Post Photorefractive Keratectomy (PRK) Use of an Eye Shield for Maintaining Vision and Mitigating Pain

Study Protocol and Statistical Analysis Plan

NCT01592643

August 19, 2011

Post Photorefractive Keratectomy (PRK) Use of an Eye Shield for Maintaining Vision and Mitigating Pain

Protocol Number: CS 003.2

August 19, 2011

SUBMITTED BY:

NEXIS VISION, INC
191 JEFFERSON DRIVE
MENLO PARK, 94025

Protocol Reviewed and Approved by:
XXXXXX

_____ _____
Principal Investigator **Date**

Table of Contents

Introduction

Laser in situ keratomileusis (LASIK) is the most popular form of refractive surgery worldwide. However, the LASIK procedure includes the creation of a corneal flap and involves a risk of both flap-related complications[1] and corneal ectasia[2]. Photorefractive keratectomy (PRK) is an older, well established, flapless refractive procedure that has been performed for over 20 years[3]. Unlike LASIK, eyes undergoing PRK incur no risk of flap-related complications and likely have a reduced risk of corneal ectasia compared to LASIK[4-6]. Unfortunately, post-operative pain and delayed visual recovery remain substantial drawbacks for PRK compared to LASIK[7]. Standard means for mitigating pain include the use of topical non-steroidal anti-inflammatory agents[8], systemic pain-relief agents[9] and the placement of a bandage contact lens[10-11]. Furthermore, this regimen does not address the visual deficit associated with the removal and subsequent re-epithelialization of the cornea. While these measures are somewhat helpful, post-operative pain remains greater than that experienced with LASIK[12] and visual recovery is significantly slower than LASIK.

Although the primary reasons for post-PRK pain are not fully understood, one hypothesis is that corneal nerve fibers are exposed following epithelial debridement and stromal ablation during the first few post operative days until the epithelium heals[13], and that even slight trauma to this area (i.e.- rubbing of eye lids against the wound) may cause severe pain. This would explain why standard bandage contact lenses reduce pain somewhat but not completely, as they still freely move over the surface of the eye and may abrade the exposed nerve fibers. Another observation is corneal swelling immediately after both PRK and LASIK. However, swelling is significantly reduced the day after surgery in LASIK whereas it increases in patients undergoing PRK. One reason for this may be the fact that the replaced LASIK flap following ablation limits hydration of the underlying tissue by preventing direct exposure of the ablated stromal tissue to the tear film. The current study is to evaluate an eye shield made of silicone with extremely high oxygen permeability and zero water content. The objective is to place the shield directly over the ablated stromal tissue in order to protect the cornea, maintain normal corneal hydration avoiding edema, and promote wound healing. Furthermore, the silicone shield is designed not to move during blinking and eye movement providing for the potential to significantly reduce pain and maintain vision following PRK.

Study Rationale

Although PRK is considered by many to be a safer refractive procedure than LASIK, the primary reason patients and doctors may be reluctant to choose PRK is the associated post operative pain and reduction in visual acuity. PRK is a very safe and well established refractive procedure, and an effective means of reducing pain and maintaining vision may allow it to be more widely adopted. Covering the exposed PRK wound with a thin silicone shield has the potential to significantly reduce pain and maintain vision following PRK.

Materials

The materials used to make the corneal eye shield all have a history of use in medical devices such as IOL's, contact lenses, and/or corneal shields. The shield materials used will include silicone and surface treatments designed to increase the wettability of the silicone. The surface treatments will include well known plasma-deposited hydrocarbon coatings in sub-micron to micron thicknesses used in standard contact lens coating.

All shields will be 300μm or less in center thickness tapering to the outer edge with an outer diameter ≤ 16mm. The shield will cover the cornea and part of the conjunctiva.

Risk Analysis

Silicone elastomer contact lenses are used to treat pediatric aphakia and also treat high myopia and keratoconus in children.

Study Objectives

Determine if silicone elastomer shields on the cornea following PRK can reduce pain and maintain vision associated with the epithelial defect during the initial post operative period following PRK.

Study Design

This will be a prospective clinical trial in which shields will be placed unilaterally or bilaterally in up to 100 healthy participants who have elected to undergo PRK to correct their refractive error. These patients will be evaluated over the course of 30 days following PRK while using the silicone shield. The shield may be enhanced and its design altered as data is gathered through the study period.

Principal Investigator

XXXXXX

Selection of Study Population

Up to 100 patients who are candidates for PRK.

Subject Inclusion Criteria

Patients who meet the following entry criteria will be eligible for enrollment in this study:

1. Patients scheduled to undergo bilateral PRK for correction of refractive error
2. FDA approved treatment guidelines for PRK
3. Age 18-60
4. Epithelial defect created with a trephine ≤ 8.0 mm
5. Patients able to understand the requirements of the study, willing to follow study instructions, provide written informed consent to participate, and comply with all study requirements, including the required study follow-up visits

Subject Exclusion Criteria

Excluded from the study will be individuals with the following characteristics:

1. Any other anterior segment abnormality other than that associated with PRK
2. Any abnormalities associated with the eye lids
3. Uncontrolled blepharitis or dry eye
4. Prior laser treatment of the retina
5. Any ophthalmic surgery performed within three (3) months prior to study excluding PRK or LASIK
6. Diagnosis of glaucoma
7. Active diabetic retinopathy
8. Clinically significant inflammation or infection within six (6) months prior to study
9. Uncontrolled systemic disease (e.g., diabetes, hypertension, etc.) in the opinion of the Investigator
10. Participation in any study involving an investigational drug within the past 30 calendar days, or ongoing participation in a study with an investigational material
11. Intolerance or hypersensitivity to topical anesthetics, antibiotics, steroids or any other pharmaceuticals that may be used pre and post surgically
12. Specifically known intolerance or hypersensitivity to contact lenses or any component of the investigative material
13. A medical condition, serious concurrent illness, or extenuating circumstance that would significantly decrease study compliance, including all prescribed follow-up

14. Any condition that, in the opinion of the investigator, would jeopardize the safety of the patient
15. Pregnancy

Completion and Termination Criteria

Patient Withdrawal

Patients are free to withdraw consent and withdraw participation in the study at any time for any reason, specified or unspecified, and without penalty or loss of benefits to which the subject is otherwise entitled and without prejudice to further treatment. Subject withdrawal from the study must be recorded on the case report form (CRF). A patient may be withdrawn at any time at the discretion of the investigator.
The following may be justifiable reasons for the investigator to withdraw a patient from the study:

- A patient who is uncooperative or misses two or more consecutive follow-up visits
- A patient noncompliant with the medical study requirements, including the prescribed use of medication
- A patient erroneously included in the study
- A patient who develops an exclusion criterion or concurrent disease (Please note that if subject reports pregnancy, that will be considered as developing exclusion criteria at any time point as per study protocol and will be withdrawn from the study.)

Moreover, a patient may be withdrawn from the study for the following medical or administrative reasons:

- Adverse Event (AE): If a patient suffers an AE that, in the judgment of the Investigator, presents an unacceptable consequence or risk to the patient, the patient will be withdrawn from further participation in the study.

If a patient decides to withdraw from participation in the study, every effort should be made to contact him or her to obtain information about the reason(s) for withdrawal and about any adverse events. Whenever possible, the patient should return to the study site for final clinical assessments. It is important for the Investigator to provide a written report on the Patient Disposition page of the CRF describing the reason for withdrawal.

Study Procedures

Study Outcomes:

- Degree of pain during the post operative period
- Degree of discomfort during the post operative period

- Ability to function during the post operative period
- Visual acuity recovery during the post operative period

Safety will be evaluated by ocular signs and symptoms, (best corrected) visual acuity and occurrence of adverse events.

Study Treatment

The study method is comprised of the placement of an eye shield to the eye after PRK similar to standard bandage lens. A standard bandage contact lens may be placed on the eye(s) after PRK at the investigator's discretion.

Methods

1. Patients planning to undergo PRK will be recruited for the study.
2. Aside from the procedure described below no alteration in patient management in the post PRK period will be made.
3. Both eyes will be treated in the same manner.
4. Following detailed explanation and signing an informed consent form each patient will receive the following:
    a. Bilateral standard PRK procedure. A trephine up to 8mm will be used to mark the debridement zone. If the surgeon decides to apply alcohol for debridement, a 20% alcohol solution placed in the trephine will be used to prepare the cornea for debridement.
    b. Standardized mitomycin use to ablation depth > 70 microns
    (For LASIK re-treatments mitomycin used in all cases)
    c. At the end of the procedure while still on the surgery table1 gtt of Ophthalmic Steroid may be administered to both eyes, then the eye shield will be placed on the study eye. A bandage contact lens may be placed at the investigator's discretion.

At 1hr, 1, 2, 3, 4, 7 days and 1 month following the procedure the patients will undergo the following evaluations. Patients may also be evaluated at days 5 and 6 - at investigator's discretion.

i. Anterior segment examination-all visits
ii. Pain Assessment-all visits, Day 5 and 6 will be optional
iii. Discomfort assessment-all visits, Day 5 and 6 will be optional

iv. Functional assessment-all visits, Day 5 and 6 will be optional
v. Uncorrected visual acuity (UCVA)-all visits
vi. Best corrected visual acuity (BCVA)-all visits, Day 5 and 6 and 1hr will be optional
vii. Contrast Sensitivity Test-(optional)
viii. Anterior segment OCT-(optional)
ix. Corneal Topography- required at baseline, post shield removal, follow up visit after post shield removal visit, 1 week and 1 month
x. Intraocular Pressure measurement: baseline, 1 week. Measurement at 1 month is optional and will be required if IOP at 1 week is increased by 3mmHg or higher from the baseline value .

Medications

Fluorescein will be used for corneal assessments. Topical anesthetics will be used as necessary during the procedure. The following medication regimen will be followed but may be adjusted at the investigator's discretion:

Preop (1 day before surgery):

- Ophthalmic Steroid 1 gtt OU q 2 hrs
- Ophthalmic Antibiotic 1 gtt OU q 2 hrs
- Ophthalmic NSAID 1 gtt OU q 2 hrs

Surgery Day

- Valium 30 minutes before surgery

Intraop

- Ophthalmic Steroid
- Ophthalmic Antibiotic
- Ophthalmic NSAID

Post Operative Day 0 (Begin after surgery until bedtime)

- Ophthalmic Steroid 1gtt OU q 1 hour
- Ophthalmic NSAID 1gtt OU q 1 hour
- Ophthalmic Antibiotic 1gtt OU q 1 hour
- Ibuprofen 600mg q 4 hour PO
- Ophthalmic Steroid/Lubricant at night

Day 1 & Day 2 (while awake)

- Ophthalmic Steroid 1 gtt OU q 4 hrs
- Ophthalmic Antibiotic 1 gtt OU 4 hrs
- Ophthalmic NSAID 1 gtt OU q 4 hrs
- Ibuprofen 600 mg q 4 hrs
- Ophthalmic Steroid/Lubricant at night

Post Operative Day 3

- Ophthalmic Steroid 1 gtt OU q 4 hrs
- Ophthalmic Antibiotic 1 gtt OU 4 hrs
- Ibuprofen 400 mg q 4 hrs

Post Operative Day4-7

- Ophthalmic Steroid 1 gtt OU q 4 hrs
- Ophthalmic Antibiotic 1 gtt OU 4 hrs
- Ibuprofen PRN

Post Operative Day 8

- Ophthalmic Steroid 1 gtt OU BID x 1 week, QD x 1 week, then stop

Time and Events Schedule: The procedures associated with each study visit are outlined and summarized in Table 1.

Table 1: Schedule of Visits and Procedures

Procedure	Baseline	Placement (0 hr)	1 hour	1 day	2 days	3 days	4 days	5 days	6 days	1 week	1 Month +/- 3 day
Visit Number	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8***	**9***	**10**	**11**
Informed Consent	X										
Demographics	X										
Ocular History	X										
Adverse Events		X	X	X	X	X	X	X	X	X	X
Systemic and topical medication profile	X									X	
Anterior Segment Examination including the Slit Lamp Exam	X		X	X	X	X	X	X	X	X	X
Visual Acuity (Uncorrected) (UCVA)	X		X	X	X	X	X	X	X	X	X
Visual Acuity (Best corrected) (BCVA)	X			X	X	X	X	X	X	X	X
Contrast Sensitivity (optional)	X			X	X	X	X	X	X	X	X
Subjective pain, discomfort and function assessment	X		X	X	X	X	X	X	X	X	X
Corneal Photography	X (optional)		X (optional)	X	X	X	X	X	X	X	X (optional)
Corneal Topography	X			X (optional)	X (optional)	X (optional)	X (optional)	X (optional)	X (optional)	X	X
OCT (optional)	X			X	X	X	X	X	X	X	X
IOP Measurement	X									X	X ***optional unless 1 week IOP value changed from B/L
Placement of eye shield (and/or bandage contact lens)		X									
Removal of shield						X**					

***If the shield is no longer on the eye, visit 8 and 9 are not required. These visits will be conducted at investigator's discretion.**
****Removal of shield (and/or bandage contact lens) will be performed at investigator's discretion.**

Study Visits and Procedures

When possible, all examinations will be scheduled for the same time of day and will be performed by the same personnel. Please refer to Appendix 1 for details of examination methods.

Screening

- Participants will be recruited from the Investigators' patient population and through referrals.
- Once patients are deemed eligible for study participation, patients will be approached for potential study participation and signing of the Informed Consent Form (ICF).
- All patients consented for study participation will be entered on a screening/enrollment log.

Visit 1 - Baseline

- The investigator or authorized study staff member will obtain signed informed consent prior to enrolling the patient into the study.
- An enrollment log will be maintained to assure that enrollment is conducted in an unbiased consecutive manner.
- Demographics, medical and ocular history, as well as concomitant systemic medications will be recorded in the case report form (CRF).
- Biomicroscopy (slit lamp exam) with corneal photography (as needed) will be performed.
- Tear film stability will be evaluated using tear breakup time (TBUT).
- Determine subjective pain, comfort and functional assessment
- Uncorrected and best corrected visual acuity will be measured using ETDRS acuity chart.
- Corneal topography
- Intraocular pressure measurement
- Contrast Sensitivity Test (optional)
- Anterior segment optical coherence tomography (OCT)- (optional)

Visit 2 - Placement (0 hour)

The placement of the corneal shield (and/or bandage contact lens) will be performed immediately following the PRK procedure (while the patients are still under the laser's microscope).

- Standard intra-operative PRK medication will be placed on the eye.
- Shield (and/or bandage contact lens) will be placed bilaterally.
- Standard post PRK medical treatment will be initiated
- Any adverse events will be recorded.

Visit 3 - 1 hour Post-PRK

This examination must occur one hour after placement of the shield (and/or bandage contact lens). The following will occur at this examination:

- Record any adverse events.
- Subjective pain and comfort questionnaire
- Perform slit lamp exam, corneal photography (optional)
- UCVA

Visit 4 – 1 day Post-PRK

This examination must occur the day after placement of the shield (and/or bandage contact lens). See patient in the morning.

The following will occur at this visit:

- Record any adverse events.
- Perform slit lamp exam with corneal photography
- Assessment of tear break up time (TBUT) over the shield
- Transparency assessment of the shield
- BCVA and UCVA
- Determine subjective pain, comfort and functional assessment
- Corneal topography (optional)
- Contrast Sensitivity Test (optional)
- Anterior segment optical coherence tomography (OCT) (optional)

Visit 5 – 2 day Post-PRK

This examination must occur two days after placement of the shield (and/or bandage contact lens). See patient in the morning.

The following will occur at this visit:

- Record any adverse events.
- Perform slit lamp exam with corneal photography.
- Assessment of tear break up time (TBUT) over shield
- Transparency assessment of the shield
- BCVA and UCVA
- Contrast Sensitivity Test (optional)
- Determine subjective pain, comfort and functional assessment
- Corneal topography (optional)
- Contrast Sensitivity Test (optional)
- Anterior segment optical coherence tomography (OCT) (optional)

Visit 6 – 3 days Post-PRK

This visit must occur three days after placement of the shield (and/or bandage contact lens).

The following will occur at this visit:

- Record any adverse events.
- Perform slit lamp exam with corneal photography
- Assessment of tear break up time (TBUT) over the shield
- Transparency assessment of the shield
- BCVA and UCVA
- Determine subjective pain, comfort and functional assessment
- Contrast Sensitivity Test (optional)
- Anterior segment optical coherence tomography (OCT) (optional)
- Removal of the shield and or bandage lens if epithelial defect has close
- Corneal topography (optional)

Visit 7 – 4 days Post-PRK

This visit must occur four days after placement of the shield (and/or bandage contact lens).
The following will occur at this visit:

- Record any adverse events.
- Perform slit lamp exam with corneal photography
- Assessment of tear break up time (TBUT) over the shield or without the shield if shield was removed
- Transparency assessment of the shield (Required only if shield is present)
- BCVA and UCVA
- Determine subjective pain, comfort and functional assessment
- Contrast Sensitivity Test (optional)
- Anterior segment optical coherence tomography (OCT) (optional)
- Removal of the shield and /or bandage lens if not removed at day 3 and epithelium is closed
- Corneal topography: Required for both cases: if shield is not present or if shield is removed at day 4 (post shield removal).

Visit 8 & 9-5 & 6 days Post-PRK-If shield is removed, this visit will be at the Investigator's discretion

The following will occur at this visit:

- Record any adverse events.
- Perform slit lamp exam with corneal photography
- Assessment of tear break up time (TBUT) over the shield or without the shield if shield was removed
- Transparency assessment of the shield (Required only if shield is present)
- BCVA and UCVA

- Determine subjective pain, comfort and functional assessment
- Contrast Sensitivity Test (optional)
- Anterior segment optical coherence tomography (OCT) (optional)
- Removal of the shield and /or bandage lens if not removed at day 3 and epithelium is closed
- Corneal topography: Required for both cases: if shield is not present or if shield is removed at day 4 (post shield removal).

Visit 10 – 1 week Post-PRK

This visit must occur seven days after placement of the shield (and/or bandage contact lens).
The following will occur at this visit:

- Record any adverse events
- Perform slit lamp exam with corneal photography
- Assessment of tear break up time (TBUT)
- BCVA and UCVA.
- Determine subjective pain, comfort and functional assessment
- Corneal topography
- Intraocular pressure measurement : Required;
- Contrast Sensitivity Test (optional)
- Anterior segment optical coherence tomography (OCT) (optional)

Visit 11 1 month Post-PRK

This visit must occur thirty days (+/- 3 day) after placement of the shield (and/or bandage contact lens).
The following will occur at this visit:

- Record any adverse events
- Perform slit lamp exam, corneal photography (optional)
- Assessment of tear break up time (TBUT)
- BCVA and UCVA
- Determine subjective pain, comfort and functional assessment
- Corneal topography
- Intraocular pressure measurement: Required-If IOP at 1wk increased by 3mmHg or higher from baseline
- Contrast Sensitivity Test (optional)
- Anterior segment optical coherence tomography (OCT) (optional)

Additional testing may be performed during the course of the study as determined by the investigator.

Unscheduled Visits

An unscheduled visit will be any visit to the clinical site other than those specified in the protocol. The Investigator or trained and qualified investigational staff will perform all procedures necessary to evaluate the study participant at these visits and will record the visit in the patient's chart and on the unscheduled visit form in the CRF.

- Any adverse event should be recorded on the adverse event (AE) form in the CRF.

Study Completion

The trial is completed when the planned enrollment has been completed and the enrolled patients exit the study.

Adverse Events and Reportable Adverse Events

An adverse event is any undesirable clinical event experienced by a patient during participation in a clinical trial whether or not that event is considered related to the investigational material. This includes a change in the patient's condition or laboratory results which has or could have a deleterious effect on the patient's health or well-being. For example, hospitalization of the patient for any reason is considered an adverse event.

Any adverse event reported by a patient or noted by the Investigator must be reported on the Adverse Event Case Report Form. The Investigator must categorize each adverse event by degree of harm to the patient (serious or not serious), relationship to study material (definite, probable, possible, or no relationship), and whether or not the adverse event was unanticipated (listed below are expected/anticipated events for this material).

A *finding* represents any objective observations made by the Investigator during the examinations. An objective finding by the Investigator will be considered an adverse event if:

- It was not present at the previous visit and not considered part of the surgical procedure (i.e.- epithelial defect)
- It was present at the previous visit(s) but with a lesser severity than the current observation

A *symptom* is a noticeable change that is perceived by the patient. Any ocular or systemic symptom, which is out of the ordinary for the patient, will be reported as an adverse event. The patient will be directly questioned about symptoms that occur between visits.

Adverse events will be carefully monitored during the study period. Minimum requirements of data to be recorded are: type of event, duration of event (start to end), severity, seriousness, action taken, outcome, relationship to material (definitely, probably, possibly, or not related), and, if

possible, the cause of the event. The investigator shall follow the participant until the condition clears, returns to baseline, or no longer warrants further follow-up.

- Intra-Operative Adverse Events:
  - Material malfunction identified prior to placement

- Post-Operative Adverse Events:
  - Visual acuity loss determined to be unacceptable as judged by treating physician
  - Pain determined to be unacceptable as judged by treating physician
  - Shield lens malposition
  - Shield malfunction (and/or bandage contact lens)
  - Persistent inflammation after 1 month postop
  - Infection
  - Corneal complications (corneal edema after 1 month, opacification)
  - Corneal sterile infiltrates

Note: Investigator or responsible staff personnel are required to notify the adverse events to the Sponsor or designee within 24 hours of knowledge of the event. The Serious Adverse Event/Unanticipated Adverse material Effect form should be completed in as much detail as possible and faxed to Sponsor at:
FAX (for reporting): (650) 618-2522
Phone (for queries): (650) 325-2050

Serious Adverse Events

Any of the following will be considered a Serious Adverse Event (SAE):

- Death
- Life-threatening event
- In-patient hospitalization or prolongation of existing hospitalization
- Complete loss of vision
- Sight-threatening complication:
  - Endophthalmitis

Trained and competent personnel in recognizing and treating adverse reactions of all types must be immediately available; personnel must also have current treatment knowledge.

An event does not need to be reported as a serious adverse event (SAE) if it represents only a relapse or an expected change or progression of pain of discomfort typically associated with PRK. This type of event needs only to be reported as an adverse event.

It is the Investigator's responsibility to inform the appropriate Institutional Review Board (IRB) and Sponsor about serious adverse events associated with the Corneal Shield.

Unanticipated Adverse Material Effects

An unanticipated adverse material effect (UADE) or event is any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a material if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigation plan, or any other unanticipated serious problem associated with a material that relates to the rights, safety, or welfare of patients. The following events are expected after the procedure:

Epithelial defect for up to 7 days
Redness
Excessive tearing
Light sensitivity for up to 3 months
Corneal edema for up to 1 month
Pain and discomfort until corneal re-epithelialization
Increased dryness for up to 6 months

The investigator will be responsible for informing the IRB of the adverse events, serious adverse events, or unanticipated adverse material effects that have occurred during the study and that have been determined attributable to the study material.

Statistical Methods

Since this is an exploratory study and no formal hypothesis testing is planned, a sample size estimate has not been calculated. Descriptive statistics will be used to present study outcomes, including demographic information, etc.

Ethical and Regulatory Considerations

This protocol was designed and will be conducted, recorded, and reported in compliance with the principles of Good Clinical Practice (GCP) regulations. These requirements are stated in global regulations as well as "Guidance for Good Clinical Practice", International Conference on Harmonization (ICH), and the most recent guidelines of the Declaration of Helsinki of Technical Requirements for Registration of Pharmaceuticals for Human Use.

Institutional Review

This protocol and patient informed consent form (ICF) must be reviewed and approved by an Institutional Review Board (IRB) before enrollment of patients.

It is the responsibility of the Investigator to obtain approval for the Study Protocol and to keep the Institutional Review Board informed of serious adverse events and any amendments to the protocol. It is also the Investigator's responsibility to maintain a file of all correspondence with the Institutional Review Board

Changes to the Study Protocol or Conduct of the Study

All changes must be documented by signed protocol amendment. If substantial changes to the design of the study are made, the amendment must be submitted to and approved by the IRB and must be agreed to and signed by the Investigator.

Patient Informed Consent

Written informed consent is required prior to enrollment in the study. It is the responsibility of the Investigator to obtain such consent.

Case Report Forms

Case Report Forms (CRFs) are provided separately from this clinical protocol document. CRFs will be filled out legibly and completely (black or blue ball point pen). The original and copy of CRFs will be kept by the investigator.

Each patient enrolled in the study will be assigned a unique patient number. The patient identifier will include the enrollment number. As the person ultimately responsible for the accuracy of all CRF data, the Investigator must sign each patient's CRF.

All study-required data will be completely documented in patient study files.

Study Material Information and Accountability

Coding/Masking: As this is a non-comparative study, no coding or masking will be used.

Dispensing: The Investigator, or designee, will be responsible for keeping current and accurate records of the materials dispensed.

Declaration of Helsinki

The study will be performed in accordance with the recommendations guiding physicians in biomedical research involving human subjects adopted by the 18th World Medical Assembly, Helsinki, Finland, 1964 and later amendments.

The investigator must retain patient identification codes after the completion or discontinuation of the trial. Patient files and other source data must be kept for the maximum period of time permitted by the practice.

Regulatory Requirements

Anonymity

The anonymity of participating patients must be maintained. Patients are identified by their initials and assigned a patient identification number on CRFs and other documents. Documents not submitted that identify the patient (e.g., the signed informed consent document) must be maintained in strict confidence by the investigator.

Monitoring

The Sponsor or Sponsor representative may visit the investigator periodically for the purpose of monitoring the progress of this study in accordance with GCP regulations. It is the responsibility of the investigator to be present or available for consultation during such scheduled monitoring visits. During these routine visits, all data pertaining to a patient's participation in this clinical investigation must be made available to the monitor. Monitoring will include personal visits and other forms of communication to assure that the investigation is conducted according to protocol and in order to comply with guidelines of good clinical practice. On-site review of CRFs will include a review of forms for completeness and clarity, and for consistency with source documents. Note that a variety of original documents, data, and records will be considered as source documents in this trial. A copy of the patient's study laboratory values will be added to the CRF, and the original document will remain in the source document file.

The Sponsor or Sponsor representative may request to witness patient evaluations occurring as part of this protocol. The Investigator and appropriate personnel may be periodically requested to attend meetings/workshops organized by the Sponsor to assure acceptable protocol execution.

APPENDIX 1

Examination Procedures, Tests, Equipment and Techniques

Visual Acuity (uncorrected)

Introduction: Distance uncorrected visual acuity will be measured at baseline and follow-up visits as shown in Table 1. Standard ETDRS acuity chart will be used for measuring VA.

In order to provide standardized and well-controlled assessment of visual acuity during the study, all visual acuity assessments for a subject must be performed consistently (e.g., the same lighting conditions, viewing distance, etc.) during the entire study.

Scoring Best-Corrected Visual Acuity

While looking through the manifest refraction in the phoropter giving the best vision according to the patient and the patient properly aligned with the ETDRS chart, the patient should be asked to read the smallest line that he can distinguish on the chart. If the patient chooses a line and reads it perfectly, he should be encouraged to read the next smallest line and so on until he makes errors in reading a line. The visual acuity is the largest Snellen fraction corresponding to the line of smallest letters that the patient can read with two or less mistakes. If one line is read with two mistakes and the next smallest line is read with three letters misread, the visual acuity should be recorded as the Snellen fraction corresponding to the line that was read with two mistakes, using "-2" to indicate the 2 mistakes. This will indicate the number of correct letters read by the subject.

Biomicroscopy

External examination and biomicroscopy will be performed using a slit lamp. Magnification will be consistent with standard clinical practice.

Observations will be documented on the appropriate Case Report Form:

The clinician will examine the conjunctiva, cornea, anterior chamber of the eye with the aid of a slit lamp, which is a table-mounted binocular microscope. Fluorescein dye will be instilled into the ocular cul-de-sac to facilitate this examination as indicated by the study method section. The patient will be seated during the examination. Grading will be done as follows:

CORNEA
Edema

None (0)=	Transparent and clear or less than mild
Mild (+1) =	Dull glassy appearance
Moderate (+2)=	Dull glassy appearance of epithelium with large number of vacuoles
Severe (+3) =	Epithelial bullae and/or stromal edema, localized or diffuse, with or without stromal striae

Staining/Erosion

None (0)=	No fluorescein staining of epithelium, OR less than mild
Mild (+1) =	Slight fluorescein staining confined to a small focus

Moderate (+2)=	Regionally dense fluorescein staining (1 mm or greater in diameter) with underlying structure moderately visible
Severe (+3) =	Marked fluorescein staining or epithelial loss

ANTERIOR CHAMBER (Anterior Segment)

Cells

None (0)=	No cells seen or less than mild
Mild (+ 1) =	+ cells
Moderate (+2) =	++ cells
Severe (+3) =	+++ cells
Hypopyon (+4)=	++++ cells, Hypopyon Formation (indicate size of hypopyon)

Flare

None (0)=	No Tyndall effect or less than mild
Mild (+1) =	Tyndall beam in the anterior chamber has a mild intensity
Moderate (+2) =	Tyndall beam in the anterior chamber is of strong intensity
Severe (+3) =	Tyndall beam is very intense. The aqueous has a white, milky appearance

Photography

As part of the biomicroscopic examination, photographs may be taken by the investigator or staff to document the status of the shield/bandage contact lens, ocular conditions, or other observations made by the Investigator. These are to be taken consistent with standard clinical practice. The patient's name or identifying features should not be included.

References

1. Schallhorn SC, Farjo AA, Huang D, Boxer Wachler BS, Trattler WB, Tanzer DJ, Majmudar PA, Sugar A; American Academy of Ophthalmology. Wavefront-guided LASIK for the correction of primary myopia and astigmatism a report by the American Academy of Ophthalmology. Ophthalmology. 2008 Jul;115(7):1249-61.
2. Alió JL, Muftuoglu O, Ortiz D, Pérez-Santonja JJ, Artola A, Ayala MJ, Garcia MJ, de Luna GC. Ten-year follow-up of laser in situ keratomileusis for high myopia. Am J Ophthalmol. 2008 Jan;145(1):55-64.
3. Ghadhfan F, Al-Rajhi A, Wagoner MD. Laser in situ keratomileusis versus surface ablation: visual outcomes and complications. J Cataract Refract Surg. 2007 Dec;33(12):2041-8.
4. Kymionis GD, Tsiklis N, Karp CL, Kalyvianaki M, Pallikaris AI. Unilateral corneal ectasia after laser in situ keratomileusis in a patient with uncomplicated photorefractive keratectomy in the fellow eye. J Cataract Refract Surg. 2007 May;33(5):859-61.
5. Javadi MA, Mohammadpour M, Rabei HM. Keratectasia after LASIK but not after PRK in one patient. J Refract Surg. 2006 Oct;22(8):817-20.
6. Rao SK, Srinivasan B, Sitalakshmi G, Padmanabhan P. Photorefractive keratectomy versus laser in situ keratomileusis to prevent keratectasia after corneal ablation. J Cataract Refract Surg. 2004 Dec;30(12):2623-8.30.
7. El-Maghraby A, Salah T, Waring GO 3rd, Klyce S, Ibrahim O. Randomized bilateral comparison of excimer laser in situ keratomileusis and photorefractive keratectomy for 2.50 to 8.00 diopters of myopia. Ophthalmology. 1999 Mar;106(3):447-57
8. Solomon KD, Donnenfeld ED, Raizman M, Sandoval HP, Stern K, VanDenburgh A, Cheetham JK, Schiffman R; Ketorolac Reformulation Study Groups 1 and 2. Safety and efficacy of ketorolac tromethamine 0.4% ophthalmic solution in post-photorefractive keratectomy patients. J Cataract Refract Surg. 2004 Aug;30(8):1653-60.
9. Nissman SA, Tractenberg RE, Babbar-Goel A, Pasternak JF. Oral gabapentin for the treatment of postoperative pain after photorefractive keratectomy. Am J Ophthalmol. 2008 Apr;145(4):623-629. Epub 2008 Jan 28.

10. Lim-Bon-Siong R, Valluri S, Gordon ME, Pepose JS. Efficacy and safety of the ProTek (Vifilcon A) therapeutic soft contact lens after photorefractive keratectomy.Am J Ophthalmol. 1998 Feb;125(2):169-76.
11. Gruenauer-Kloevekorn C, Kloevekorn-Fischer U, Duncker GI. Contact lenses and special back surface design after penetrating keratoplasty to improve contact lens fit and visual outcome. Br J Ophthalmol. 2005 Dec;89(12):1601-8.
12. El-Agha MS, Johnston EW, Bowman RW, Cavanagh HD, McCulley JP. Photorefractive keratectomy versus laser in situ keratomileusis for the treatment of spherical hyperopia. Eye Contact Lens. 2003 Jan;29(1):31-7.
13. Gallar J, Acosta MC, Gutiérrez AR, Belmonte C. Impulse activity in corneal sensory nerve fibers after photorefractive keratectomy. Invest Ophthalmol Vis Sci. 2007 Sep;48(9):4033-7.
14 Gurland JE. Use of Silicone Lenses in Infants and Children, *Ophthalmology* 1979; 86:1599-1604.
15. Aasuri MK, Venkata N, Preetam P, Rao NT. Management of pediatric aphakia with silsoft contact lenses. CLAO J. 1999 Oct; 25(4):209-12.