Study: Autologous Serum Tears for Dry Eye Disease Study Protocol
Protocol: TOYOS-GENIUSPRP-19-01
Date: October 16, 2019

Cover Page
NCT03287635
Clinical Efficacy of H.P. Acthar Gel 80 Units/ml to Improve the Signs and Symptoms in Subjects with Dry Eye Disease

Date May 10, 2018

Participant Informed Consent Form and Authorization to Use and Disclose Medical Information

TITLE: Evaluation of the Safety and Efficacy of Autologous Serum Tears Prepared with the Genius PRP for Dry Eye Disease

PROTOCOL NO: TOYOS-GENIUSPRP-19-01

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INTRODUCTION

You are being asked to participate in a medical research study. Before agreeing to participate in this research study. It is important that you read the following explanation of this research study. No guarantees or assurances can be made as to the results of the study.

The decision to participate in this study is up to you. Your participation is completely voluntary. Your decision will not affect your relationship with your regular doctor or your current or future medical care.

Please read this form carefully. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision whether to participate. Ask about anything you don't understand or would like explained better. Take time to decide whether or not you want to take part in this study and ask the study doctor or study staff as many questions about the study as you would like. You cannot take part in this research study until you sign this form.

This form explains the following:

- Purpose of the study
- Procedures involved in the study
- Possible benefits
- Possible risks
- How your medical information will be used and who may view it

Background and Purpose

Dry eye disease is a condition that can affect a patient's quality of life. Symptoms of dry eye include but are not limited to irritation, redness, burning, foreign body sensation, dryness, pain and blurry vision. In many cases, dry eye disease is caused by chronic inflammation that can damage both the surface of the eye and the nerves in the ocular surface that help to maintain normal health.

In dry eye disease due to neurotrophic keratitis, the nerves in the eye may be damaged enough to allow ongoing and worsening damage to the surface of the eye as well as a loss of feeling or pain due to the chronic nature of the disease.

Dry eye disease may be caused by a variety of factors including hormonal changes, bacterial infections, systemic medications, allergies, use of eye drops that contain preservatives or inflammation, pollution or poor diet. Dry eye disease is especially prevalent in Asian populations.

In recent years, a growing number of doctors have observed that application of the topical application of growth factors including nerve growth factor which is contained within platelet rich plasma (PRP) prepared from a patient's own blood can help to improve the signs and symptoms of dry eye disease.

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PURPOSE OF STUDY
You are being asked to take part in this study because you have been diagnosed with dry eye disease.

The purpose of this research study is to study the effects, safety and efficacy of intense pulse light with the Lumenis M22 applied to the upper eyelids of subjects who have a diagnosis of dry eye disease caused by MGD>

The Genius PRP has been approved for use the United States for the preparation of platelet rich plasma (PRP) for intraoperative use during orthopedic procedures. This system is a cleared (approved) device (by the United States Food and Drug Administration (FDA) for orthopedic use. The use of GENIUS PRP for reducing the symptoms of dry eye caused by dry eye disease in this study is investigational. An investigational use is one that is not approved by the United States Food and Drug Administration (FDA). Because this is a research study, IPL for dry eye disease caused by dry eye disease will be used only during this study and not after the study is over.

Approximately 20 men and women between the ages of 18-85 will be enrolled in this study being conducted with enrollment, data collection and follow up visits at Tianjin Eye Hospital and data analysis and manuscript preparation primarily at Toyos Clinic's Nashville location.

DURATION OF THE STUDY

Participation in the study will last 4 weeks. During this period, you will receive study treatment twice daily for four consecutive weeks. Four (4) weeks after initiation of the study treatment, you will be asked to return to the clinic for a follow up visit.

YOUR RESPONSIBILITIES

If you agree to participate in the study, you will attend 2 visits at the clinic, enrollment and final follow up visit.

Screening/baseline visit: At this first visit, the study doctor will determine if you are eligible to participate in the study. The study doctor or staff will give you a detailed explanation about the study and review this consent document. Before any study-related tests or procedures are performed, you will be asked to read and sign this document. You may sign it at this visit or if you wish to have some time to think more about, consult with others, you may elect to take it home for as long as you wish. If you decide that you wish to participate in the study, you must return with a signed informed consent form.

After the informed consent is signed, you will be asked questions about your medical history or demographic information including age, gender, race and skin type). This visit can occur on the

same day as the screening visit or up to a week later. If you are eligible to participate in the study you will have a brief examination including:

Visual acuity test: the doctor or study staff will use a chart and ask them to read them from top to bottom as the letters become smaller.

Slit lamp exam: the doctor will examine the structures of the eye using a microscope and beam of light.

Confocal imaging: the doctor will examine the nerves in the front of the eye with a special high resolution microscope.

VAS Scales: you will be asked to rate your current ocular pain and dryness symptoms at each study visit.

Tear film break up time: the study doctor will measure the time it takes from a blink of the eye to the time a dry spot is formed on the surface of the eye using a yellow dye and a topical anesthetic or a drop of liquid dye. The doctor will ask you to blink and start a stopwatch. Your doctor will repeat this three time and take the average of these measurements.

First study visit: The first study will consist of a blood draw by an approved technician and preparation of the PRP by an investigator. The patient will have their visual acuity tested with a slit lamp examination of the front of the eye, a subjective visual analog pain scale will be completed by the patients, and a confocal image will be taken.

Final study visit. The same procedures except the blood draw and PRP prepartion will be done at this study visit.

Procedures		Enrollment/Baseline Visit 1, Day 1	Study Visit 2 Day 30+/-3 day
Informed Consent		x	
Demographics		x	
Medical History		x	
VAS Scale pain		x	x
Administer Study Intervention		X	
Concomitant medication review		X	X

BCVA		X	X
Slit Lamp Biomicroscopy		X	X
Dilated ophthalmoscopy		X	X
Confocal imaging		X	x
Non-invasive tear break up time		X	x

POTENTIAL SIDE EFFECTS AND RISKS

The Genius PRP treatment used in this study may cause all, some or none of the listed risks/side effects. There may be potential risks to you by taking part in this study including risks that are currently unknown.

Possible risks of this procedure include:
*eye pain
*eye irritation
*autoimmune deposits in eye that disappear after stopping study drug
*eye watering

Risks of procedures and tests for this study

You will have various eye examinations which may product temporary eye irritation.

-Blood draw, which allows the investigator to create PRP with the patient's own blood. This procedure involves a needle for venipuncture that will allow for 60 cc of blood to be removed. There may be some minor discomfort with the blood draw, local irritation or bruising or need to re-stick if blood flow is insufficient. The PRP will be prepared aseptically.

-Slit lamp examination which allows an examination of the frontal eye structures of the eye, including the eyelid, sclera (the white of the eye), conjunctiva (a clear mucous membrane that covers the sclera just behind the iris), and the cornea. The instrument used for this test consists of a high-intensity light source that can be focused to shine a thin sheet of light into the eye.

-Dilated ophthalmoscopy, which allows examination of the back of the eye. The test may involve placing drops in the eye in order to dilate (expand) the pupils, which may cause you to experience some light sensitivity for a few hours after this examination. The dilating drops may rarely cause increased pressure in the eye leading to nausea and pain.

- Confocal imaging, which allows for high resolution of the nerves within the front of the eye may or may not require contact with the front of the eye.

- Tear Break Up Time – depending on the type of testing, a drop of fluorescein stain may be instilled into the eye, the lids held open for several seconds until the tear film breaks up or the patient may sit in front of a technology with open eyes until the technician observes tear break up.

Pregnant women are not eligible to take part in the trial. If you are a woman who may become pregnant, you must use an effective method of birth control while participating in the study and for four weeks after your last dose of study drug. If you become pregnant during the study, please let your study staff known immediately and cease use of the study product. If you become pregnant during the study, the study staff will ask to follow your pregnancy to its outcome. You should tell your study doctor about physical or emotional changes or side effects that may occur while taking part in this study. Promptly report any health problems or changes to a member of the study staff or your study doctor.

New Findings
We will tell you about any new information that may affect your health, welfare, or choice to stay in this research.

Potential Benefits
You may benefit as a result of your participation in this study. However, there is no assurance that you will benefit from your participation in this study. Results from this study may benefit other patients in the future.

Your dry eye disease may worsen, improve or stay the same while receiving the study product.

Alternative Treatment
This clinical study is for research purposes only. You do not have to participate in the study to receive treatment for dry eye. There are other options available to you may include warm compresses, artificial tears, topical cyclosporine, topical lifitiegrast topical steroids, non-steroidals, autologous serum tears or IPL. You may choose to take part in a different study, if one is available and for which you may be eligible.

Costs
There will be no charge to you for your participation in this study. Study-related procedures and study visits will be provided to you at no charge or to your insurance company. If you are injured or get sick because of being in this research, call the study doctor immediately. The study doctor will provide emergency medical treatment. Your insurance may be billed for this treatment. No other payment is available from the study doctor.

You will not be paid for being in this study.

Voluntary Participation/Withdrawal
Your decision to participate in this clinical research study is voluntary. You may choose not to participate or you may withdraw from the study for any reason at any time without penalty or loss of any benefits you are otherwise entitled. You should tell the study doctor or study team if you decide to leave the study.

The study doctor can stop the study or your participation in the study at any time without your consent if it appears to be medically harmful to you, if you fail to follow directions for participating in the study, if the study is canceled, or for administrative reasons. If you withdraw or are withdrawn from the study, you will no longer receive access to study product but may be asked to continue in the study for safety measures.

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.

It is possible that regulatory agencies such as the U.S. Food and Drug Administration (FDA) may inspect confidential study materials and absolute confidentiality cannot be assured. However, all medical records and research materials will be held confidential to the extent permitted by law. Medical records which identify you and the consent form signed by you may also be looked at and/or copied for research or regulatory purposes by:

1. Department of Health and Human Services (DHHS) agencies
2. The institution where the research is being done, and

If the results of this study are published or presented at meetings, you will not be identified. This permission or authorization has no end date. You have a right to see your study records but will not be able to do so until the study has ended.

You may withdraw your permission at any time by writing your study doctor a letter. If you withdraw permission after you have entered the study, you cannot continue participating in the study. If you refuse to give permission or withdraw permission, your medical care and relationship with your health care providers at the study center will not be affected.

If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the research team at the phone number listed above on the first page.

This research is being overseen by an Institutional Review Board ("IRB"). An IRB is a group of people who perform independent review of research studies. You may talk to them at XXXX if:

You have questions, concerns, or complaints that are not being answered by the research team
You are not getting answers from the research team.
You cannot reach the research team.
You want to talk to someone else about the research.
You have questions about your rights as a research subject.

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Consent

I have read the statements in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study, if and until I decide otherwise. I do not give up any of my legal rights by signed this consent document. I may request a copy of this signed consent document.

Printed Name of Participant

_____ _____

Signature of Participant Date

I have carefully explained to the participant the nature and purpose of the above study. There has been an opportunity for the participant to ask questions about this research study. I have been available to answer any questions that the participant has about the study.

Printed Name of Person Conducting Consent Discussion

_____ _____

Signature of Person Conducting Consent Discussion Date

Authorization to Use and Disclose Protected Health Information

During your participation in this research study, the study doctor and study staff will collect or create health information about you and record it on study documents. The study doctor will keep this protected health information.

Under federal law, your protected health information (PHI) that is created or obtained during this research study cannot be used or disclosed without your permission. This permission is called an "Authorization." You do not have to sign this Authorization, however, you may not participate in this study unless you give your permission to use and disclose your PHI by signing this authorization. By signing, you are agreeing to allow the study doctor and study staff to use your health information to conduct this study.

This Authorization will never expire unless and until you revoke (cancel or withdraw) it.

You have a right to revoke your Authorization at any time. If you revoke it, your health information will no longer be used for this study, except to the extent the parties have already taken action based upon your prior Authorization or need the information to complete analysis and reports for this research. To revoke your Authorization, you must write to the study doctor, state that you are revoking your Authorization to Use or Disclose Protected Health Information. The study doctor's mailing address is Toyos Clinic, 2204 Crestmoor Road, Nashville, TN 37215. If you revoke this Authorization, you will not be allowed to continue in the study.

You may receive a copy of this Authorization after you have signed it.

_____

Printed Name of Participant

_____ _____

Signature of Participant Date

I have carefully explained to the participant the nature and purpose of this form. I have been available to answer any questions that the participant has about this form.

_____

Printed Name of Person Obtaining the Authorization

_____ _____

Signature of Person Obtaining the Authorization Date