Study Title	A Phase I/II Randomized, Double-Masked Placebo-Controlled Study for Determining the Safety of Processed Amniotic Fluid (PAF) Drops after Photorefractive Keratectomy
ClinicalTrials.gov ID (NCT Number)	NCT04281004
Principal Investigator (PI)	Mark Mifflin, MD
Document (ICF, Protocol, SAP)	ICF
Update Date (Approval Date)	November 28, 2022

Consent and Authorization Document

STUDY TITLE: **A Phase I/II Randomized, Double-Masked Placebo-Controlled Study for Determining the Safety of Processed Amniotic Fluid (PAF) Drops after Photorefractive Keratectomy**

PRINCIPAL INVESTIGATOR: **Mark Mifflin, M.D.** **TELEPHONE:** **(801) 583-4152**

ADDRESS: **John A. Moran Eye Center**
65 Mario Capecchi Drive
Salt Lake City, UT 84132

CONSICE SUMMARY

You are being asked to join a research study for people who are considering photorefractive keratectomy (PRK) surgery. Before you consider the research, you should be aware of the following information:

Research is voluntary. You do not have to be in this study. You will get standard medical care for PRK surgery even if you decide not to join the study.

This study uses an investigational eye drop made from processed amniotic fluid (pAF). The pAF eye drop has not been approved by the U.S. Food and Drug Administration. We hope the study eye drop will help your eye heal more quickly after PRK surgery, but we don't know if it works yet. We are doing this study to evaluate the safety of the pAF eye drops and their effect on corneal healing and discomfort following PRK. This is the first time these eye drops have been tried in people after PRK surgery.

This study also uses placebo eye drops consisting of saline solution. If you join the study, you will receive either the pAF drops or the placebo drops. Everyone in the study gets standard medical treatment for PRK surgery, in addition to getting the pAF drops or the placebo.

This study lasts about one year. If you sign up now, you can still take yourself out of the study later on.

You might benefit from being in the study, but there is no guarantee of benefit. The pAF drops have some risks, which are explained later in this document.

If you think you want to be in the study, please read the rest of this document and discuss it with the study team and get answers to your questions before you decide to be in the study. The document explains what will happen during the study.

BACKGROUND

PRK surgery uses a laser to sculpt the clear surface of the eye (the cornea) to correct near sightedness or far sightedness. During PRK, the top layer of the cornea is removed, and the laser reshapes the middle layer. This procedure is FDA approved and used widely. One disadvantage of PRK compared to other laser surgeries like LASIK is that healing takes longer. This is in part due to the defect created in the surface of the eye during PRK, which is the like a large scratch. Some patients experience pain as the surface of the eye heals, a process that can take several days to a week.

One product that has been used to help with healing after other types of eye surgery is amniotic membrane. Amniotic membrane is the inner layer of the placenta. This type of tissue has been used to help the surface of the eye to heal after surgery. In this study, we want to study the impact of a similar product, amniotic fluid. This product is thought to have similar properties that may increase the rate of healing after PRK, and possibly reduce pain during the healing period.

This study is being conducted by Dr. Mark Mifflin at the Moran Eye Center in collaboration with the Department of Cell Therapy & Regenerative Medicine at the University of Utah.

The University of Utah has a significant institutional financial interest in intellectual property being used in this study (U-5650 "Amnion/Chorion Membrane as a Wound Cover to Control Adhesions and Heal Wounds, Amniotic Fluid (Supernatant) and Amniotic Fluid (Whole) to Reduce Inflammation, Heal Wounds and Stimulate Bone Growth") and a significant institutional financial interest in Eliksa (a non-publicly traded company which is licensing the technology for commercialization). This is a conflict of interest as determined by the University of Utah Institutional Conflict of Interest Officer and a management plan has been implemented to ensure transparency, promote data integrity, and to safeguard human subjects in the research.

Investigator Jan Pierce has a financial interest in Eliksa, (a non-publicly traded company which is licensing the technology for commercialization), which is a conflict of interest as determined by the University of Utah Individual Conflict of Interest Committee, and a management plan has been implemented to ensure transparency, promote data integrity, and to safeguard human subjects in the research.

STUDY PROCEDURES

Screening/Baseline Visit

If you are interested and eligible to participate in this study, we will ask you to read and sign this study informed consent prior to surgery. As is standard for our PRK cases, you will also speak with our surgery coordinator about PRK. In preparation for your surgery, we will review your medical history and any medications you are currently taking. We will check your vision, examine the surface of your eyes and determine what your vision should be after you have surgery. Our surgical coordinator will work with you to schedule your surgery on a mutually agreeable day.

Surgery (Day 1 AM)
Your surgery will take place early in the morning. Before surgery, we will review any changes in your medications and you will be assigned to receive either the placebo or the pAF eye drops. Neither you nor your surgeon will be able to choose which type of drop you receive, because you will be assigned randomly. Neither you nor your surgeon will not know if you are getting the pAF drops or placebo because this study is double-masked. If we need to, for safety reasons, we can find out which type of study drop you have been assigned to.

Your surgeon will perform PRK surgery according to standard practices and will administer the first dose of placebo or pAF fluid directly after surgery.

As part of our standard procedures for PRK, you will have a bandage contact lens placed on your eyes after surgery. The bandage contact lens is typically removed one week after surgery. You will also be instructed to use preservative free artificial tears in both eyes several times a day for the first week, and as needed thereafter.

Days 1 (PM) through 8
We will send you home with labeled vials of study eye drops and instructions on how to store and use them.

You will use the assigned study eye drops 4 times daily for the first 7 days. We will ask you about all medications you take and any problems you've had with your eyes during this time. We will examine your eyes on days 3, 4, 5, 6, 7, and 8 after surgery to measure the rate of healing of each eye. If your eyes have healed prior to Day 8, you may be able to skip subsequent in-person examinations except for Day 8. For example, you may be able to skip Days 4, 5, 6, and 7 if your eyes have healed by Day 3.

On Days 1 through 7 we will ask you to complete a pain scale. On day 8 we will check your vision.

Months 1, 3, 6 and 12
You will have checkups one month, 3 months, 6 months and one year after your PRK surgery. At each of these visits, we will check your vision and examine the surface of your eyes. You would have these procedures whether or not you were in this study. For the purposes of this study, we will collect and analyze the information we get from these checkups. We will also ask you about any problems you've had with your eyes and the medications you have taken during this time.

RISKS
Risks of the study include those normally associated with PRK surgery including, but not limited to, decreased vision, over-correction, under-correction, pain, glare, halos, dry eye, corneal haze, swelling of the eye and itchy eye.

There is a theoretical risk of infection with amniotic fluid drops. The manufacturer utilizes strict donor screening procedures to avoid the collection of tissues from donors who may carry infection. These standards are the same standards used in other eye surgeries such as corneal transplantation. Despite rigorous donor screening and laboratory testing, the drops may transmit infection. The donors from whom the drops were derived are tested and found negative for Hepatitis B & C, HIV (Human Immunodeficiency Virus) and Syphilis.

You could have an immune reaction to the study drops. We will monitor you for any signs of such a reaction and provide treatment if needed.

Because we need to collect information from your medical record for this study, there is a risk of loss of confidentiality. We follow strict privacy policies to minimize this risk.

UNFORESEEABLE RISKS
In addition to the risks listed above, you may experience a previously unknown risk or side effect.

BENEFITS
We cannot promise any benefits to you from your being in the study. If you are assigned to the pAF drops, there may be a potential benefit of decreased pain and healing time. The information we get from this study may help us treat future patients.

ALTERNATIVE PROCEDURES
You may choose not to be in this study. If you do not want to take part in the study, there are other choices such as receiving the PRK procedure outside of this research study. You may discuss these options with your doctor.

PERSON TO CONTACT
If you have questions, complaints or concerns about this study, or if you think you may have been injured from being in this study, please contact Dr. Mifflin at 801-583-4152. In case of medical issues that occur after hours, the University of Utah Hospital Operator can be reached at (801) 581-2121. The operator can page the ophthalmologist on call. This number is available 24-hours a day.

Institutional Review Board: Contact the Institutional Review Board (IRB) if you have questions regarding your rights as a research participant. Also, contact the IRB if you have questions, complaints or concerns which you do not feel you can discuss with the investigator. The University of Utah IRB may be reached by phone at (801) 581-3655 or by e-mail at irb@hsc.utah.edu.

Research Participant Advocate: You may also contact the Research Participant Advocate (RPA) by phone at (801) 581-3803 or by email at participant.advocate@hsc.utah.edu.

University of Utah
Institutional Review Board
Approved 1/18/2023
Expires 1/17/2024
IRB_00099569

RESEARCH-RELATED INJURY

If you are injured from being in this study, medical care is available to you at the University of Utah Health Sciences Center, as it is to all sick or injured people. The University of Utah has not set aside any money to pay the costs for such care. The University of Utah will work with you to address costs from injuries. Costs would be charged to you or your insurance company (if you have insurance), to the study sponsor or other third party (if applicable), to the extent those parties are responsible for paying for medical care you receive. Since this is a research study, some health insurance plans may not pay for the costs. By signing this consent form you are not giving up your right to pursue legal action against any parties involved with this research.

The University of Utah is a part of the government. If you are injured in this study, and want to sue the University or the doctors, nurses, students, or other people who work for the University, special laws may apply. The Governmental Immunity Act of Utah is a law that controls when a person needs to bring a claim against the government, and limits the amount of money a person may recover. See sections 63G -7-101 to -904 of the Utah Code.

VOLUNTARY PARTICIPATION

Research studies include only people who choose to take part. You can tell us that you don't want to be in this study. You can start the study and then choose to stop the study later. We will still give you medical care and answer any questions you have. Your decision will not affect your relationship with your doctor or the study team in any way.

If you want to stop being in this study, please let the research doctor know. That way you can find out what should be done about your normal medical care outside of the study.

RIGHT OF INVESTIGATOR TO WITHDRAW

The investigator can withdraw you without your approval. He may withdraw you from the study if he feels it is in your best interest.

COSTS AND COMPENSATION TO PARTICIPANTS

The study eye drops will be provided free of charge. All procedures are considered within the standard of care for PRK surgery and will be billed to you in the usual manner; however, you will be eligible for a reduced study fee for their surgery and post-operative care. PRK surgery is considered cosmetic surgery and is never billed to insurance. The surgery charge includes standard post-operative examinations up to one year.

If enhancement surgery is deemed necessary during the one-year post-operative period, this will be included in your initial fee, as is standard of care. Any other costs related to management of adverse events, or if additional refractive correction is necessary at some time after the one-year postoperative period, will remain your responsibility and are not included in the study surgery fee.

You will receive a $40 check after you complete your 3 month study visit. If you need help with transportation for the post-surgery visits, please talk with your surgeon. Cab vouchers or similar assistance may be provided.

NEW INFORMATION
Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study.

NUMBER OF PARTICIPANTS
We expect to enroll 63 participants at the University of Utah.

AUTHORIZATION FOR USE OF YOUR PROTECTED HEALTH INFORMATION
Signing this document means you allow us, the researchers in this study, and others working with us to use some information about your health for this research study. The FDA may also review research records that are a part of this study.

This is the information we will use and include in our research records:

- Demographic and identifying information like your name, address, telephone number, and email address
- Related medical information about you such as your family medical history, allergies, current and past medications and therapies, and information from ophthalmic examinations.
- All tests and procedures that will be done in the study

How we will protect and share your information:

- We will do everything we can to keep your information private but we cannot guarantee this. Study information will be kept in a secured manner and electronic records will be password protected. Study information may be stored with other information in your medical record. Other doctors, nurses, and third parties (like insurance companies) may be able to see this information as part of the regular treatment, payment, and health care operations of the hospital. We may also need to disclose information if required by law.

- In order to conduct this study and make sure it is conducted as described in this form, the research records may be used and reviewed by others who are working with us on this research:
    - Members of the research team and the University of Utah Health Sciences Center
    - The University of Utah Institutional Review Board (IRB), who reviews research involving people to make sure the study protects your rights
    - The Food and Drug Administration, who is authorized to ensure the integrity of the research
- If we share your identifying information with groups outside of *University of Utah Health Sciences Center,* they may not be required to follow the same federal privacy laws that we follow. They may also share your information again with others not described in this form.

- If you do not want us to use information about your health, you should not be part of this research. If you choose not to participate, you can still receive health care services at the University of Utah Health Sciences Center.

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

What if I decide to Not Participate after I sign the Consent and Authorization Form?

You can tell us anytime that you do not want to be in this study and do not want us to use your health information. You can also tell us in writing. If you change your mind, we will not be able to collect new information about you, and you will be withdrawn from the research study. However, we can continue to use information we have already started to use in our research, as needed to maintain the integrity of the research.

This authorization does not have an expiration date.

PARTICIPANT CONSENT

I confirm that I have read this consent and authorization document and have had the opportunity to ask questions. I will be given a signed copy of the consent and authorization form to keep. **I agree to take part in this research study and authorize you to use and disclose health information about me for this study, as you have explained in this document.**

_____	_____	_____
Participant's Name	Participant's Signature	Date

STATEMENT OF STAFF OBTAINING AUTHORIZATION AND CONSENT

I have carefully explained to the participant the nature and purpose of the above study in language understood by the participant. I provided the participant enough time and an adequate place to read and review this form and discuss the study with study investigators and/or family members. I have answered the participant's questions to their satisfaction. The participant voluntarily agreed to participate in the study and personally signed and dated the consent prior to any study procedures being done. A copy of the signed & dated consent form was given to the participant.

_____	_____	_____
Name of Person Obtaining Authorization and Consent	Signature of Person Obtaining Authorization and Consent	Date