A Multi-center Study Comparing the Ex-PRESS™ Mini Glaucoma Shunt to Trabeculectomy in Subjects with Open Angle Glaucoma

XVT-01

Revision D: September 5, 2011

Protocol Table of Changes

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Revision	Date	Description	Paragraphs Changed
	05 July 2006	Original	NA
B	15 March 2007	See below section	1.0 investigational plan 9.1 Study synopsis – subject population 9.2 Study Device 9.3.3 Inclusion criteria 9.3.4 Exclusion criteria 12.0 Statistical analysis
C	19 March 2008	See below section	1.0 investigational plan 9.8 Subjects compensation 14.0 Participating investigators (will be updated for each site under a current amendment version)
D	05 September 2011	See below section	10.5 Record Retention 14.0 Participating investigators

Amendment 2 – Revision C from 19 March 2008

Purpose / Justification:

In order to enhance the recruitment rate, Dr. Edward Barnet and Carla Siegfried from Washington university in Missouri were added to the XVT study as investigators. In the future more sites will be added.

Sites participating in the XVT study:

Site Number	Investigator	Address
1.	Peter A. Netland, MD*	University of Tennessee Memphis 956 Court Ave. Memphis, TN 38163
2.	Iqbal K. Ahmed, MD	3200 Erin Mills Pkwy. Unit 1 Millway Plaza, Mississauga, ON. L5L 1W8. Canada
3.	Robert L. Stamper, MD	University of California 10 Koret Street. Box 0730. San Francisco, CA 94143-0730
4.	Marlene R. Moster, MD	Wills Eye Hospital 840 Walnut Street 11th floor. Philadelphia, PA 19107
5.	Mark B. Sherwood, MD	University of Florida Box 100284, J.H.M.H.C. Gainesville, FL 32610
6.	Steve R. Sarkisian, MD	Dean A. McGee Eye Institute 608 Stanton L. Young Boulevard. Oklahoma City, OK 73104
7.	Edward Barnett	Washington University 660 South Euclid Ave., CB 8009. St. Louis, MO 63110

Amendment 3 – Revision D from 05 September 2011

Purpose / Justification:

10.5 Record Retention: In accordance with the Coordinating Center's interpretation of HIPAA, all investigators will retain any and all clinical trial material (documentation, photographs, etc) for a period of six (6) years following the completion of the study.

14.0 Participating investigators: Dr. Netland is now Faculty at the University of Virginia and the University of Virginia is now the Study Coordinating Center. Dr. Sarwat Salim is now the Investigator at the University of Tennessee, Memphis.

Sites participating in the XVT study:

Site Number	Investigator	Address
1.	Sarwat Salim, MD	University of Tennessee Memphis 956 Court Ave. Memphis, TN 38163
2.	Iqbal K. Ahmed, MD	3200 Erin Mills Pkwy. Unit 1 Millway Plaza, Mississauga, ON. L5L 1W8. Canada
3.	Robert L. Stamper, MD	University of California 10 Koret Street. Box 0730. San Francisco, CA 94143-0730
4.	Marlene R. Moster, MD	Wills Eye Hospital 840 Walnut Street 11th floor. Philadelphia, PA 19107
5.	Mark B. Sherwood, MD	University of Florida Box 100284, J.H.M.H.C. Gainesville, FL 32610
6.	Steve R. Sarkisian, MD	Dean A. McGee Eye Institute 608 Stanton L. Young Boulevard. Oklahoma City, OK 73104
7.	Edward Barnett	Washington University 660 South Euclid Ave., CB 8009. St. Louis, MO 63110
8.	Garry Condon, MD	Allegheny General Hospital East Wing Office Building 420 East North Avenue, Suite 116 Pittsburgh, PA 15212
9.	Peter A. Netland, MD, PhD*	University of Virginia 1300 Jefferson Park Ave. Charlottesville, VA 22903

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Protocol of Investigational Study

Study XVT-01

1.0 Investigational Plan

A multicenter clinical research study will be conducted in the United States and Canada. A total of 120 subjects will be enrolled with 60 subjects in each arm to compare the safety and efficacy of the Ex-PRESS mini glaucoma shunt implantation versus trabeculectomy in patients suffering from glaucoma.

2.0 Study Purpose

The purpose of this study is to compare the safety and effectiveness of the Ex-PRESS mini glaucoma shunt to trabeculectomy in reducing the number of post operative complications, reducing intraocular pressure (IOP) and reducing the use of hypotensive medications in subjects with open-angle glaucoma or ocular hypertension.

3.0 Rationale for the Study

Trabeculectomy has been the surgical treatment of choice for primary open angle glaucoma since 1970s (1), its success rates and complications however are less than ideal. Early hypotony and bleb infections are still of concern.
The Ex-PRESS, a miniature stainless steel glaucoma device approved by FDA since March 2002, is widely used worldwide for open angle glaucoma patients. This procedure is theoretically more reproducible and simple to perform as well as less traumatic to the ocular tissue than traditional filtering surgery.
With regard to the inclusion of subjects diagnosed and being treated for ocular hypertension, several recently published studies demonstrate that in patients with elevated IOP, with or without the visual field loss or optic nerve damage of glaucoma, lowering IOP provides benefit in long-term outcome of subsequent visual field loss (2-5). In any case, all subjects enrolled in the study have the opportunity to be treated with ocular hypotensive medications during the follow-up period as judged appropriate by the investigator.

4.0 Potential Risks and Benefits

The potential risks with the use of the Ex-PRESS are the same, with the same probability of occurrence and of the same magnitude, as would be found with conventional glaucoma drainage surgery. They include a risk of bleeding, infection, too low an intraocular pressure after surgery, failure of the operation to control the intraocular pressure, corneal swelling, risk of implant erosion, and double vision.
The following potential benefits have been identified:

- If the implant is effective and reduces intraocular pressure, the subject may reduce or eliminate glaucoma medication therapy.
- If the implant is effective and reduces intraocular pressure, the subject may not require additional glaucoma surgery.

- If the subject requires additional glaucoma surgery post Ex-PRESS implantation, this option requires a smaller conjunctival incision than trabeculectomy, therefore sparing more conjunctival tissue..
- This procedure is less invasive than other conventional glaucoma surgeries, thus resulting in potentially fewer complications.

5.0 Background

Glaucoma filtering surgery is indicated when glaucomatous damage progresses despite the attempt to lower the intraocular pressure (IOP) obtained with pharmacological and/or laser treatment. In the past few years, filtering surgery has improved, with an increased likelihood of successfully lowering the IOP while minimizing complications. While full thickness filtration procedures considerably reduced the IOP, they were associated with early postoperative hypotony and related side effects and became progressively less popular. Trabeculectomy has been the surgical treatment of choice for open angle glaucoma (OAG) since the 1970s; its success rate and complication rate however are less than ideal. Early hypotony and bleb infections are still of concern.
The Ex-PRESS is a miniature stainless steel glaucoma device, developed as an alternative to trabeculectomy and to the other types of glaucoma filtering surgery for patients with OAG. The Ex-PRESS mini glaucoma shunt is FDA approved since March 2002. This procedure is theoretically more reproducible and simple to perform as well as less traumatic to the ocular tissue than traditional filtering surgery.

5.1 Clinical Studies

Since the Ex-PRESS mini glaucoma shunt was FDA approved, post marketing studies were performed and presented in paper publications and meetings (1, 6-20). The Ex-PRESS was found to be safe and effective in the treatment of glaucoma subjects. A prospective randomized study comparing the Ex-PRESS to trabeculectomy in open angle glaucoma patients was performed in the Netherlands. A total of 40 subjects with primary open angle glaucoma were enrolled in each study arm and followed for 1 year. The Ex-PRESS implant under a scleral flap was found to have a more effective success rate, % IOP reduction and medication reduction compared to trabeculectomy (20).

6.0 Device Description

The Ex-PRESS is a miniature drainage device designed to regulate intraocular pressure in eyes suffering from glaucoma. The concept behind the Ex-PRESS is to divert aqueous humor through the implant from the anterior chamber to an intrascleral space - the bleb. The Ex-PRESS glaucoma implant is manufactured from implantable stainless steel. It consists of a 2-3 mm long and 0.4mm outer diameter and 50 micron inner diameter tube, which connects the anterior chamber to the intrascleral space. Despite its miniature size, the Ex-PRESS features several major structural elements (figure 1):

1. A cannula for draining aqueous humor from the anterior chamber to the intrascleral space.
2. A plate to prevent excessive penetration.
3. A spur to prevent extrusion of the Ex-PRESS^{TM} from the eye.

4. Reserve orifices near the distal end, which constitute an alternative conduit for aqueous humor drainage in case of occlusion of the primary (axial) opening of the cannula by the iris.

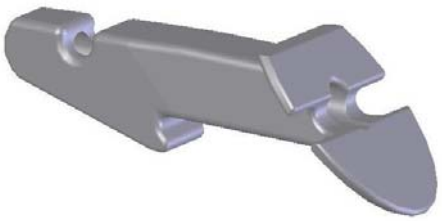

Figure 1: Ex-PRESS

The Ex-PRESS is loaded on a specially designed disposable introducer. The introducer has a female Luer Lock base and mounted on a disposable 1 ml syringe.

7.0 Study Objective

The study objective is to compare the safety and effectiveness of Ex-PRESS implantation under a scleral flap versus trabeculectomy.

7.1 Primary Effectiveness End Points

The primary effectiveness measure will be qualified and complete success rate defined as IOP≤18mmHg with or without medications in the test group as compared to complete and qualified success rate in the concurrent control group at 12 months.

7.2 Secondary Effectiveness End points

The secondary effectiveness measure will be qualified and complete success rate defined as IOP≤18mmHg with or without medications in the test group as compared to qualified and complete success rate in the concurrent control group at 24 months.

7.3 Primary Safety End Points

Post operative safety profile defined as vitreous loss and hypotony (IOP≤5mmHg) and related complications (choroidal effusion, hyphema, shallow/flat AC, leaking bleb).

7.4 Secondary Safety End Points

Comparison of the incidence of all adverse events that occur during the intra-operative and postoperative periods between the two study arms.
To evaluate and compare the incidence of elevated IOP (IOP spikes) in the immediate postoperative period in both study arms. For this study, an IOP spike will be considered an increase of 10mmHg or more from baseline (21). However, all measurements will be collected and analyzed.

8.0 Study Claim

The safety of the Ex-PRESS™ is superior and efficacy as good as trabeculectomy in open angle glaucoma patients.

9.0 Study Protocol

9.1 Study Synopsis

Title:	A prospective randomized multi-center study to compare the Ex-PRESS™ to trabeculectomy in patients with open angle glaucoma who failed medical treatment and for which filtering surgery is indicated
Protocol Number:	XVT-01
Number of Sites:	7 sites were approved.
Study Period:	2 year, 10 visits: Pre-operation, day of surgery, day 1, 1-2 Weeks, Months 1, 3, 6, 12, 18 and 24 post operation. Additional visits will be performed and recorded as required for the optimal treatment and follow up of the patient. Additional visits are defined as visits that were not preplanned and considered emergent.
Study design:	A prospective, two arm, active control, unmasked, randomized study
Objectives:	A prospective randomized trial to compare the safety and efficacy of the Ex-PRESS to trabeculectomy in patients with open angle glaucoma who failed medical or are allergic to medical treatment and for which filtering surgery is indicated
Control Arm	Subjects undergoing trabeculectomy with the use of Mitomycin C
Treatment Arm	Subjects undergoing Ex-PRESS Under Scleral Flap implantation procedure with the use of Mitomycin C
Subject Population:	Open angle glaucoma patient's candidates for filtering surgery. The patients may have a history of cataract phacoemulsification surgery.
Sample Size:	Total of 120 subjects with 60 subjects in each arm. Each site can enroll a maximum of 30 subjects and a minimum of 5 subjects for each study arm.
Follow-up duration:	2 years
Target enrollment period:	Up to 1 year

9.2 Study Device

The Ex-PRESS R version miniature glaucoma shunt.

9.3 Study Population

9.3.1 Number of Subjects

A total of 120 subjects will be enrolled into the study with 60 subjects in each arm.

9.3.2 Study Population

The study population will consist of subjects diagnosed with open-angle glaucoma (OAG) (which includes pseudoexfoliative and pigmentary glaucoma) and subjects diagnosed with ocular hypertension (OHT). Subjects must be currently taking ocular hypotensive medications or found to be allergic to hypotensive medications. Subjects may also have a history of cataract phacoemulsification surgery.

All subjects will have IOP of 19mmHg or more. For example, a subject who is currently taking two medications and has a pressure of 21mmHg with cataract phacoemulsification surgery performed 12 months before will qualify for enrollment in the study. A complete listing of inclusion and exclusion criteria is presented in section 9.3.3 below.

9.3.3 Inclusion Criteria

- Adult subject over the age of 18
- Subject diagnosed with open angle glaucoma (POAG, PXFG or PDSG) or ocular hypertension
- Subject is a candidate for filtering surgery with intra-operative anti-metabolites
- IOP > 18 mmHg on maximum tolerated medial therapy based on two measurements taken 1 hour apart at the same visit.
- Subject willing to attend all follow-up evaluations
- Subject willing to sign informed consent.

9.3.4 Exclusion Criteria

- Subject diagnosed with: PACG, NTG, secondary glaucoma, neovascular glaucoma
- Subject has history of glaucoma surgery (filtering, glaucoma drainage device, cyclo destructive procedures)
- Subject has history of penetrating keratoplasty (PKP)
- Subject underwent large incision extra capsular cataract extraction
- Subject underwent cataract phacoemulsification within the last month
- Subject has a visually significant cataract that is planned for extraction at the time of filtering surgery or within 12 months thereafter
- Any ocular disease or history in the operated eye other than glaucoma and cataract, such as uveitis, ocular infection, severe dry eye, severe blepharitis , active proliferative retinopathy, ICE syndrome, epithelial or fibrous down growth, aphakia, and ocular pathology that may interfere with accurate IOP measurements
- Subject has vitreous present in the anterior chamber for which vitrectomy is anticipated
- IOP of ≤18mmHg
- Subject participates in any other concurrent ocular investigation.

9.4 Subject Enrollment

9.4.1 Informed Consent and Enrollment

The informed consent/patient information sheet written in the subject's native language will be explained to each prospective subject by the investigator or a trained clinical professional. The final informed consent form must be approved by the Institutional Review Board (IRB).
Once the subject has been informed of all aspects of the study, the subject will then be given a choice to voluntarily confirm his or her participation in the study as documented by completion of the Informed Consent. After signing the Informed Consent and the HIPAA (Health Insurance Portability and Accountability Act) authorization, the subject can then proceed with the screening evaluation.

The subject has the right to withdraw from the study at any time without consequences, as indicated in the Patient Informed Consent documentation.

9.4.2 Baseline Evaluation

After obtaining an understanding of the purpose of this study, reviewing and signing the informed consent form, all potential subjects will undergo an examination in order to determine their eligibility for this study.

The screening examination will consist of applanation tonometry to measure IOP, general slit-lamp biomicroscopy to review the overall health of the eye, visual acuity (VA) measurements, and a review of current medications and prior surgeries. All information should be compared to the specific inclusion and exclusion criteria in order to determine if the subject is eligible to participate in the study.
The following criteria are provided below to assist with appropriate screening for all subjects in this study:

- Diagnosis

Investigator is to provide the diagnosis in each eye, as either ocular hypertension (elevated IOP without evidence of visual field loss or cupping of the optic nerve head) or glaucoma (elevated IOP with either glaucomatous visual field loss, as judged by automated threshold visual field testing, or cupping of the optic nerve head.

- Measurement of intraocular pressure

Each time IOP is measured, the surgeon or technician is to utilize a Goldmann tonometer, however, an independent observer should read the measurement and then record the measurement to minimize observer bias.
Two measurements should be taken and the mean recorded on the case report form UNLESS they differ by more than 2 mmHg in which case a third measurement is taken and the median value is recorded.

- Visual Field Examination

Visual fields must be automated threshold visual fields (e.g., 30-2 or 24-2 Humphrey). SITA Standard visual fields are required. Visual fields must be reliable, defined as less than 33% false positives, false negatives, and fixation losses.

The visual field must be performed within three to six months of study entry and meet the aforementioned requirements. Both the test eye and the fellow eye should have visual field data.

Visual fields are to be performed with a non-dilated pupil unless, in the opinion of the investigator, the pupil is so miotic that dilation is required (e.g., < 3 mm). If dilation was performed at baseline, it should be performed at all subsequent visual field examinations. However, dilation should not be performed before the IOP measurement on the appropriate visits.

For OAG subjects and in accordance with the American Academy of Ophthalmology (AAO) Preferred Practice Patterns, the severity of glaucoma damage can be assessed as follows: (1) Mild – characteristic optic nerve abnormalities are consistent with glaucoma, but there is a normal visual field and (2) Moderate – visual field abnormalities are in one hemifield and not within 5 degrees of fixation.

For OHT subjects, qualifying visual fields must be normal and reliable in the study eye.

- Cup-to-Disc Ratio

A numerical expression indicating the percentage of disc occupied by the optic cup. A score from 0.1 to 0.9 (in 0.1 increments) should be indicated.

- Visual Acuity

Best corrected visual acuity will be measured at baseline and at each follow-up visit. Visual acuity will be measured using Snellen line method.

If a subject satisfies all inclusion and exclusion criteria the subject will be enrolled into the study. The subject is then randomized to participate in either Group A or Group B using the sealed envelope method of randomization.

Group A
Subjects will undergo implantation of the Ex-PRESS mini glaucoma shunt.
Group B
Subjects will undergo standard trabeculectomy.

9.5 Surgical Procedure

9.5.1 Materials and Equipment

A listing of general equipment and materials needed for the preoperative, operative, and postoperative steps of the investigational study is provided below.
Goldmann Applanation Tonometer, Handheld direct ophthalmoscope, Viscoelastic Solution, Balanced Salt Solution, toothed forceps, tying forceps, non-toothed forceps, scissors, cautery, speculum, blades, punch, 25G or 23G needle and Ex-PRESS mini glaucoma shunt.

9.5.2 Surgical procedure

Ex-PRESS implantation procedure

Local or topical anesthesia is administered and the eye is prepared and covered using conventional sterile procedures. Implantation is performed using a special introducer, conventional microsurgical instruments and a surgical microscope.
The Ex-PRESS, mounted on its introducer is inserted into the anterior chamber at the limbus through the sclera under the scleral flap.
The implantation procedure may be performed as follows:

1. Creation of a fornix or limbal based conjunctival flap in the upper quadrants
2. Creation of a limbal-based scleral flap extending into clear cornea
3. Delicate application of MMC solution onto the sclerectomy bed. (MMC concentration 0.4mg/ml for 1-3 minutes)
4. Penetration into the anterior chamber using a 23-25G needle, halfway between the white sclera and the clear cornea (in the center of the grey zone), and creation of a track incision at the limbus
5. Prior to implantation, a thorough mobility check should be performed
6. Implantation of the Ex-PRESS implant loaded on its introducer, through that pre-incision
7. Withdrawal of the introducer
8. Tucking the plate under the scleral flap, and verification of its position
9. Suturing the scleral flap with sutures

After the implantation procedure, antibiotics and steroids are administered topically, the eye is covered with a pad and the patient is discharged.

Standard trabeculectomy procedure

1. Creation of a fornix or limbal based conjunctival flap in the upper quadrants
2. Creation of a limbal-based scleral flap extending into clear cornea
3. Delicate application of MMC solution onto the sclerectomy bed. (MMC concentration 0.4mg/ml for 1-3 minutes)
4. Creation of fistula 1mm x 2mm in size
5. Iridectomy
6. Suturing the scleral flap
7. Repositioning of the conjunctiva with sutures

After the procedure, antibiotics and steroids are administered topically, the eye is covered with a pad and the patient is discharged.

9.6 Follow up

All subjects will participate in defined follow-up visits for two years. Follow up visits include day of surgery, day 1, 1-2 Weeks, Months 1, 3, 6, 12, 18 and 24 post surgery. Additional visits will be performed and recorded as required for the optimal treatment and follow up of the patient. Additional visits are defined as visits that were not preplanned and considered emergent. Table 1 presents the activities to be performed at each follow up visit.

Table 1: Follow-up Activities

Activity	Screening	Surgery	1 Day	1-2 Wk	1 Mo	3 Mo	6 Mo	12 Mo	18 Mo	24 Mo
Ophthalmology Exam	X									
Medical History	X									
Medication Assessment	X		X	X	X	X	X	X	X	X
Visual Field	X							X		X
CD ratio	X							X		X
Slit-lamp Exam	X		X	X	X	X	X	X	X	X
Visual Acuity	X		X	X	X	X	X	X	X	X
Fundus Exam	X							X		X
IOP	X		X	X	X	X	X	X	X	X
Procedure		X								
Adverse Event Assessment		X	X	X	X	X	X	X	X	X
Protocol Deviation Assessment		X	X	X	X	X	X	X	X	X

- Intraocular pressure measurements during follow-up visits

Each time IOP is measured, the surgeon or technician is to utilize a Goldmann tonometer, however, an independent observer should read the measurement and then record the measurement to minimize observer bias.
Two measurements should be taken and the mean recorded on the case report form UNLESS they differ by more than 2 mmHg in which case a third measurement is taken and the median value is recorded.
All attempts should be made to conduct each follow-up evaluation within the specified time intervals (Table 2).

Table 2: Follow up examination schedule

Follow up visit	Acceptable Time Interval (Days from Procedure)
Day 1 pos-op	Day 1 post op
7-14 days post-op	7-14 days post-op
1 month post-op	30 days ± 7 days
3 months post-op	90 days ± 14 days
6 months post-op	180 days ± 21 days
12 months post-op	360 days ± 30 days
18 months post-op	540 days ± 30 days
24 months post-op	720 days ± 30 days

9.7 Study Withdrawal

All subjects have the right to withdraw at any point during the treatment without prejudice. The investigator can discontinue any subject at any time if medically necessary. If a subject withdraws prematurely from the study, a genuine effort must be made to determine the reason(s) why the subject discontinued the study. The reason must be recorded.

9.8 Subjects Compensation

Subjects will be compensated up to 100 USD for traveling and parking fee, against receipts. Half of the payment and up to 50 USD will be given at 12 months visit, and 50 USD at 24 months visit. The payment will be given by the study staff (e.g. site study coordinator/ clinical administrator/ investigator).

10.0 Data Handling

10.1 Subject Identification

The subjects will be identified by a 2 digit sequential subject number. The initials for each subject will also be included on CRFs. In this way, information contained in the study records will be kept as confidential as possible. The allocation subject number will be as follows: XVT __ __ (Site number) - __ __ __ (subject enrollment number). Subject initials will include three letters, first letter of first name, middle name and last name. In cases where subject does not have a middle name a dash sign will be entered.

10.2 Confidentiality

All medical records associated with this clinical investigation will be made available for review by designated personel and governmental agencies involved. The results of the study may be published in the future for scientific purposes, but the identity (name) of each subject will not be revealed. All records will be stored in a secure area at the investigator's facility

10.3 Case Report Forms

The data from this study will be collected using the following forms:
CRF 1 – Initial Data Sheet
CRF 2 – Operative Form
CRF 3 – Follow-Up Form (to be used for all follow-up visits)
CRF 4 – Adverse Event Form
CRF 5 – Protocol Deviation Form

10.4 Administrative Forms

The administrative forms include the Subject Log Form.

10.5 Record Retention

The investigator will retain any and all clinical trial material (documentation, photographs, etc.) for a period of six (6) years following the completion of the study.

11.0 Safety

At each visit, the ocular health of each subject will be assessed. The cornea, anterior chamber, trabecular meshwork, and implant location (if applicable) will be examined. If any abnormalities are observed, they are to be noted (type and location) within the case report forms.

11.1 Adverse Events

Any ocular adverse events occurring during the trial whether they are considered to be device related or not must be documented in the subject's records. Date and time of the event, its severity, treatment (if any) and the assessed relationship of the event to the study will be recorded on CRF 4 Adverse Event Form. Conditions which exist at the time the subject is enrolled do not need to be recorded on the Adverse Event Form as adverse events unless they increase in severity during the study.

A brief overview of the differences between anticipated, unanticipated and serious adverse events is provided below:

- Anticipated Adverse Events

Anticipated adverse events include those that might reasonably be expected to occur in this study because they are associated with glaucoma surgical procedures.

- Unanticipated Adverse Events

Unanticipated adverse device effects (UADE) include any serious adverse effects on health or safety or any life-threatening problem or death caused by or likely directly related to the Ex-PRESS mini shunt or the placement of the Ex-PRESS mini shunt within the eye that are not typically associated with glaucoma surgical procedures.

- Serious Adverse Events

Serious adverse events include those events that require or prolong hospitalization, require surgical intervention, are sight or life-threatening or fatal, or result in significant disability or incapacity.

11.2 Reporting Adverse Events

All serious adverse events (whether anticipated or unanticipated) must be reported to the reviewing IRB according to their guidelines given..
All adverse events should be documented by completing CRF 4, Adverse Event Form and a specific IRB AE form (if applicable).

Identification and collection of adverse event information will be the responsibility of the study investigator. The investigator will follow the Declaration of Helsinki in order to ensure the safety of all subjects.

11.3 Type and duration of follow-up after adverse events

The investigator is responsible for recommending the type and duration of follow-up for each subject who experiences an adverse event. All events must be followed until study completion, complete resolution or resolution with sequelae. All details must be documented on CRF 6, Adverse Event Form.

12.0 Statistical Analysis

The data provided from this randomized controlled study are intended to provide a reasonable assurance of safety and effectiveness for the Ex-PRESS mini shunt compared to standard trabeculectomy.

The primary safety and effectiveness end points are provided in sections 7.1-7.4 of this protocol. The data will be analyzed using the Fishers exact test p-value and Student's paired *t* test p-value comparison. Success rate will be analyzed using Kaplan-Meier survival analysis curves. Phakic and pseudophakic patients will be explored as a possible covariate in the efficacy and safety analysis.

13.0 Compliance with Protocol

The investigator shall conduct this investigation in accordance with the investigational plan, applicable FDA regulations, HIPAA Health Insurance and Accountability Act and any conditions of approval imposed by an IRB.

14.0 Participating Investigators

The investigational sites recruited to participate in this multicenter study are listed below in Table 3:

Table 3: Investigational sites for the XVT-01 study

Site Number	Investigator	Address
1.	Sarwat Salim, MD	University of Tennessee Memphis 956 Court Ave Memphis, TN 38163
2.	Iqbal(Ike) K. Ahmed, MD	3200 Erin Mills Pkwy. Unit 1 Millway Plaza Mississauga, ON. L5L 1W8. Canada
3.	Robert L. Stamper, MD	University of California Box 0730 10 Koret Street San Francisco, CA 94143-0730
4.	Marlene R. Moster, MD	Wills Eye Hospital 840 Walnut Street 11th floor Philadelphia, PA 19107
5.	Mark B. Sherwood, MD	University of Florida Box 100284, J.H.M.H.C. Gainesville, FL 32610
6.	Steve R. Sarkisian, MD	Dean A. McGee Eye Institute 608 Stanton L. Young Boulevard Oklahoma City, OK 73104
7.	Edward Barnett	Washington University 660 South Euclid Ave., CB 8009 St. Louis, MO 63110
8.	Garry Condon, MD	Allegheny General Hospital East Wing Office Building 420 East North Avenue, Suite 116 Pittsburgh, PA 15212
9.	Peter A. Netland, MD, PhD*	University of Virginia 1300 Jefferson Park Ave. Charlottesville, VA 22903

* Principal Investigator

15.0 References

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