Informed Consent
And
Authorization To Disclose Health Information

Sponsor / Study Title:	**Gynecologic Cancer Research Foundation/ "A Double Blind Placebo Controlled Trial of Autologous Platelet Rich Plasma (PRP) Intradermal Injections for the Treatment of Vulvar Lichen Sclerosus."**
Principal Investigator: (Study Doctor)	**Andrew Goldstein, M.D.**
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Introduction:

You are being invited to take part in a research study. Research studies are voluntary and include only those who wish to take part. This research study is for an experimental treatment for lichen sclerosus. It is not known if this experimental treatment will be an effective (good) treatment for lichen sclerosus. Before you decide if you want to participate in this research study, it is important for you to understand why the research is being done and what it will involve. This consent form describes the purpose, procedures, benefits, risks, discomforts, and precautions of the study. It also describes the alternative procedures available to you and your right to withdraw from the study at any time. No guarantees or assurances can be made as to the results of the study.

Please take time to read the following information carefully and discuss it with friends, relatives, or your family doctor if you wish. Please ask if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. You will be given a signed and dated copy of this consent to take home with you.

If you are not completely truthful with your study doctor regarding your health history, you may harm yourself by participating in this study.

You may not use additional medications for lichen sclerosus while participating in this study.

Financial Disclosure:
Dr. Andrew Goldstein, the principal investigator, holds a position on the board of the organization that is funding this research. Due to this potential conflict of interest, Dr. Goldstein will not be involved in the informed consent process or recruitment for this study. Additional

costs of this study are being funded by The Center for Vulvovaginal Disorders, the medical practice of Dr. Andrew Goldstein. Speak with the study doctor if you have additional questions.

Purpose of the Study:

Lichen sclerosus (LS) is a skin condition of the external genitals (vulva) of women. LS causes vulvar itching, pain, and burning. In addition, LS causes scarring of the vulva which may cause significant sexual dysfunction or pain. Lastly, 4-6% of women with LS will develop vulvar cancer.

The current "gold standard" treatment for lichen sclerosus is potent steroids creams. When used correctly, steroid creams help to decrease the symptoms of itching and burning and can prevent further vulvar scarring. In addition, proper treatment reverses the underlying inflammation of LS, and may lower the risk of getting cancer. While useful, steroid creams may have serious side effects that include thinning of the skin, fungal infections, and lowering the immune system.

Platelet-rich plasma (PRP) is a platelet concentrate that helps to speed up tissue healing, without serious side effects, in a very wide range of medical conditions such as diabetic foot ulcers, muscle injury, tendon injury, and in a variety of cosmetic procedures. The PRP works because of its high level of proteins that help with wound healing. It is also apparent from the majority of published studies that PRP therapy has minimal risk of scar tissue formation or significant bad side effects.

Recently, there was an exploratory study of twelve subjects that used PRP for the study treatment of lichen sclerosus. While this study showed good success, the study was limited because of its small size and lack of placebo (a drug or study treatment that contains no active ingredient) control.

Length of the Study and Number of Subjects:

The study will consist of four visits to the study center. Each visit is expected to last approximately one hour. The total amount of time you will participate in the study is 14 weeks, including a 2 week pretreatment period and a 12 week study treatment period. You will fill out questionnaires at each visit. Your safety will be assessed for the entire 12 week study treatment period.

Up to 30 women may participate in this study.

Who May Participate:

You *may* participate if you:

- are 18 years or older.

- have a diagnosis of active lichen sclerosus (Dr. Goldstein will remove a pea size amount of skin (a biopsy) and will do a physical assessment of the vulva area at the beginning of the study to confirm this diagnosis).
- are willing and able to comply with the study requirements.
- have a negative pregnancy test prior to enrolling in this study and will use at least one form of birth control during the course of the study if you are sexually active and are fertile.
- Have at least a 5 out of 10 on a questionnaire that measures the amount of itching you are having.

You *may not* participate if you:

- are immunocompromised (have a lowered immune system) (for example, you have been diagnosed with or have a history of lymphoma, AIDS, or Wiskott-Aldrich Syndrome), or have an uncontrolled malignant disease.
- have a generalized infection (bacterial, viral or fungal), or obvious localized infections in the vulva area.
- have swollen lymph nodes (lymphadenopathy)
- have any active sexually transmitted diseases on the vulva (herpes, molluscum, condyloma)
- have been diagnosed with diabetes.
- have been diagnosed with other vulvar dermatologic conditions including lichen planus, psoriasis, lichen simplex chronicus, candidiasis, intraepithelial neoplasia, or carcinoma.
- are pregnant or breastfeeding.
- if you become pregnant while on the study, you must withdraw from the study.
- have received an investigational drug within four weeks prior to the study or who plan to use other investigational drugs during the course of this study.
- have severe medical condition(s) that in the view of the investigator prohibits participation in the study.
- have a history of substance abuse or any factor, which limits your ability to cooperate with the study procedures.
- are uncooperative or are not willing to attend regular visits.
- have received systemic immunosuppressants (steroids), other systemic therapies or any other systemic therapies known or suspected to have an effect on vulvar lichen sclerosus within 12 weeks prior to participation in the study.
- have been treated with topical therapy (for example, topical corticosteroids, pimecrolimus, tacrolimus, doxepin, phenol, menthol, camphor, pramoxine, topical estrogen, topical testosterone) or any other topical therapies known or suspected to have an effect on vulvar lichen sclerosus or its symptoms within 16 weeks prior to participation in the study.

Your Role in the Study:

Taking part in a research study can be an inconvenience to your daily life. Please consider the study time commitments and responsibilities as a research subject when you are deciding to take part. Your responsibilities as a study subject include the following:

- Tell the truth about your medical history and current conditions.
- Tell the study doctor if you have been in a research study in the last 30 days or are in another research study now.
- Tell the study doctor about any problems you have during the study.

Procedures to Be Followed During the Study:

Visit 1 Screening

This visit will include a detailed history and physical examination. You will fill out a questionnaire about your itching, burning, soreness, and pain with intercourse. A digital photograph of your vulva will be taken. To see if you have vulvar cancer, Dr. Goldstein will put acetic acid on your vulva and examine your vulva with a microscope (colposcope). The acetic acid solution will be washed off with water after approximately 4 minutes. A 4mm (¼ inch) skin biopsy of the vulva will be taken. Prior to the biopsy, a numbing medication (lidocaine) will be injected in the biopsy site. After the biopsy, you will get one or two stitches at the biopsy site. These stitches dissolve and do not have to be removed.

Visit 2 Baseline

You will return approximately 2 weeks after visit 1. If you meet the inclusion criteria, you will have sixty ccs of blood drawn (4 tablespoons) from your arm to make the PRP.

You will then be randomized to either receive the PRP or a placebo (saline). Two thirds of the women (20 out of 30) will receive the PRP and one third (10 out of 30) will receive the placebo. Only a research coordinator will know if you will be receiving the PRP or the placebo. Neither you nor Dr. Goldstein will know if you are to receive the PRP or placebo. If you have been randomized to receive the PRP you will get it throughout the entire study. If you have been randomized to receive placebo, you will get it throughout the entire study and you will not be getting PRP. If you are randomized to receive the placebo, the PRP will be discarded.

You will then receive either the PRP injection or placebo injection into the skin of the vulva. The syringe containing the PRP or placebo is blackened so that neither you, nor Dr. Goldstein, will know if you are receiving the PRP or placebo.

Visit 3

You will return approximately 6 weeks after visit 2. You will tell the study doctor if you are having any side effects from the prior injections. Sixty cc of blood will be drawn (4 tablespoons)

from your arm to make the PRP. You will then receive either the PRP or placebo injections into the skin of the vulva.

Visit 4

You will return approximately 6 weeks after visit 3. You will tell the study doctor if you are having any side effects from the prior injections. You will have a limited physical exam. A digital photograph of your vulva will be taken. Your vulva will be examined with a microscope (colposcope) after application of a very dilute acetic acid solution to make sure that you do not have vulvar cancer. The acetic acid solution will be washed off with water after approximately 4 minutes. A 4mm (¼ inch) skin biopsy will be taken. Prior to the biopsy, a numbing medication (lidocaine) will be injected in the biopsy site. After the biopsy, you will get one or two stitches at the biopsy site. These stitches dissolve and do not have to be removed.

Foreseeable Discomforts and Risks of the Study:

1) If the PRP is not an effective study treatment of lichen sclerosus:

Your symptoms of vulvar itching, burning, pain during intercourse may not improve, or they may get worse.

Scarring of your vulva may get worse.

You may develop vulvar cancer.

2) Possible side effects from the intervention during this study:

Because the PRP is derived from your own blood there is no risk of an allergic or immune reaction.

The risks related to the PRP injections include:

Very likely:

1) mild or moderate pain from the injection

Less likely

1) bruising at injection sites

Rare but potentially serious

1) infection at injection sites

The risks related to the venipunctures (blood removal):

Very likely:

1) mild discomfort

Less likely

1) bruising
2) anemia

Risks related to the vulvar biopsies:

Very Likely:

1) Pain from injection of anesthetic
2) Mild or moderate discomfort while the biopsy heals (typically less than 10 days)
3) Need to refrain from intercourse until biopsy heals

Less Likely

1) Infection at biopsy site requiring antibiotics

Rare but Serious

1) long-lasting discomfort at the biopsy site

Risks of Lidocaine Injection

Tell your caregivers at once if you have any of these serious side effects:

1) feeling anxious, shaky, dizzy, restless, or depressed;
2) drowsiness, vomiting, ringing in your ears, blurred vision;
3) confusion, twitching, seizure (convulsions);
4) fast heart rate, rapid breathing, feeling hot or cold;
5) weak or shallow breathing, slow heart rate, weak pulse; or
6) feeling like you might pass out.

Less serious side effects include:

1) mild bruising, redness, itching, or swelling where the medication was injected;
2) mild dizziness;
3) nausea;
4) numbness in places where the medicine is accidentally applied

Get emergency medical help if you have any of these signs of an allergic reaction: hives; difficulty breathing; swelling of your face, lips, tongue, or throat.

Application of the dilute acid solution usually causes mild or moderate stinging or burning depending on the presence of cracks or ulcers in the skin. The stinging or burning will usually stop within a few minutes after washing off this acid solution.

In order to protect you from the risk of loss of confidentiality, individual subject names will not be used for any purpose and you will be tracked only by a unique subject number. All data files will be password-protected and no hard copies with medical record numbers or account numbers will be printed. All of your study data will be kept in a secure location. Information published will be in group form without individual identifying facts.

New Findings:

Any new important information which is discovered during the study and which may influence your willingness to continue participation in the study will be made available to you in a timely fashion.

Potential Benefits of the Study:

There is the hope that the itching, burning, pain, ulceration, and skin thickening from your lichen sclerosus might be decreased. There is the hope that the PRP will prevent further scarring of your vulva and may lower your risks of developing vulvar cancer. There is, however, no guarantee that you will benefit from your participation in the study. The itching, burning, pain, ulceration, and skin thickening from your lichen sclerosus could stay the same or even worsen.

Alternatives to Being in the Study:

You do not need to take part in this research study. Treatments for lichen sclerosus include steroids creams. Your study doctor can discuss the alternatives and the risks and benefits of these alternatives with you.

Compensation:

You will not receive compensation for participation in this study.

Disclosure of Protected Health Information (HIPAA):

For purposes of this study:

- The investigators will use medical information collected or created as part of the study, such as medical records and test results, that identifies you by name or in another way.
- Your consent to participate in the study means that you agree that the Investigators may obtain your medical information that he requests for study purposes from your physicians and your other health care providers.
- You are also agreeing that the Investigators may use and share this information with the parties described below. In addition, you agree that, during the study, you may not have access to some of your medical information obtained or created as part of this study. You will be allowed to access this information once the study is finished.
- Unless required by law, the Investigators will share this medical information only with the Study Team and other professionals involved in the Study, and the US Food and Drug Administration (FDA), governmental agencies in other countries where the study drug may be considered for approval, and Chesapeake Institutional Review Board.
- The purpose for using and sharing this information with these parties is to perform the study and to ensure the accuracy of the study data. Not all of the parties who will have access to your medical information as part of the study are prohibited by federal law from further sharing it, so the information, once received by them, may no longer be protected by federal law.

- You have the right to cancel this consent at any time by giving written notice to any of the Investigators. If you cancel this consent, then the Investigators will no longer use or disclose your medical information, unless it is necessary to do so to preserve the scientific integrity of the study. However, canceling this consent will not affect previous uses and disclosures and your medical information would not be removed from the study records.
- If you fail to give your consent by signing and dating this document, or if you cancel your consent later, then you will not be eligible to participate in this study and will not receive any study treatment provided as part of the study. Unless and until you cancel the consent, it will remain valid and effective.
- All documents will be retained for 10 years after completion of the study.

In Case of Research- Related Injury:

If you become ill or are hurt while you are in the study, get the medical care that you need right away. You should inform the healthcare professional treating you that you are participating in this study.

You understand that you must report any suspected study-related illness or injury to the study investigator immediately. Medical therapy will be arranged for you by the study doctor (Dr. Andrew Goldstein) for any physical injuries or illnesses which occur as a direct result of your participation in this research. You will not be reimbursed for your medical expenses that are not covered by your medical insurance or third party coverage. Compensation for lost wages and/or direct or indirect losses is not available. Dr. Andrew Goldstein will not provide any other form of compensation for injury. You will not lose any of your legal rights as a research subject by signing and dating this form nor does it relieve the investigators, Sponsor or involved institutions from their legal and professional responsibilities.

Costs:

There will be no charge to you for your participation in this study. The study treatment, study related procedures, tests, and study visits will be provided to you at no charge to you or your insurance company. Routine medical care not required for this study is not covered.

Serious Adverse Events:

Every serious adverse medical event, whether related to, or not related to the investigational protocol will be reported to the Chesapeake IRB Officer within 24 hours of the report being received by Dr. Goldstein.

Getting Answers to Your Questions or Concerns About the Study:

You can ask questions about this consent form or the study (before you decide to start the study, at any time during the study, or after completion of the study). Questions may include:

- Who to contact in the case of a research-related injury or illness;

- Payment or compensation for being in the study, if any;
- Your responsibilities as a study subject;
- Eligibility to participate in the research;
- The study doctor's or study site's decision to exclude you from participation;
- Results of tests and/or procedures;
- Other questions, concerns, or complaints.

Contact the study doctor or study staff listed on the first page of this form with any questions, concerns or complaints.

Getting Answers to Your Questions About Your Rights as a Research Subject:

This study has been reviewed by an Institutional Review Board (IRB). This Committee reviewed this study to help ensure that your rights and welfare are protected and that this study is carried out in an ethical manner.

For questions about your rights as a research subject, contact:

- By mail:
  Study Subject Adviser
  Chesapeake IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@chesapeakeirb.com

Please reference the following number when contacting the Study Subject Adviser: Pro00019511.

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.

Voluntary Participation/Withdraw:

Your participation in this study is voluntary. You may decide not to participate or you may withdraw from this study at any given time without penalty or loss of benefits to which you are otherwise entitled and without effect on your future medical care. There will be no change in your medical care or eligibility to participate in future research studies.

In addition, the study doctor can stop your participation at any time without your consent for the following reasons: if it appears to be medically harmful to you, if you fail to follow directions for participating in the study, if it is discovered that you do not meet the study requirements, if you become pregnant, at the discretion of the study doctor, or if the study is cancelled.

If you withdraw from the study, please be aware that to meet regulatory requirements, the information collected about you will still be processed and used in submissions to regulatory agencies.

Primary Care Physician Notification:

Participation in this study should not be considered a substitute for treatment by your primary care physician or specialist. Please ask your study doctor questions about the results of your laboratory tests or diagnostic procedures. Please review this information with your primary care physician or specialist. Unless specifically requested, your primary care physician or specialist will not be contacted by your study doctor regarding your participation in this study.

Consent:

This consent form contains important facts so that you can decide if it is in your best interest to participate in this research study. If you have any questions that are not answered in this consent form, the study doctor can give you further information.

All of your questions about the study have been answered. Based on this information, you voluntarily agree to participate in the study. All oral and written information and discussion about the study are in English, a language you can read and understand. You will not lose any of your legal rights as a research subject by signing and dating this consent form. You will receive a copy of this signed and dated consent form.

_____	_____	_____	_____
Printed Name of Subject	Signature	Date	Time

Statement of Person Explaining Consent:

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

_____	_____	_____	_____
Printed Name of Person Obtaining Consent	Signature	Date	Time