from all subjects. The study will adhere to the Declaration of Helsinki and the Health Insurance Portability and Accountability Act. This study is registered in http://www.clinicaltrials.gov (NCT00666237).

Study Organization

Participating centers and committees in the PTVT Study are listed in the Appendix (available at http://aaojournal.org). Investigators at 16 Clinical Centers will be responsible for screening potential study patients, enrolling eligible patients, and following the patients according to the study protocol set forth in detail in the *Primary Tube Versus Trabeculectomy (PTVT) Study Manual of Procedures*. An independent Safety and Data Monitoring Committee (SDMC) will monitor all aspects of the study, including evidence of adverse and beneficial treatment effects. The Statistical Coordinating Center (SCC) will generate the random allocation sequence and assign patients to the two surgical treatments. The SCC will receive, edit, process, analyze, and store all study data. The SCC will coordinate activities at the Clinical Centers and monitor adherence to the study protocol. The Steering Committee is composed of the principal investigators from each Clinical Center and the study chairmen. The Steering Committee will provide leadership for the study, and this committee has overall responsibility for directing activities and formulating policy for the study.

Eligibility Criteria

Patients age 18 to 85 years who have had no previous incisional ocular surgery and inadequately controlled glaucoma with IOP ≥ 18 mm Hg and ≤ 40 mm Hg on tolerated medical therapy will be eligible for the PTVT Study. Exclusion criteria include no light perception vision, pregnant or nursing women, narrow anterior chamber angle, iris neovascularization or proliferative retinopathy, iridocorneal endothelial syndrome, epithelial or fibrous downgrowth, chronic or recurrent uveitis, steroid-induced glaucoma, severe posterior blepharitis, unwillingness to discontinue contact lens use after surgery, previous cyclodestructive procedure, conjunctival scarring from prior ocular trauma or cicatrizing disease precluding a superior trabeculectomy, functionally significant cataract, need for glaucoma surgery combined with other ocular procedures or anticipated need for additional ocular surgery, unwillingness or inability to give consent, unwillingness to accept randomization, or inability to return for scheduled protocol visits. Among patients in whom both eyes are eligible, only the first eye undergoing surgical treatment will be enrolled in the study.

Treatment Assignment

Randomization to placement of a Baerveldt glaucoma implant (Abbott Medical Optics, Santa Ana, CA) or trabeculectomy with MMC will occur at the time the patient is enrolled in the PTVT Study. Patients will be stratified by Clinical Center and based upon prognostic factors including age (< 50 years or ≥ 50 years), ethnicity (African American or other), and previous failed filtering surgery in the non-study eye (present or absent). Patients will be randomized using a randomly permuted block scheme in which the block size varies between 2 and 6 with an equal number of patients randomized to each treatment group at the end of each block at each Clinical Center and within each stratum. Neither the patient nor the clinician will be masked to the randomization assignment.

Surgical Procedures

The surgical procedures under investigation in the PTVT Study have been standardized to ensure consistency, while allowing each surgeon sufficient latitude to perform the operations in a manner with which he or she feels comfortable.

Baerveldt Implantation: A 350-mm^2 Baerveldt glaucoma implant will be placed in the superotemporal quadrant in patients randomized to the tube group. A limbus-based or fornix-based conjunctival flap may be used, based on the surgeon's preference. The wings of the end plate will be positioned under the superior and lateral rectus muscles. The implant will be secured to sclera with nonabsorbable suture at a measured distance of 10 mm posterior to the limbus through the two fixation holes in the end plate. The tube will be completely occluded to temporarily restrict aqueous flow to the end plate until it becomes encapsulated, minimizing the risk of early postoperative hypotony. The method of temporary tube occlusion will be left to the discretion of the surgeon, who will also be given the option of fenestrating the tube for early IOP reduction. The tube will be trimmed bevel-up to extend approximately 2 mm into the anterior chamber. A 23-gauge needle will be used to create an entry incision into the anterior chamber at the posterior limbus. The tube will be inserted through this entry incision and positioned away from the corneal endothelium, just above the iris. A patch graft will be used to cover the limbal portion of the tube. The type of suture material used to fixate the patch graft and close the conjunctiva, and the method of conjunctival closure will be determined by the surgeon. Intraoperative antifibrotic agents will not be used during tube shunt surgery. Otherwise, intraoperative and postoperative medications will be prescribed in keeping with the surgeon's usual practice.

Trabeculectomy with MMC: Patients randomized to the trabeculectomy group will undergo a superior trabeculectomy with MMC. A limbus-based or fornix-based conjunctival flap will be dissected, depending on the surgeon's preference. A fluid retaining sponge soaked in MMC (0.4 mg/ml) will be applied to the superior sclera for 2 minutes before or after scleral flap dissection, according to the surgeon's usual practice. This area will then be copiously irrigated with balanced salt solution (BSS). A paracentesis will be created in the peripheral cornea, and a corneal-based scleral flap will be dissected approximately half scleral thickness. A block of limbal tissue will be excised underneath the trabeculectomy flap. The scleral flap will be reapproximated to the scleral bed with interrupted or releasable 10–0 nylon suture. The dimensions of the scleral flap, size of the inner block, and number and tension of the scleral flap sutures will be determined at the surgeon's discretion. Following injection of BSS into the anterior chamber through the paracentesis, the anterior chamber will remain formed with a visible leak present around the scleral flap at equilibrium; if the chamber shallows or the visible leak is judged too brisk, additional scleral flap sutures will be placed (or the original sutures will be replaced with tighter ones) to minimize the risk of hypotony and/or anterior chamber shallowing. The type of suture material and method of conjunctival closure (single-layered or double-layered closure) will be of the surgeon's choice. BSS will be injected through the paracentesis to elevate the bleb at the conclusion of the case. A moistened fluorescein strip will be used to check for leakage from the paracentesis or conjunctiva, and additional sutures will be placed as needed. The use of intraoperative and postoperative medications will be determined by the surgeon.

Study Measurements

A list of study measurements for scheduled follow-up visits is presented in Table 2. An appointment schedule will be generated by the SCC for each patient at enrollment and sent to the patient's Clinical Center. The date of surgery will be the study entry date for patients in the PTVT Study, and all follow-up visits will be calculated from this date. Enrolled patients will complete follow-up visits 1 day, 1 week, 1 month, 3 months, 6 months, 1 year, 18 months, 2 years, 3 years, 4 years, and 5 years postoperatively. All study measurements will be made as described in detail in the *Primary Tube Versus Trabeculectomy (PTVT) Study Manual of Procedures*.

Visual Acuity: Distance visual acuity (VA) will be measured with two techniques, Snellen VA and the standard procedure developed for the Early Treatment Diabetic Retinopathy Study (ETDRS).[6] Refraction will be performed prior to measurement of VA at the baseline examination and at the annual follow-up visits. Snellen VA will be measured at the baseline examination and every follow-up visit. ETDRS visual acuity will be tested at the baseline examination and the 1-year, 3-year, and 5-year follow-up visits. Investigators will provide an explanation for loss of ≥ 2 lines of Snellen VA at follow-up visits after 3 months.

Slit-lamp Biomicroscopy: Examination of the anterior segment with slit lamp biomicroscopy will be performed at the baseline examination to document the preoperative condition of the eye, and at all follow-up visits to detect any changes in ocular status during the course of the study that may be attributable to the disease or treatment. The presence or absence of a bleb (perilimbal bleb after trabeculectomy and bleb overlying the end plate after tube shunt placement) will be documented at each follow-up visit. Mechanical trauma to the corneal endothelium by the tube may produce corneal decompensation after tube shunt implantation. In eyes treated with tube shunt surgery, the position and length of the tube in the anterior chamber will be recorded at all follow-up visits.

Seidel Testing: Seidel testing will be performed at each follow-up visit. If the Seidel test is positive, the leak will be graded as an ooze, frank leak, or brisk leak.

Tonometry: Goldmann applanation tonometry will be used to measure IOP, except when irregular corneal astigmatism, corneal scarring, or corneal edema precludes accurate readings. In these cases, the Tono-Pen (Reichert Ophthalmic Instruments, Depew, NY) will be used. IOP readings will be repeated until 2 measurements are obtained differing by 1 mm Hg or less, and the average of the 2 readings will serve as the IOP measurement for the follow-up visit.

Motility Evaluation: Diplopia is an important complication associated with Baerveldt implantation. A formal motility evaluation will be performed in all patients at baseline and at the 1-year and 5-year follow-up visits. Additionally, motility evaluation will be performed in patients with diplopia at or after the 6-month follow-up visit. Transient diplopia following Baerveldt implantation is not uncommon. This study will focus on the incidence and nature of permanent restrictive strabismus associated with the Baerveldt glaucoma implant. The cover-uncover and alternate cover tests will be performed with the patient looking in primary

gaze, as well as in upgaze, downgaze, left gaze, and right gaze. Motility evaluation will be performed both with the patient fixating at distance and near. Any heterophorias or heterotropias will be identified, and the deviation will be measured with hand-held prism. In patients who are unable to fixate for cover testing, the deviation will be measured by centering the corneal light reflexes with prism using the modified Krimsky method.

Gonioscopy: Gonioscopy will be performed at the baseline examination to establish the type of glaucoma and to identify patients who should be excluded because of anatomically narrow angles.

Ophthalmoscopy: A dilated fundus examination will be performed at the baseline examination and at the 1-week, 1-month, 3-month and annual follow-up visits. The fundus will also be examined at other follow-up visits in the presence of shallowing of the anterior chamber, IOP ≤ 5 mm Hg, or unexplained vision loss. Ophthalmoscopy will be used to detect posterior segment complications, such as serous choroidal effusions, suprachoroidal hemorrhage, or hypotony maculopathy.

Perimetry: Quantitative automated perimetry will be performed within one month of enrollment and at the annual follow-up visits. The Humphrey Field Analyzer will be used to conduct a 24–2 threshold test with a size III white stimulus in all patients.

Outcome Measures

The primary outcome measure in the PTVT Study is the rate of surgical failure at 5 years. Failure is defined as IOP > 21 mm Hg or < 20% reduction below baseline on 2 consecutive follow-up visits after 3 months, IOP ≤ 5 mm Hg on 2 consecutive follow-up visits after 3 months, reoperation for glaucoma, or loss of light perception vision. Reoperation for glaucoma is defined as additional glaucoma surgery requiring a return to the operating room, such as placement of a tube shunt. Cyclodestruction is also regarded as a reoperation for glaucoma, whether done in the clinic or operating room. Interventions performed at the slit lamp, such as needling procedures and laser suture lysis, are not considered glaucoma reoperations. Eyes that have not failed and are not on supplemental medical therapy are considered complete successes. Eyes that have not failed but require supplemental medical therapy are defined as qualified successes. Secondary outcome measures in the PTVT Study include IOP, VA, use of glaucoma medical therapy, surgical complications, and visual fields. Treatment outcomes will follow the intention-to-treat principle in which patients are analyzed according to their randomized treatment assignment.

Sample Size Calculations

Sample size calculations have been performed based on projected differences in failure rates between treatment groups. Enrollment of 88 patients in each treatment group is expected to detect a relative risk of failure of 2.0 at 5 years assuming a 20% failure rate in the lower risk group with a two-sided significance level of 0.05, a power of 0.80, and analysis with Yates corrected chi-square. An attrition rate of 6% per year was observed in the Tube Versus Trabeculectomy (TVT) Study, and similar loss to follow-up is anticipated in this study. Therefore, a total of 242 patients will be recruited for the study.

Quality Assurance

Data collection has been standardized through description of all study measures in the *Primary Tube Versus Trabeculectomy (PTVT) Study Manual of Procedures* and use of uniform data collection forms. Patient eligibility will be independently reviewed by the SCC before enrollment. All data forms will be received and secured at the SCC. Each form will be data entered by the SCC Research Coordinator and then verified by double entry. Edit checks, including missing and questionable data, will be clarified with Clinical Centers.

The study will be regularly reviewed by the SDMC. This committee will monitor adherence to the study protocol at each Clinical Center and review treatment reports prepared by the SCC for evidence of adverse or beneficial treatment effects. The SDMC will terminate enrollment in the study if treatment benefits or treatment risks are so great for one treatment group that continuation of the trial is deemed unethical.

Statistical Analysis

Univariate comparisons between treatment groups will be performed with the two-sided Student t-test for continuous variables and the chi-square test, asymptotic, Yates corrected, or exact permutation as appropriate for categorical variables. The time to failure is defined as the time from surgical treatment to reoperation for glaucoma, loss of light perception vision, or the first of 2 consecutive study visits after 3 months in which the patient has persistent hypotony (i.e., IOP ≤ 5 mm Hg) or inadequately reduced IOP (i.e., IOP > 21 mm Hg or reduced < 20% below baseline). Treatment comparisons of time to failure and reoperation for glaucoma or complications will be assessed with the stratified Kaplan-Meier survival analysis log-rank test. A p-value ≤ 0.05 will be considered statistically significant in our analyses. Interim analyses will be regularly prepared by the SCC and reviewed by the SDMC to assess benefits and risks for each treatment group.

DISCUSSION

Practice patterns vary in the surgical treatment of glaucoma. A recent survey of the American Glaucoma Society membership demonstrated that several different approaches are commonly used in the operative management of primary open-angle glaucoma in eyes without previous ocular surgery.[4,5] Trabeculectomy with MMC and tube shunt implantation were the most popular incisional procedures for managing glaucoma in eyes at low risk for filtration failure. The lack of consensus among glaucoma surgeons regarding the preferred initial operation for medically uncontrolled glaucoma likely relates to the fact that limited clinical data are available comparing trabeculectomy and tube shunts as primary glaucoma procedures.

Numerous studies have evaluated trabeculectomy with MMC as an initial operation for glaucoma,[7–23] and a smaller number have assessed tube shunt implantation as a primary glaucoma procedure.[21–25] A summary of these studies is shown in Table 3. Success rates ranged from 26.7% to 98.1% for trabeculectomy with MMC,[7–23] and 69.8% to 96% for tube shunts[21–25] as an initial surgical procedure for glaucoma with various definitions of success. There are obvious difficulties in making comparisons across studies because of

differences in patient populations, disease severity, surgical technique, length of follow-up, and definitions of success/failure. However, comparable success rates have been reported for both trabeculectomy with MMC and tubes shunts as primary glaucoma procedures.

Investigations have directly compared trabeculectomy and tube shunt surgery as initial glaucoma operations. Panarelli and colleagues retrospectively examined the outcomes of primary Baerveldt implantation and trabeculectomy with MMC in 125 eyes without previous ocular surgery at low risk for surgical failure.[22] The cumulative probability of success (IOP ≤ 21 mm Hg and reduced ≥ 20%, IOP > 5 mm Hg, no glaucoma reoperation, and no loss of light perception vision) was similar with both procedures at 3 years (87% Baerveldt group vs 76% trabeculectomy group, p = 0.23). Primary trabeculectomy with MMC produced greater IOP reduction with fewer glaucoma medications compared with Baerveldt implantation during 3 years of follow-up, and no significant difference in the rate of surgical complications was observed between the two procedures (20% Baerveldt group vs 29% trabeculectomy group, p = 0.27).

A prospective, nonrandomized study by Molteno and colleagues compared the long-term outcomes of trabeculectomy and Molteno implantation as an initial glaucoma procedure.[23] A total of 978 eyes were enrolled in this study, including 718 eyes that underwent trabeculectomy and 260 eyes that had placement of a Molteno implant (Molteno Ophthalmic Limited, Dunedin, New Zealand). There were 15 (2%) eyes in the trabeculectomy group and 28 (11%) eyes in the Molteno group that were pseudophakic at baseline, and 127 (18%) eyes receiving trabeculectomy and 63 (24%) eyes undergoing Molteno implantation had cataract extraction at the time of glaucoma surgery. An intraoperative antifibrotic agent was used in only 15 (2%) trabeculectomy cases. The failure rate (IOP > 21 mm Hg, phthisis bulbi, repeated surgery, loss of light perception vision) with Kaplan-Meier survival analysis was higher after trabeculectomy compared with Molteno implant surgery at 10 years (18% trabeculectomy group vs 4% Molteno group). Mean IOP, use of ocular hypotensive medications, complications, and vision loss were similar after primary trabeculectomy and primary Molteno implant placement during a mean follow-up of 7.7 years and 5.0 years, respectively.

Selection bias in retrospective and prospective, non-randomized comparative case series may produce treatment groups with different underlying risk factors for failure. Therefore, results from these study designs must be interpreted with caution. Randomized clinical trials aim to produce comparison groups that differ only by the treatment received, and they are considered the gold standard for evaluating therapies.

Wilson and associates compared the Ahmed glaucoma valve implant (New World Medical, Inc., Rancho Cucamonga, CA) to trabeculectomy with or without an antifibrotic agent in a randomized clinical trial involving 117 patients with a mean follow-up of 9.7 months.[26] Lower mean IOP was observed in the trabeculectomy group relative to the Ahmed group after 11–13 months (11.4 mm Hg trabeculectomy group vs 17.2 mm Hg Ahmed group, p = 0.001), and a greater proportion of the Ahmed group required at least one topical glaucoma medication at final follow-up (16% trabeculectomy group vs 35% Ahmed group, p = 0.01). The cumulative probability of success (IOP < 21 mm Hg and reduced ≥ 15%, IOP > 5

mm Hg, no additional glaucoma surgery, and no loss of light perception vision) was similar between the two treatment groups at 11–13 months (83.6% trabeculectomy group vs 88.1% Ahmed group, p = 0.43). This study was performed in Saudi Arabia and Sri Lanka, and included patients with all glaucoma types and some eyes that had undergone previous ocular surgery. A follow-up study continued enrollment in Sri Lanka to a total of 123 patients with primary open-angle glaucoma and angle-closure glaucoma without previous ocular surgery, and mean follow-up was 31 months.[21] Success rates were comparable between the trabeculectomy and Ahmed groups at 41–52 months (68.1% trabeculectomy group vs 69.8% Ahmed group, p = 0.86).

The TVT Study is a multicenter randomized clinical trial comparing the safety and efficacy of tube shunt surgery and trabeculectomy with MMC in eyes with previous cataract and/or glaucoma surgery.[27] A total of 212 patients were enrolled, including 107 patients who received a Baerveldt implant and 105 patients who underwent trabeculectomy with MMC. Tube shunt implantation had a higher rate of surgical success (IOP ≤ 21 mm Hg and reduced ≥ 20%, IOP > 5 mm Hg, no glaucoma reoperation, and no loss of light perception vision) compared with trabeculectomy with MMC at 5 years (70.2% tube group vs 53.1% trabeculectomy group, p = 0.025).[28] Similar mean IOP (14.4 mm Hg tube group vs 12.6 mm Hg trabeculectomy group, p = 0.12) and number of glaucoma medications (1.4 tube group vs 1.2 trabeculectomy group, p = 0.23) were observed with both surgical procedures after 5 years of follow-up. Early postoperative complications occurred more frequently after trabeculectomy with MMC than tube shunt placement (21% tube group vs 37% trabeculectomy group, p = 0.012), but both procedures had similar rates of late complications (34% tube group vs 36% trabeculectomy group, p = 0.81) and serious complications (22% tube group vs 20% trabeculectomy group, p = 0.79) after 5 years.[29]

Eyes were stratified at enrollment in the TVT Study based on type of previous intraocular surgery.[27] The largest stratum consisted of eyes with cataract extraction and intraocular lens implantation as the only prior ocular surgery at baseline, which included 94 (44%) patients. It is noteworthy that the greatest absolute difference in 5-year success rates between treatment groups was observed among patients in this stratum (74% tube group vs 41% trabeculectomy group).[28] This observation provided a major rationale for the PTVT Study.

The PTVT Study will restrict enrollment to patients without previous ocular surgery. Ocular surgery can produce conjunctival scarring that reduces the success of glaucoma filtering surgery. Eyes with conjunctival scarring from other causes, such as trauma or cicatrizing disease (e.g., Stevens Johnson syndrome, ocular cicatricial pemphigoid) are ineligible for this study. Several secondary glaucomas will be excluded from the PTVT Study, including neovascular glaucoma, uveitic glaucoma, and glaucoma associated with the iridocorneal endothelial syndrome and epithelial or fibrous downgrowth. It was the consensus opinion of the investigators that use of a tube shunt is the preferred surgical approach in these refractory glaucomas. Eyes with steroid-induced glaucoma will be excluded to avoid the potential confounding effect of postoperative steroids in a patient group in which these agents are known to produce IOP elevation. Severe posterior blepharitis and patient unwillingness to discontinue contact lens use postoperatively are exclusion criteria because of concern about an increased risk of infection should these patients be randomized to the trabeculectomy

group. Eyes with previous cyclodestructive procedures are ineligible due to a greater risk of hypotony with subsequent glaucoma surgery. The presence of a narrow anterior chamber angle is an exclusion criterion because of concerns about the adequacy of space in the anterior chamber to allow positioning of the tube away from the corneal endothelium, should randomization to the tube group occur. Eyes with a functionally significant cataract or a need for glaucoma surgery combined with other ocular procedures will be excluded, or if there is an anticipated need for additional ocular surgery. Several studies have demonstrated reduced trabecular function when various ocular procedures are performed in eyes with a pre-existing filtering bleb.[30–34]

The PTVT Study was designed to compare the safety and efficacy of tube shunt surgery to trabeculectomy with MMC in eyes without previous ocular surgery. Enrolled patients will be randomly assigned to treatment with a 350-mm^2 Baerveldt glaucoma implant or trabeculectomy with MMC. We plan to report study results after 1 year, 3 years, and 5 years of follow-up. We anticipate that the PTVT Study will provide valuable information to guide surgical decision-making in similar patient groups.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Presented as a paper at the 2016 American Academy of Ophthalmology Annual Meeting and 2017 American Glaucoma Society Annual Meeting

Supported by research grants from Abbott Medical Optics, Santa Ana, California, the National Eye Institute (grant EY014801), National Institutes of Health, Bethesda, Maryland, and Research to Prevent Blindness, Inc., New York, New York.

The sponsors had no role in the design or conduct of this research.

Mr. Feuer and Ms. Shi have received grant support from Abbott Medical Optics. The other authors report no financial interest in the subject matter of this paper.

Abbreviations/acronyms:

BSS	balanced salt solution
ETDRS	Early Treatment Diabetic Retinopathy Study
IOP	intraocular pressure
MMC	mitomycin C
PTVT	Primary Tube Versus Trabeculectomy
SCC	Statistical Coordinating Center
SDMC	Safety and Data Monitoring Committee
TVT	Tube Versus Trabeculectomy

VA visual acuity

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Table 1.

PTVT Study Synopsis

Purpose	**To compare the safety and efficacy of tube shunt surgery and trabeculectomy with MMC**
Treatment groups	350-mm^2 Baerveldt glaucoma implant
	Trabeculectomy with MMC (0.4 mg/ml for 2 minutes)
Patient eligibility	
Inclusion criteria	Age 18 to 85 years
	Glaucoma inadequately controlled on tolerated medical therapy with IOP ≥ 18 mm Hg and ≤ 40 mm Hg
	No previous incisional ocular surgery
Exclusion criteria	No light perception vision
	Pregnant or nursing women
	Narrow anterior chamber angle
	Iris neovascularization or active proliferative retinopathy
	Iridocorneal endothelial syndrome
	Epithelial or fibrous downgrowth
	Chronic or recurrent uveitis
	Steroid-induced glaucoma
	Severe posterior blepharitis
	Unwilling to discontinue contact lens use after surgery
	Previous cyclodestructive procedure
	Conjunctival scarring from prior ocular trauma of cicatrizing disease precluding a trabeculectomy superiorly
	Functionally significant cataract
	Need for glaucoma surgery combined with other ocular procedures (i.e. cataract surgery, penetrating keratoplasty, or retinal surgery) or anticipated need for additional ocular surgery
	Unwilling or unable to give consent, unwilling to accept randomization, or unable to return for scheduled protocol visits
Treatment assignment	Random
	Stratified by Clinical Center, age, ethnicity, and previous failed filtering surgery in nonstudy eye
Follow-up examinations	1 day, 1 week, 1 month, 3 months, 6 months, 12 months, 18 months, 1 year, 2 years, 3 years, 4 years, 5 years
Outcome measures	Failure (IOP > 21 mm Hg or reduced < 20% from baseline, IOP ≤ 5 mm Hg, reoperation for glaucoma, or loss of light perception vision)
	IOP

Purpose	To compare the safety and efficacy of tube shunt surgery and trabeculectomy with MMC
	Glaucoma medical therapy
	VA
	Visual fields
	Surgical complications
Enrollment	242 patients
Study centers and committees	16 Clinical Centers
	Safety and Data Monitoring Committee
	Statistical Coordinating Center
	Steering Committee

IOP = intraocular pressure; MMC = mitomycin C; VA = visual acuity

Table 2.

Study Measures at Scheduled PTVT Study Visits

	Baseline	1 Day	1 Week	1 Month	3 Months	6 Months	1 Year	18 Months	2 Years	3 Years	4 Years	5 Years
Snellen VA	X	X	X	X	X	X	X	X	X	X	X	X
ETDRS VA	X						X			X		X
Slit-lamp biomicroscopy	X	X	X	X	X	X	X	X	X	X	X	X
Seidel testing		X	X	X	X	X	X	X	X	X	X	X
Tonometry	X	X	X	X	X	X	X	X	X	X	X	X
Pachymetry	X						X		X	X	X	X
Motility evaluation	X					*	X	*	*	*	*	X
Gonioscopy	X											
Ophthalmoscopy	X	†	X	X	X	†	X	†	X	X	X	X
Perimetry	X						X		X	X	X	X

*If diplopia

†If shallowing of the anterior chamber, intraocular pressure ≤ 5 mm Hg, or unexplained vision loss

Table 3.

Studies Evaluating Primary Tube Shunt Surgery and Trabeculectomy with MMC

Author	Procedure	Number of Eyes	Success Rate	IOP Success Criteria (mm Hg)	Mean Follow-up (months)
Martini et al[7]	Trabeculectomy with MMC	30	96.6% at 1 year	≤ 18	12.0
Scott et al[8]	Trabeculectomy with MMC	89	77.9% at 2 years	≤ 21 and ≥ 30% reduction	18.4
Rasheed[9]	Trabeculectomy with MMC	25	92% at last follow-up	< 20	17.8
			72% at last follow-up	< 15	
			60% at last follow-up	< 12	
Singh et al[10]	Trabeculectomy with MMC	54	98.1% at 1 year	< 18	11.1
			96.3% at 1 year	< 21	
			83.3% at 1 year	< 15	
			57.4% at 1 year	< 12	
Bindlish et al[11]	Trabeculectomy with MMC	123	57.7% at 5 years	< target and > 6	NR
Beckers et al[12]	Trabeculectomy with MMC	60	60% at 5 years	≤ 15	NR
Fontana et al[13]	Trabeculectomy with MMC	292	62% at 3 years	≤ 18 and ≥ 20% reduction	NR
			56% at 3 years	≤ 15 and ≥ 25% reduction	
			46% at 3 years	≤ 12 and ≥ 30% reduction	
Shigeeda et al[14]	Trabeculectomy with MMC	123	74.1% at 8 years	< 21 and ≥ 30% reduction	81.6
			67.0% at 8 years	< 18	
			44.5% at 8 years	< 16	
Kim et al[15]	Trabeculectomy with MMC	30	73.3% at last follow-up	< 21	78.0
			40.0% at last follow-up	< 18	
			26.7% at last follow-up	< 15	
			26.7% at last follow-up	< 12	
Reibaldi et al[16]	Trabeculectomy with MMC	67	73.1% at last follow-up	≤ 18	127
			64.2% at last follow-up	≤ 16	
			56.7% at last follow-up	≤ 14	
Alwitry et al[17]	Trabeculectomy with MMC	59	93.2% at 1 year	≤ 21	19.3
			88.2% at 1 year	≤ 18	

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Author	Procedure	Number of Eyes	Success Rate	IOP Success Criteria (mm Hg)	Mean Follow-up (months)
			83.1% at 1 year	≤ 16	
Palanca-Capistrano et al[18]	Trabeculectomy with MMC	58	66% at 5 years	≤ 21 and ≥ 20% reduction and ≥ 6	45.3
Takihara et al[19]	Trabeculectomy with MMC	175	92.6% at 3 years	< 21	37.5
			81.3% at 3 years	< 18	
			54.2% at 3 years	< 15	
Cillino et al[20]	Trabeculectomy with MMC	20	85% at 5 years	≤ 21	NR
			70% at 5 years	≤ 17	
			40% at 5 years	≤ 15	
Wilson et al	Trabeculectomy with MMC*	64	68.1% at 41–52 months	< 21 and ≥ 15% reduction and > 5	31
	Ahmed implant	59	69.8% at 41–52 months		31
Panarelli et al	Trabeculectomy with MMC	70	76% at 3 years	≤ 21 and ≥ 20% reduction and > 5	33
	Baerveldt implant	55	87% at 3 years		27
Molteno et al[23]	Trabeculectomy†	718‡	82% at 10 years	≤ 21	92
	SP/DP Molteno implant, Molteno3 implant	260‡	96% at 10 years		60
Valimaki and Ylilehto[24]	Molteno3 implant	106‡	91% at 3 years	≤ 21 and ≥ 20% reduction and > 5	35
Namavari et al[25]	Baerveldt implant	37	84% at last follow-up	≤ 21 and ≥ 20% reduction and > 5	NR

DP = double-plate; IOP = intraocular pressure; MMC = mitomycin C; NR = not reported; SP = single-plate

*6 eyes did not receive MMC

†An intraoperative antifibrotic agent was used in 15 (2%) patients

‡Some patients were pseudophakic at baseline