APPROVED
AS MODIFIED
Mar 16, 2017
WIRB®

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE: Epithelium-On Corneal Collagen Crosslinking for Keratoconus

PROTOCOL NO.: 001
WIRB® Protocol #20170265

SPONSOR/ INVESTIGATOR:
Name: Kenneth Beckman, MD
Address: 450 Alkyre Run Dr #100
City, State, Zip Code: Westerville, Ohio 43082
Country: USA

STUDY-RELATED PHONE NUMBER(S):
Name: Kenneth Beckman, MD
Phone Number(s): 614-506-4720 or 614-890-5692 (24 hours)

A person who takes part in a research study is called a research or study subject. In this consent form "you" always refers to the research subject. If you are a parent or guardian, please remember that "you" means the research (study) subject.

SUMMARY

You are being asked to be in a research study. The purpose of this consent form is to help you decide if you want to be in the research study.

You should not join this research study until all of your questions are answered.

Things to know before deciding to take part in a research study:

- The main goal of a research study is to learn things to help patients in the future.
- The main goal of regular medical care is to help each patient.
- The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.
- Parts of this study may involve standard medical care. Standard care is the treatment normally given for a certain condition or illness.
- Other parts of this study may involve experimental (investigational) procedures that are being tested for a certain condition or illness. An investigational drug, device is one that has not been approved by the U.S. Food & Drug Administration (FDA).
- After reading the consent form and having a discussion with the research staff, you should know which parts of the study are experimental and which are standard medical care.

- Your medical records may become part of the research record. If that happens, your medical records may be looked at and/or copied by the sponsor of this study and government agencies or other groups associated with the study.
- Your medical insurance may be billed for any standard medical care you receive during the research study. If your insurance company is billed then it may have access to the research records. Insurance companies may not pay for treatment that is part of a research study. Taking part in a research study could affect your current or future insurance coverage.

PURPOSE OF THE STUDY

The purpose of this study is to determine the safety and effectiveness of cross-linking treatment using Photrexa® eye drops and UV light from the KXL® System for reducing corneal curvature (curve). You may be eligible to take part in this study because you have been diagnosed with Keratoconus, a condition in which the cornea (clear front part of the eye) thins and becomes cone-shaped causing visual problems.

The cross-linking procedure is intended to strengthen the corneal tissue. The cross-linking treatment using Photrexa (riboflavin eye drops) and the KXL System (UV light) are approved by the U.S. Food and Drug Administration (FDA) for the treatment of keratoconus and currently available in this country. During this procedure, the first layer of the cornea (epithelium) is removed, riboflavin (which is Vitamin B) eye drops are applied to the eye, and then the eye is exposed to UV light. The interaction between the riboflavin and UV light creates bonds between the collagen fibers in the cornea resulting in the strengthening of the cornea.

In this study, the crosslinking procedure will be performed using the FDA approved Photrexa and KXL System, however, the experimental part of the procedure is that the front layer of the cornea (epithelium) will not be removed.

PROCEDURES

The first part of the study is called a screening period. The screening period can begin up to 45 days before you receive study treatment. During this time, the study doctor will decide if you qualify to be in the study. To be in this study, you must:

- be at least 14 years of age
- have a diagnosis of progressive keratoconus
- willingness and ability to comply with the schedule for follow-up visits
- be willing (if a current contact lens wearer) to go without wearing your contact lenses for 1 week before screening
- have not had any other corneal condition that might affect the treatment or might make you more likely to have corneal problems in the future
- not be pregnant or planning pregnancy during the course of the study
- be able to maintain your eye position steady during the course of the treatment
- have a current condition that would not make you a good candidate for the study.

Before you can start the study, the study doctor or study staff will talk to you about the study. Then you have to read and sign this consent form before the study doctor or study staff can begin the screening process.

If you decide to be in this study and the study doctor says you qualify to be in the study, your participation will last for 12 months after treatment. This includes 8 office visits. You should ask the study staff how much of your time each visit will require.

Estimates for the visit times are as follows:

- Screening Visit, including the eye examination, special tests, a survey and any pictures of your eye required - about three hours
- Treatment visit: - will last about 2 hours, after which it is expected you could return home
- Day after treatment visit - this visit will take about 30 minutes
- Other post- treatment visits (at 1 week, 1 month, and 3, 6 and 12 months) should take between one and two hours, including any special tests.
- You will be instructed to remove your contact lenses 1 week prior to each follow up visit.

Visit 1 Screening Visit (Up to 45 days before assignment to a study group)

After you sign this consent form, the study doctor or study staff will do the things listed below during your screening visit to make sure that you are eligible to be in the study. The screening visit could be combined with part of your routine office visit. If you agree to participate in the study, then any tests that are done on your initial evaluation (which is being billed to insurance) as part of the normal testing for that exam (UCVA, BCVA, pentacam) prior to entering the study may be used as your initial screening tests for the study. The data from that visit may be used as your screening visit so you do not need to repeat the same tests.

- You will be asked questions about your health, your medical history, and any medications that you take. You will be asked about your eye history and about other procedures you have had done to your eyes.
- Your vision will be checked by reading an eye chart.
- Your corneal thickness will be measured by taking images of your eye with a special camera.
- Special measurements of the curvature (curve) of your cornea will be taken.
- Your eye will be examined by the study doctor using a special microscope.

Refraction Stability Visit(s) - (Contact Lens Wearers Only) and at Least 7 Days after Visit 1 and any additional visits must be 7 Days apart

- You will be asked questions about how you are feeling and any medications that you are taking, as well as questions to be sure your eye and medical history have not changed.
- Your vision will be checked by reading an eye chart.
- Your refraction (measurement for eyeglasses) will be done, although you will not be given a prescription for new glasses. If your refraction is stable, when compared to a previous refraction, you will be scheduled for Visit 2. If your refraction is not stable at this visit, you may be scheduled to return for an additional visit to recheck the refraction stability.

- Your eye will be examined by the study doctor using a special microscope.
- Special measurements of the curvature (curve) of your cornea will be taken.
- Your study doctor will decide if this Visit will occur on the same day as your Visit 2 (treatment day) or on a date before the Visit 2. Your treatment will happen at Visit 2 after the Refraction Stability assessments are complete.

Visit 2 Treatment Day (Study Day 0)

- You will be asked questions about how you are feeling and any medications that you are taking, as well as questions to be sure your eye and medical history have not changed.
- Prior to randomization, if you are a woman and you are able to have children, a urine test will be administered to see if you are pregnant. The results must be negative (meaning you are not pregnant) for you to continue in this study.
- Once in the room where the treatment will take place, you will be positioned to make you comfortable for the treatment, then some numbing eye drops will be put into your eye. Your eyelids will be held open with a small instrument and numbing eye drops used to help you be comfortable during the treatment will be dropped at the rate of one drop every 20 seconds for one minute. The cornea surface is then prepped with a sponge. Then, Photrexa riboflavin will be administered at a rate of 1-2 drops every 2 minutes for 30 minutes, along with continued application of the numbing drop every 2 minutes for 10 minutes. The doctor will exam your eye with a special microscope and additional drops will be added if needed. Your eye must remain open during the procedure for this treatment to work.
- The doctor will exam your eye with a special microscope and additional drops will be added if needed. Your eye must remain open during the procedure for this treatment to work.
- During the treatment period, the UVA light is turned on and Photrexa will be dropped at a rate of 1 to 2 drops every 2 minutes along with the UV light. You will continue to receive numbing drops every 5 minutes. The procedure will last 30 minutes. At the end of 30 minutes, the UV light turns off.
- Your study doctor will give you instructions for after care and may also give you a prescription(s) for you to take if needed. Please refer to the instruction sheet that your pharmacist gives you for any warnings and possible side effects if you are provided with a prescription.

Follow-Up Visits

These visits will occur as follows:

- Visit 3 (1 day after treatment)
- Visit 4 (1 week after treatment)
- Visit 5 (1 month after treatment)
- Visit 6 (3 months after treatment)
- Visit 7 (6 months after treatment)
- Visit 8 (12 months after treatment)

The procedures for these visits are as follows:

- You will be asked questions about how you are feeling and any medications that you are taking. You should report any changes in your health or changes in the medications you are currently taking.
- Your vision will be checked by reading an eye chart.
- Your eye will be examined by the study doctor using a special microscope.
- Special measurements of the curvature (curve) of your cornea will be taken.

While you are in the study, you must:

- Follow the instructions you are given.
- Come to the study centers for all visits with the study doctor.
- Tell the study doctor or study staff about any changes in your health or changes in medication.
- Tell the study doctor or study staff if you want to stop being in the study at any time.
- Ask questions if you think of them.

RISKS AND DISCOMFORTS

Photrexa is an approved drug and Cross-Linking is an approved procedure but there may be side effects from the Photrexa or the Cross-Linking procedure that are not known at this time. Any time you are enrolled in a study, there may be risks, discomfort, and side effects.

Some known side effects of the Cross-Linking procedure for keratoconus are haze, punctate keratitis (dry eye), corneal striae (white lines seen using a special microscope), corneal epithelium (outermost layer of the eye) defect, eye pain, reduced (vision) visual acuity and blurred vision.

There are some risks that we do not know about. They are listed below and divided into sections, and then by how common certain things we might expect are. If you have any questions about things happening to your eyes or health, contact the study doctor or study staff.

Your condition may not get better, and it may even get worse as a result of your being in this study.

There may be side effects of the cross-linking treatment that are not known at this time.

The most and less common risks and discomforts expected in this study are:

Using Numbing Eye Drops:

Common:	Redness of your eyes, tearing or stinging, blurred vision lasting a few minutes
Uncommon:	Feeling faint or dizzy, blurred vision lasting longer than a few minutes.

Using Dilating Eye Drops:

Common: Redness of your eyes, tearing or stinging, and glare & blurry vision for reading and distance which lasts for up to 6 hours

Uncommon: Feeling faint or dizzy, glare or blurred vision at distance or near that lasts longer than 6 hours, allergic reactions (see below)

Your study doctor will provide you with additional risks and discomforts with any medications he/she may prescribe.

Using the post-treatment eye drops (antibiotic drops):

Common: Redness, tearing, increased tearing, inflammation, allergic reactions, dry eye, eye pain, eye itching, broken blood vessels in the eyes, cough, eye discharge, swollen eyelids, unpleasant taste

Uncommon: sore throat, fever, ear pain, rash, hives, itching, difficulty breathing or swallowing, hoarseness

Using the post-treatment eye drops (steroid or NSAID drops):

Common: Redness, tearing or stinging, blurred vision lasting a few minutes

Uncommon: Temporary increase in eye pressure, allergic reactions (see below)

Rare but possible risks include:

Rare: Cataract formation, corneal thinning, glaucoma (increased pressure in the eye), optic (eye) nerve damage, loss of vision

Measurement of your eye pressure with a tonometer or thickness of your cornea with a pachymeter:

Common: Redness, stinging, or tearing of your eyes, blurred vision lasting less than 30 minutes

Uncommon: Blurred vision lasting longer than 30 minutes, dizziness or feeling faint, scratching your cornea requiring treatment by your study doctor

Allergic reactions to drops or medications of any kind:

Common: Redness of your eyes, a rash on your skin

Uncommon: Difficulty breathing, wheezing, a sudden drop in blood pressure, a fast pulse, sweating, or swelling around your mouth, throat, or eyes

Rare but possible risks include:

Rare: Death

Taking prescription pain medication (by mouth):

Common: Nausea, vomiting, constipation, lightheadedness, dizziness, drowsiness, flushing, vision changes, or mental/mood changes

Uncommon: Slow/irregular breathing, slow/irregular heartbeat

Rare but possible risks include:

Rare: Liver or kidney damage if high doses are taken

Please tell the study doctor or study staff right away if you have any side effects. Also, please tell them if you have any other problems with your health or the way you feel during the study, whether or not you think they are related to the study.

PREGNANCY

To protect against possible side effects of Photrexa, women who are pregnant or nursing a child may not take part in this study. If you are a woman who is able to become pregnant, you and the study doctor must agree on a method of birth control to use throughout the study. If you think that you have gotten pregnant during the study, you must tell the study doctor immediately. Pregnant women will be taken out of the study.

The effect of the Photrexa on sperm is not known. To protect against possible side effects, if you are a man you should not get a sexual partner pregnant while taking the Photrexa. You and the study doctor should agree on a method of birth control to use throughout the study.

For females capable of becoming pregnant, you must first have a urine pregnancy test performed prior to randomization and prior to treatment of the cross-over (placebo) or fellow eye. You must agree to use a medically acceptable form of birth control for at least one week prior to the randomization visit and one week prior to the treatment of a fellow eye or cross-over eye and continue to use the method until one month after the last corneal collagen cross-linking procedure.

You and the study doctor should agree on a method of birth control to use throughout the study. Acceptable methods of birth control include oral hormonal contraceptives (the pill), injection, patch, implant, ring), condom with spermicide, diaphragm with spermicide, diaphragm and male condom, or IUD. Another option is to only have intercourse with a partner who has had a vasectomy (male surgical sterilization). You may participate in the study if you are not sexually active and agree to utilize an acceptable method of birth control should you become sexually active.

Women considered capable of becoming pregnant include all females who have experienced menarche (first menstruation) and have not experienced menopause (have not had a period for greater than 12 consecutive months) or have not undergone successful surgical sterilization (e.g. hysterectomy, bilateral tubal ligation (both tubes tied), or bilateral oophorectomy [both ovaries removed]).

Women who are pregnant or nursing a child may not take part in this study. If you think that you have become pregnant during the study, you must tell your study doctor immediately. You should not participate in this study if you plan to become pregnant during the approximately 12-18 months that is required for participation in this study.

NEW INFORMATION

It is possible that the researchers will learn something new during the study about the risks of being in it. If this happens, they will tell you about it so you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

BENEFITS

Your keratoconus may improve while you are in this study; however, this cannot be promised. The results of this study may help people with keratoconus in the future.

OTHER RISKS

Your condition may not get better or may get worse during this study.

COSTS

This includes the treatment and all scheduled study visits, including testing done as part of the study on post treatment visits. Your initial evaluation prior to being included in the study will be charged to you or your insurance as a standard office visit would. Any exams or tests that are done during the one year study course that are not related to the study will be billed to you or your insurance company as with any standard appointment.

You might have unexpected expenses from being in this study. Ask your study doctor to discuss the costs that will or will not be covered by the sponsor. This discussion should include who will pay the costs of treating possible side effects.

PAYMENT FOR PARTICIPATION

You will not be paid for being in this study.

ALTERNATIVE TREATMENT

If you decide not to enter this study, there is care available to you outside of research, such as: contact lenses, INTACS implantation, and corneal transplantation. The study doctor will discuss these with you. You do not have to be in this study to be treated for Keratoconus.

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

What information may be used and given to others?
The study doctor will get your personal and medical information. For example:

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits

Who may use and give out information about you?
The study doctor, the study staff, and sponsor

Who might get this information?
The sponsor of this research. "Sponsor" means any persons or companies that are:

- working for or with the sponsor, or
- owned by the sponsor.

Your information may be given to:

- The U.S. Food and Drug Administration (FDA),
- Department of Health and Human Services (DHHS) agencies,
- Governmental agencies in other countries,
- Governmental agencies to whom certain diseases (reportable diseases) must be reported, and
- Western Institutional Review Board® (WIRB®).

Why will this information be used and/or given to others?

- to do the research,
- to study the results, and
- to see if the research was done right.

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

May I withdraw or revoke (cancel) my permission?
This authorization does not automatically expire. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
There is a risk that your information will be given to others without your permission.

Confidentiality
Information from this study will be given to the sponsor. "Sponsor" includes any persons or companies that are contracted by the sponsor to have access to the research information during and after the study.

The information will also be given to the U.S. Food and Drug Administration (FDA). It may be given to governmental agencies in other countries where the study drug or device may be considered for approval. Medical records which identify you and the consent form signed by you will be looked at and/or copied for research or regulatory purposes by:

- the sponsor,

and may be looked at and/or copied for research or regulatory purposes by:

- the FDA,
- Department of Health and Human Services (DHHS) agencies,
- governmental agencies in other countries, and
- Western Institutional Review Board® (WIRB®).

Absolute confidentiality cannot be guaranteed because of the need to give information to these parties. The results of this research study may be presented at meetings or in publications. Your identity will not be disclosed in those presentations.

COMPENSATION FOR INJURY

If you are injured or get sick as a result of being in this study, call the study doctor immediately. The study doctor will provide emergency medical treatment. If your injury or illness is not a direct result of being in this study, you, your medical insurance, or another third party payer (responsible for paying) will be responsible for those medical costs. You should be aware that if your medical insurance does not cover the costs of study-related injuries or illnesses, then you would be responsible for those costs. By signing this consent form, you are not giving up your right to seek legal recourse for your injury.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Your participation in this study is voluntary. You may decide not to participate or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are entitled.

Your participation in this study may be stopped at any time by the study doctor or the sponsor without your consent for any reason, including:

- if it is in your best interest
- if you do not consent to continue in the study after being told of changes in the research that may affect you

If you leave the study before the planned final visit, you may be asked by the study doctor to have some tests or procedures done so that you leave the study safely.

SOURCE OF FUNDING FOR THE STUDY

The sponsor Dr. Kenneth Beckman will pay for this research study.

QUESTIONS

Contact the CECCO staff at 614-506-4720 or 614-890-5692 (24 hours) for any of the following reasons:

- if you have any questions about your participation in this study,
- if you feel you have had a research-related injury or a reaction to Photrexa or the procedure, or
- if you have questions, concerns or complaints about the research.

If you have questions about your rights as a research subject or if you have questions, concerns or complaints about the research, you may contact:

Western Institutional Review Board® (WIRB®)
1019 39th Avenue SE Suite 120
Puyallup, Washington 98374-2115
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: Help@wirb.com

WIRB is a group of people who independently review research.

WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WIRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

Do not sign this consent form unless you have had a chance to ask questions and have gotten satisfactory answers.

If you agree to be in this study, you will receive a signed and dated copy of this consent form for your records.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

CONSENT

I have read this consent form (or it has been read to me). All my questions about the study and my part in it have been answered. I freely consent to be in this research study.

I authorize the release of my medical and research records for the purpose of this study.
By signing this consent form, I have not given up any of my legal rights.

Consent and Assent Instructions:

Consent:

* Adults must sign on the subject line below

* For children, consent is provided by the parent or guardian

* For subjects who are children when they begin participation and become adults during the study, consent to continue must be provided by the subject at that time using the section below

Assent:

* Assent is required for subjects for whom the investigator determines it is appropriate using the Assent section below.

CONSENT SIGNATURE:

_____ _____

Signature of Adult Subject Date

_____ _____

Signature of Parent or Guardian Date

ASSENT SECTION:

Statement of person conducting assent discussion:

- I have explained all aspects of the research to the subject to the best of his or her ability to understand.
- I have answered all the questions of the subject relating to this research.
- The subject agrees to be in the research.
- I believe the subject's decision to enroll is voluntary.
- The study doctor and study staff agree to respect the subject's physical or emotional dissent at any time during this research when that dissent pertains to anything being done solely for the purpose of this research.

Statement of Parent or Guardian:

My child appears to understand the research to the best of his or her ability and has agreed to participate.

Signature of Parent or Guardian	Date
Printed Name of Person Conducting the Informed Consent Discussion	Position
Signature of Person Conducting the Informed Consent Discussion	Date

Ver. 06/15/2015