Descemets Endothelial Thickness Comparison Trial

Manual of Operations and Procedures

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1. INTRODUCTION AND BACKGROUND

Corneal transplantation has evolved rapidly in recent years. Lamellar keratoplasty to replace diseased endothelium has led to faster recovery times, fewer complications, and better visual acuity outcomes.[1] Currently, Descemet's Stripping Endothelial Keratoplasty (DSAEK) is the most common procedure because of its relative ease and good outcomes.[2] Newer techniques such as Descemet's Membrane Endothelial Keratoplasty (DMEK), where Descemet's membrane alone is transplanted, has the potential to further improve visual acuity outcomes, produce fewer higher-order corneal aberrations and decrease rejection rates.[3-7] However, donor preparation, increased intra-operative times, and problems with donor attachment in DMEK are all important limitations.[8-10]

There are three potential mechanisms by which DMEK may provide better visual acuity outcomes than DSAEK: graft thickness, interface haze and corneal higher-order aberrations. Graft thickness has been correlated with best spectacle corrected visual acuity (BSCVA) outcomes among thinner grafts. One retrospective case series found that 71% of thin endothelial grafts (defined as <131μm) had BSCVA of 20/25 or better while only 50% of thick grafts (defined as ≥131) achieved this.[11] In addition, higher-order aberrations, in particular of the posterior cornea, are increased after DSAEK. Theoretically, given the decreased tissue transplanted after DMEK this would be lessened; however, one retrospective series looking at higher order aberrations in DMEK compared with DSAEK found no difference in posterior aberrations of the central 4.0 mm zone between the two groups.[10] Finally, interface haze may be increased in DSAEK and has been correlated with BSCVA.[12]

Ultrathin DSAEK involves donor preparation with a double microkeratome pass to produce donor grafts less than 100 um thick. This procedure may have similar results to DMEK but without the technical difficulties. Several large prospective series show similar visual outcome results and rates of immunologic rejection between ultrathin DSAEK and DMEK, however comparisons are difficult.[11,13-15] This randomized controlled trial could directly address these important issues. We also anticipate that secondary analyses of the trial data will allow us to address several more.

Research Question: Are BSCVA outcomes, endothelial cell counts, and post-operative corneal light scatter and higher-order aberrations different between patients undergoing ultrathin DSAEK versus DMEK?

1.1 Specific Aims

1) **To determine whether there is a difference in best spectacle-corrected visual acuity (BSCVA) at 6 months between patients receiving ultrathin DSAEK and DMEK.** We hypothesize that the DMEK group will have improved visual acuity compared with DSAEK at 3 months, but not at 6 months. By randomizing 25 patients per arm, we anticipate 80% power to detect a one standard deviation, or approximately 1.2 Snellen lines, difference in BSCVA between the DMEK and DSAEK groups.

2) **To evaluate endothelial cell loss at 6 months between patients receiving ultrathin DSAEK and DMEK.** We hypothesize that there will be a difference in endothelial cell loss at 6 months between patients receiving ultrathin DSAEK and DMEK, accounting for pre-operative endothelial cell count.

3) **To assess the relative role of light scatter, higher-order aberrations and graft thickness on visual acuity.** We predict that there will be increased light scatter at the

graft-host interface and but no difference in posterior corneal higher-order aberrations of the central 4mm in DSAEK versus DMEK.[10]

While long-term outcomes such as graft rejection and survival are beyond the scope of the initial phase of this study, we anticipate we will be able to evaluate these as we follow patients at 12 and 24 months.

1.2 Study Outcomes

Primary Outcome:

- BSCVA *at 6 months*

Secondary Outcomes:

- Endothelial cell counts
- Corneal higher-order aberrations as measured by Pentacam
- Interface haze as measured by Pentacam densitometry
- Change in NEI-VFQ *from baseline to 3 months and 12 months*
- Primary graft failure, defined as a lack of graft clearing or need for re-graft within the first 2 months
- Graft rejection, defined as loss of graft clarity due to edema with evidence of inflammation such as anterior chamber cell or keratic precipitates.

Other Outcomes measured:

- Refraction
- Graft thickness as measured by OCT and pachymetry
- Operative times
- Adverse events/Complication rates

1.3 Study Design

Descemets Endothelial Thickness Comparison Trial (DETECT) is a randomized double-masked, two-arm clinical trial. The purpose of this study is to determine differences in visual outcomes between two types of corneal transplant surgeries. There will be 1:1 randomization to one of two treatment groups – 1.) Ultrathin Descemet's Stripping Endothelial Keratoplasty (DSAEK) OR 2.) Descemet's Membrane Endothelial Keratoplasty (DMEK). The enrollment period is 24 months.

2. ORGANIZATION

Oregon Health & Science University (OHSU) along with the University of California San Francisco (UCSF) will jointly execute this clinical trial. OHSU will mainly be responsible for recruitment and enrollment, intervention implementation, and follow-up visits. UCSF will take the lead on all data analysis, writing of study-related materials, and journal publications.

2.1 Collaborating Institutions

Oregon Health & Science University

As a teaching institution and part of OHSU, Casey Eye Institute has state-of-the-art facilities and access to specialists in all areas of eye care. The Casey Eye Institute will serve as one of the sites for recruitment, treatment/intervention, and follow-up visits. All study personnel assisting with the research will be adequately informed about the protocol, the research procedures, and their duties and functions through ongoing communication between Casey Eye Institute and UCSF.

Winston Chamberlain, MD, PhD is the PI for this study and works as a lead surgeon at Casey Eye Institute. Dr. Chamberlain received his BS in biology from California Institute of Technology. He holds a PhD in immunology and an MD from the University of Colorado Health Sciences Center. He is board certified in ophthalmology, and a member of the American Academy of Ophthalmology. His research interests include the outcomes of corneal transplant surgery with the femtosecond laser and DSAEK techniques, and inflammatory responses in the cornea.

Brenda Purvis is the OHSU study coordinator. She works as the Cornea Division Manager at Casey Eye Institute.

Stanford University
The Byers Eye Institute at Stanford University is dedicated to combating blindness and preserving sight by delivering an effective, integrated collection of comprehensive vision care specialties. The Byers Eye Institute will be a second site for recruitment, treatment/intervention, and follow-up visits. All study personnel assisting with the research will be adequately informed about the protocol, the research procedures, and their duties and functions through ongoing communication between Byers Eye Institute and UCSF.

Charles C. Lin, MD is a board-certified ophthalmologist and cornea specialist. He is the co-PI at the Byers Eye Institute at Stanford University School of Medicine. Dr. Lin received his AB in Environmental Science and Public Policy from Harvard University, graduating summa cum laude. He attended medical school at the University of California, San Francisco, where he received his M.D. with honors. Following an internship in Internal Medicine at Cedars-Sinai Hospital, he completed his ophthalmology residency at the University of California, San Francisco. He received subspecialty Cornea, External Disease, and Refractive Surgery training at the F.I. Proctor Foundation and University of California, San Francisco, one of the premier fellowships in the country. He spearheads the cornea transplant program at Stanford University and has launched cutting edge surgical procedures including ultra-thin DSAEK, DMEK and DALK at Stanford.

Pauline Lacoste has strong expertise working on ophthalmology studies and is successfully trained to CITI, HIPAA and GCP.

Francis I. Proctor Foundation
The Proctor Foundation is an organized research unit at the University of California, San Francisco. The Foundation has a 56-year history of research in ocular infectious and inflammatory disease and runs one of the leading corneal fellowship training programs in the United States. Proctor Foundation faculty have been involved in prevention of blindness research in developing countries since the Foundation's inception. The impetus for establishing the Foundation in 1947 was to eradicate trachoma in the American Southwest and other parts of the world.

UCSF will perform the data analysis. UCSF will not consent any participants, perform surgeries, or collect study data. UCSF will have the most current protocol, consent documents and HIPAA authorization for reference. UCSF has received IRB approval for this study (IRB number: 14-13728). All modifications to either IRB of record will be communicated between sites. UCSF will ensure protection of all study-related data by using de-identified information over a secure server. All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy. There will be ongoing communication of problems, interim results, and study closure between both sites.

Jennifer Rose-Nussbaumer, MD is the co-PI at UCSF for this study. Dr. Rose-Nussbaumer is a Cornea fellowship trained Ophthalmologist at F. I. Proctor Foundation. In addition to her clinical work in cataract and corneal transplant surgery, she is an NIH funded clinical researcher. She is studying corneal ulcer treatment in India and Nepal and corneal transplant outcomes in Ethiopia. She is the principle investigator on the Corneal Preservation Time study at UCSF. Her previous vision research in Ophthalmology includes work with the World Health Organization on Trachoma, as well as investigating the ocular manifestations of HIV disease. Dr. Rose-Nussbaumer's role in this study will be to perform data analysis, to collaborate with surgery site and eye bank, and to collaborate with OHSU and Stanford PIs regarding study design and protocols.

Ariana Austin, MS is the UCSF study coordinator for this study. She has experience working on international and ophthalmology studies and currently serves as a study coordinator for several surgical studies at F. I. Proctor Foundation.

3. PATIENT FLOW

3.1 Study Timeline

The enrollment period will be 24 months. Study participants will be required to have follow-up visits at months 3 (visit window: 2-4 months), 6 (visit window: 5-7 months), 12 (visit window: 10-14 months), and 24 (visit window: 20-28) from the time of surgery. Additional visits may be needed and will be determined by the surgeon/investigator.

3.2 Eligibility Requirements

3.2.1 Study Area

Recruitment of eligible participants will be done at the Casey Eye Institute and Byers Eye Institute. Eligible participants will be screened by the primary surgeon and research staff at OHSU and Stanford. Potential participants will be approached during a standard of care clinical visit in the outpatient practice of the primary investigator at Casey Eye Institute, OHSU. These are patients that need to have corneal surgery whether or not they participate in this study.

3.2.2 Eligibility criteria for study participants

Only those who meet all of the inclusion criteria and none of the exclusion criteria will be enrolled in this study.

Inclusion Criteria:

- Damaged or diseased endothelium from Fuchs or Pseudophakic Bullous Keratopathy
- Good candidates for corneal transplantation for either DMEK or DSAEK
- Willingness and ability to undergo a cornea transplantation
- Willingness to participate in follow-up visits

Exclusion Criteria:

- Participants who are decisionally and/or cognitively impaired
- Participants who are not suitable for the DMEK or DSAEK surgeries
- Prior Endothelial Keratoplasty (EK) or any other ophthalmic surgery except uncomplicated cataract surgery

- Indication for surgery that is not suitable for EK (e.g. keratoconus, stromal dystrophies and scars)
- Presence of a condition that increases the probability for failure (e.g., heavily vascularized cornea, uncontrolled uveitis)
- Other primary endothelial dysfunction conditions including posterior polymorphous corneal dystrophy and congenital hereditary corneal dystrophy
- Aphakia, or anterior chamber IOL in study eye prior to or anticipated during EK
- Planned intraocular lens exchange of an anterior chamber IOL with a posterior chamber IOL in study at time of study EK
- Pre-operative central sub-epithelial or stromal scarring that the investigator believes is visually significant and could impact post-operative stromal clarity assessment
- Peripheral anterior synechiae (iris to angle) in the angle greater than a total of three clock hours
- Hypotony (Intraocular pressure <10mmHg)
- Uncontrolled (defined as intraocular pressure >25mmHg) glaucoma
- Visually significant optic nerve or macular pathology

3.3 Randomization

Each study eye will be randomly assigned to the 1) DSAEK or 2) DMEK treatment group. Block randomization will be performed using a computer program (Statistical package R; Version 2.12; R Foundation for Statistical Computing, Vienna, Austria) by the coordinating site.

Once an eye is enrolled in the study, the study coordinator will assign the study participant's eye an ID (alpha-numeric code) and inform the eye bank (Note: The eye bank will assign tissue to the study participant prior to knowing which arm the study participant is assigned to). The eye bank will then sign into the Dropbox account associated with this study, open the "New Patient" folder, and then open the file named with the particular study participant ID.

Once the eye bank has opened the file, the study eye has been assigned a study participant ID and randomized to treatment group; therefore, they will be included in the intention to treat analysis. (Note: See eye bank protocol for full donor tissue procurement and assignment information).

The treatment assignment will not contain identifiable patient information and will be shared using a password that is only known by the eye bank. The eye bank may only open the document for a given study participant and not for past or future study participants. The treatment assignment document should be moved from the "New Patients" folder to the "Old Patients" folder once opened.

3.4 Study Visits

3.4.1 Baseline Visit

During this visit, eligible patients who are enrolling for the first time will be enrolled in the study and will give consent. The baseline patient form will be completed and the NEI-VFQ will also be administered. If a patient includes a second eye in the study, they will complete an abbreviated baseline patient form for that study eye prior to surgery. They will not complete a second NEI-VFQ at the baseline visit for their second eye. Patients will also complete BSCVA, IOP, Pachymetry, and Pentacam tests at baseline.

3.4.2 Surgery Visit

The enrolled study participant's eye(s) will undergo either DSAEK or DMEK surgery. If both of a participant's eyes are included in the study, randomization to DSAEK or DMEK will be performed independently for each eye.

3.4.3 Follow-Up Visits

The follow-up patient form will be completed at each visit, for each enrolled eye. Data collected for each follow-up visit will include:

3 month follow-up: BSCVA, IOP, pentacam topography and densitometry pachymetry, optical coherence tomography, and endothelial imaging will be performed. The NEI-VFQ form will also be completed

6 month follow-up data: BSCVA, IOP, pentacam topography and densitometry pachymetry, optical coherence tomography, endothelial imaging, and slit-lamp photography will be performed.

12 month follow-up: BSCVA, IOP, pentacam topography and densitometry pachymetry, optical coherence tomography, and endothelial imaging will be performed. The NEI-VFQ form will also be completed

3.4.4 Final Visit

During the Month 24 final visit, the final status and follow-up patient forms will be completed. BSCVA, IOP, pentacam topography and densitometry pachymetry, optical coherence tomography, and endothelial imaging will also be performed.

3.5 Adverse Events (AEs)

During each study visit, the subject will be questioned about AEs in a non-leading manner. All AEs, whether observed by the Investigator, elicited by the Investigator, or spontaneously reported by the subject, will be documented in the subject's chart and the adverse event form. Slit lamp photography will also be completed after any adverse event takes place.

All AEs should be followed until they are resolved or until a stable clinical endpoint is reached. Each AE is to be classified by the Investigator as SERIOUS (SAE) or NONSERIOUS (NSAE).

If a SAE occurs, the investigator at OHSU or Stanford must verbally and/or in writing notify OHSU/Stanford or its designee within 24 hours of the occurrence of the SAE.

The initial SAE report must be followed by a written report, signed by the investigator, and received by OHSU/Stanford or its designee via fax within two working days. The investigator must provide written follow-up reports until the SAE or clinically significant AE has resolved or until a stable clinical endpoint is reached. Notification of an SAE or clinically significant AE must also be submitted to the Institutional Review Board (IRB)/Ethics Committee (EC) in accordance with its requirements. All AEs must be reported from the time that the subject provides informed consent through the last study visit.

4. PROCEDURES

4.1 Masking

All study participants will be masked to their intervention. The refractionist performing the BSCVA will also be masked. Due to the nature of the intervention, the surgeon and technician performing study visit endothelial cell counts and other imaging will not be masked; however, graders will be masked when possible. Eye bank and UCSF study personnel will not be given any identifying information.

4.2 Treatment

For each procedure, the tissue will be prepared by either Lions VisionGift or Sightlife. Each participant will undergo surgery only once and will take approximately 1-2 hours. This study requires 6 visits to the clinic over a period of 2 years, there may be additional post-operative visits (above what the study requires) following this surgical procedure.

4.2.1 DSAEK

For DSAEK, tissue grafts will be cut to the right thickness using a microkeratome prepared at the eye bank per standard eye bank protocol (about 60-90 microns thick). A 4 mm corneal incision will be used, with Endoserter as the means of inserting the graft, an FDA approved device for this purpose.

4.2.2 DMEK

For DMEK, endothelial grafts will be pre-peeled at the eyebank (70%). In the operating room the remaining 30% will be peeled, and the endothelium will be stained with trypan blue. A 3.5 mm corneal incision will be used and the graft will be inserted with a modified jones tube injector. The tap technique will be used to position the graft.

4.3 Examinations During Follow-up Visits

There will be 4 follow-up visits for this study – Month 3, 6, 12, and 24; all of these visits would be expected in normal post-operative care. During each follow-up appointment, tests will be done on the participant's study eye; these include: BSCVA, intraocular pressure (IOP), corneal thickness using a Pachymeter, manifest refraction, slit lamp and slit lamp photography, endothelial imaging, Pentacam topography and densitometry, and optical coherence tomography (OCT) testing. Dilated retinal exam will be performed at the discretion of the surgeon.

4.4 Study Schedule

Table 1: Study Schedule

	Visit 1 Pre-op	Visit 2 Surgery	Visit 3 Month 3	Visit 4 Month 6	Visit 5 Month 12	Visit 6 Month 24
Forms						
Consent and Authorization form	X					
Baseline form	X					
NEI-VFQ	X (for 1st eye)				X	
Follow-up form			X	X	X	X
Final form						X
Procedures						
DMEK or DSAEK surgery		X				
Tests						
IOP	X		X	X	X	X
Pachymetry U/S	X		X	X	X	X
Pentacam (densiometry & topography)	X		X	X	X	X
OCT			X	X	X	X
Endothelial imaging			X	X	X	X
Slit Lamp Photography*	A few patients			X		
BSCVA/ETDRS/MRx	X		X	X	X	X
Total visit time	2 hours	2 hours	1 hour	1 hour	1 hour	1 hour

* Slit lamp photography also taken upon an adverse event

5. STUDY MEDICATIONS

5.1 Prednisolone, Ofloxacin, and Tropicamide/Phenylephrine

The following medications will be administered for treatment purposes: Prednisolone, Ofloxacin, and Tropicamide/Phenylephrine.

5.1.1 Treatment schedule for study medications

The following drug schedule will be followed by all participants: Prednisolone and Ofloxacin four times a day post-operation. Standardized protocol will be to continue Ofloxacin for 1 week, then stop. Prednisolone will be taken four times a day for 4 months, then decreased by 1 drop per month until at 1 drop per day. Participants will stay on 1 drop for at least one year. Steroid treatment can be altered at the discretion of the clinician. The aforementioned drugs will be used for FDA approved indications and will not require an IND. All medications will be protected and only appropriate personnel will administer the drugs. Tropicamide/Phenylephrine drops will be used at the screening exam and at postoperative visits when required. They would be used for pre- and postoperative eye monitoring whether participants are involved in the study or not. These drops are not included in the below dosing schedule since they will be utilized on an as needed bases.

Table 2: Dosing schedule for Prednisolone and Ofloxacin

Medication	Day 1-Day 8	Day 9-Month 3	Month 4	Month 5	Month 6- 12
Prednisolone	4 times/day	4 times/day	3 times/day	2 times/day	1 time/day
Ofloxacin	4 times/day				

5.2 Possible Side Effects of Study Medications

Prednisolone: eye irritation, swelling, pain, or redness; pressure within the eye; cataract growth; eye infection

Ofloxacin: eye irritation, swelling, pain, or redness

Tropicamide/Phenylephrine: eye irritation, swelling, pain, or redness; Eye dilation may result in temporary blurred vision, light sensitivity, and increased heart rate.

6. PROTECTION OF HUMAN SUBJECTS

6.1 Institutional Review Board Approval

6.1.1 Oregon Health & Science University Institutional Review Board (OHSU IRB)

The OHSU IRB will annually review study protocol for ethical approval.

6.1.2 University of California, San Francisco Committee on Human Research (UCSF CHR)

The UCSF CHR will annually review study protocol for ethical approval.

6.1.3 Stanford University Institutional Review Board (Stanford IRB)

The Stanford IRB will annually review study protocol for ethical approval.

6.2 Informed Consent

OHSU and Stanford personnel will obtain full written consent from each patient enrolled. The primary surgeon will screen participants and determine their eligibility. He/she will clearly explain the process and risks involved and will also ask the patient to sign any necessary consent documents. The study participant will have 6 visits total per eye included in the study; visits include surgery and will take place over a period of 2 years. The patient has the ability to withdraw at any time and will not be forced into anything with which he/she is not comfortable. Consent documents have been uploaded to the IRB application.

6.3 Risks to Study Participants

Study participants will not have any increased risk or cost for participating in this study. Participants in the study have the same risks as those undergoing corneal transplantation in other settings. Many of the risks in this study are inherent risks of corneal transplantation; thus, there is no known increased risk associated with participation in this study.

As with any surgery, there are risks associated with these surgeries, and both surgeries have similar risks. There is a risk of infection or bleeding which could result in vision loss. There may be damage to the tissue graft during tissue preparation, and the tissue graft can fail to attach to the cornea; thus, there may be a need for repeat air injection. Below, the other risks associated with each type of surgery are listed:

- DSAEK: There may be slightly decreased vision after surgery compared to DMEK, although this is unknown. The healing process may also be slower. Some think there is an increased risk of rejection compared to DMEK, although this is also unknown.

- DMEK: There may be increased risk of tissue loss, repeat air injection, detachment of the tissue graft to the cornea compared with DSAEK. There may be higher costs associated with this surgery, although these additional costs will be covered by insurance.

Blindness due to infection may occur in extremely rare cases. There may also be differences in rates of difficulty with donor preparation, increased intra-operative times, graft rejection and graft survival, and donor attachment in DMEK versus DSAEK. Even if there is a total detachment during DMEK, we will continue to move forward with secondary treatment. These risks will be addressed by OHSU by making sure all protocols are being followed thoroughly and by following up with participants after surgery.

There are no known risks directly related to the Endoserter and jones tube. There may be some discomfort during follow-up testing (BSCVA, IOP, slit lamp, Pachymeter, Pentacam, endothelial imaging and OCT testing and photo imaging inside the eye), but this will be kept to a minimum. The participant will be asked to tell the doctor if any of this testing feels painful.

Anesthesiology will be determined as per the participants needs. They will generally be awake with medications given to help them relax and feel comfortable. This is called monitored anesthesia care. Other participants may require general anesthesia care. While this is generally safe, there are small increased risks to the heart and lungs which will be discussed with the anesthesiologist. Both types of anesthesia are routinely used for DMEK and DSAEK surgeries, although generally monitored anesthesia care is the typical route.

6.4 Privacy, Confidentiality, and Data Security

All data will be stored and transferred using a secure server with de-identified information.

We will take steps to keep the participant's personal information confidential. Health information will be kept secure and separate from information which identifies participants. Upon enrollment, participants will be assigned a code that will be used instead of their name, medical record number or other personally identifying information. Electronic files for data analysis will contain only the participant code. The code will be stored at OHSU/Stanford on a secure server and will only be accessed by study personnel – the PI, study coordinator, or other member of the study team). Access to study-related patient information will be limited only to members of the study team.

Only a small number of researchers related to this study will have direct access to the participant's medical information. Paper files will be stored in locked filing cabinets in restricted access offices at OHSU. Access to data/specimens is restricted to study personnel.

Information may be released to others outside of OHSU/Stanford who are involved in coordinating or overseeing research, but information which identifies the participant will be kept secure. To ensure the success of this study, OHSU and Stanford have partnered with University of California, San Francisco (UCSF)'s F.I. Proctor Foundation, which is a center that specializes in ophthalmology research. The coordinating center at UCSF will have access to de-identified information using a code number. UCSF's role is to support OHSU and Stanford on the data analysis portion of this study and assisting with the development of consent and study-related materials. UCSF has received IRB approval to take part in this study (IRB number: 14-13728).

6.5 Exclusion of Vulnerable Populations

The following populations will not be enrolled in this study: children (18 years and under), pregnant women, decisionally impaired adults, and prisoners.

6.6 Compensation to Participants

There is no additional cost or compensation for the study participant. There will be no compensation for research-related injury.

7. DATA COLLECTION AND MANAGEMENT

7.1 Data Collection and Entry

All data will be collected using hardcopy patient forms at OHSU and Stanford during baseline and follow-up visits. De-identified data will be uploaded to a Dropbox account in order to share the data with the UCSF study coordinator. De-identified data will be input into a database using double data entry at UCSF.

7.2 Data Consistency, Validity, and Monitoring

Data monitoring reports will be prepared using STATA and Excel. If the forms are not filled out completely, the UCSF study coordinator will contact the person responsible for completing the form to provide the missing data, or clarify any inconsistent data. The OHSU and Stanford study coordinators are the only people who are authorized to add missing data or make any changes to the study forms. All changes should be made with a red ink pen, and then signed and dated.

7.3 Data Storage and Security

De-identified data will then be input into a database using double data entry at UCSF. Data will be stored at UCSF for about 10 years.

8. STATISTICAL ANALYSIS

Please see the **Statistical Analysis Plan (SAP)** for details on the statistical analysis.

9. REFERENCES

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10.APPENDICES

10.1 Study Forms

Please see appropriate separate documents for the study forms.

Study forms include:

- Study visit checklist
- Baseline edibility and patient form
- NEI-VFQ
- Follow-up patient form
- Final patient forms

10.2 Protocols

Please see appropriate separate documents for the study protocols.

Protocols include:

- Best Spectacle-Corrected Visual Acuity Protocol
- Eye Bank Protocol; Donor Eligibility and Assignment
- Pentacam Protocol
- Pachymetry Protocol
- Endothelial Cell Count Protocol
- Slit Lamp Photography Protocol
- Optic Coherence Tomography Protocol