Platelet-rich Plasma (PRP) for Endometrial Regeneration and Repair NCT02825849

Document Date: Oct 24 2019

Consent

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: PLATELET-RICH-PLASMA FOR ENDOMETRIAL REGENERATION AND REPAIR: A PROSPECTIVE PILOT STUDY

This is a medical research study. Your study doctor(s), Heather Huddleston, M.D., Lusine Aghajanova, M.D, Ph.D. and colleagues from the UCSF Division of Reproductive Endocrinology and Infertility will explain this study to you.

Medical research studies include only people who choose to take part. Take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor.

You are being asked to take part in this study because you either have Asherman's Syndrome (scar tissue inside the uterus) or have thin lining in preparation for frozen embryo transfer (FET).

Why is this study being done?

The purpose of this study is to determine if a specific type of blood cells, platelets, derived from patient's own blood can enhance the repair and regeneration of uterine lining in cases of persistent thin uterine lining in patients undergoing procedures related to in vitro fertilization (IVF), or in patients with moderate-severe scar tissue inside the uterus (Asherman's syndrome).

Who pays for this study?

The Reproductive Endocrinology and Infertility Division will allocate funds. The special kits to isolate platelets from patients' blood will be donated by a manufacturer to the study.

How many people will take part in this study?

This is a pilot study. Therefore, a total of 70 female patients will take part in this study. 35 patients will receive PRP for their diagnosis of thin lining or Asherman's, while an additional 35 will serve as controls to whom the PRP group is compared.

What will happen if I take part in this research study?

If you agree to take part in this study, you will undergo a standard protocol used in our clinic and chosen by your doctor to prepare you for the frozen embryo transfer (FET) or to manage your Asherman's Syndrome. In addition to standard treatment, you will also receive the study treatment (platelet rich plasma (PRP) intrauterine infusion).

FET Patients: For the FET patients with **thin lining**, you will have a baseline transvaginal ultrasound performed to determine if you have an ovarian cyst that may delay your FET cycle. If the baseline ultrasound is normal, you will be able to start the medications in preparation for the

transfer. The treating physician will be able to explain more of this to you at your appointment. You will then have another ultrasound after 10-12 days of medication to evaluate your uterine lining. If your lining is thin, <6mm on that day, and if you agree to participate, you will be given the study treatment (platelet rich plasma (PRP) intrauterine infusion). If you participate in the study, the only difference between the study and standard care will be that you will undergo an additional blood draw in order to create the platelet rich plasma (PRP). For PRP, the platelets (thrombocytes) will be isolated from the obtained blood, and small amount (0.5-1ml) of this PRP will be slowly infused into the uterus through a tiny catheter that we usually use for the intrauterine inseminations (IUI). If after this first treatment we do not see significant improvement in uterine lining thickness, we will perform second infusion of PRP, for a total of two infusions.

Asherman's Syndrome: For the moderate-severe **Asherman's Syndrome patients**, you will undergo the hysteroscopic procedure for resection of intrauterine adhesions, as determined by and discussed with you by your doctor. Per standard of care in our clinic, a tiny balloon will placed into the uterine cavity to prevent re-scarring. If you participate in the study, the only difference between the study and standard care will be that you will undergo an additional blood draw in order to create the platelet rich plasma (PRP). For PRP, the platelets (thrombocytes) will be isolated from the obtained blood, and small amount (0.5-1ml) of this PRP will be slowly infused into the uterus through a tiny catheter that we usually use for the intrauterine inseminations (IUI). If after this first treatment we do not see significant improvement in uterine lining thickness, we will perform second infusion of PRP, for a total of two infusions.

You will be discharged home following the surgery and have the infusion of PRP on day 1 following your surgery. You will be instructed to start on 30 days of hormonal medications per standard practice to help regrowth of the uterine lining. You will receive doxycycline antibiotic for the duration of the intrauterine balloon placement (5-7 days) to prevent possible infection. You will then have uterine lining assessment with transvaginal ultrasound at 2 and 4 weeks during the first month post-procedure. Second look hysteroscopy may be performed after 1 month to assess the uterine cavity. You will be asked to record the menstrual flow diary before treatment and for the next 1-3 months.

During the main part of the study

You will undergo all procedures of a normal standard FET cycle or standard treatment of moderate-severe Asherman's syndrome. This will include using standard of care medications to suppress your ovaries in preparation for FET and growing your uterine lining with estrogens, periodic monitoring of your ovaries and uterus by transvaginal ultrasound, or undergoing surgical removal of scar tissue under anesthesia.

You will be signing a separate FET or surgical consent forms with your nurse or physician, which covers these procedures in greater details.

Please see below for more information about the standard of care FET treatment and Asherman's Syndrome treatment, as well as additional treatment associated with the study.

FET cycle/Thin Lining

FET cycle/thin lining patients	Standard care	Study Treatment
Cycle suppression/preparation of uterine lining	Standard protocol with Lupron and estrogen patches	Standard protocol with Lupron and estrogen patches
Ultrasound Monitoring Visit (Ultrasound visit #1 (Baseline))	Average of 5-10 minutes of time	Average of 5-10 minutes of time
Ultrasound monitoring Visit #2 around CD12	Average of 5-10 minutes of time	Average 5 min of 5-10 minutes of time
Blood draw during visit #2	none	One blood draw about 1 teaspoon (5ml) for hormonal assay and 2 tablespoons (30ml) for PRP preparation
Intrauterine PRP infusion (during visit #2)	none	#1 Intrauterine PRP infusion 0.5ml in office
Ultrasound monitoring visit #3 72 hours after Visit #2.	Average 5 min	Average 5 min. If lining <7mm, will get second treatment
Blood draw during visit #3 around CD15 (72 hours later)	none	One blood draw about 1 teaspoon (5ml) for hormonal assay and 2 tablespoons (30ml) for PRP preparation
Intrauterine PRP infusion (during visit #3)	none	#2 Intrauterine PRP infusion 0.5
Ultrasound Monitoring visit #4 around CD 18 (72 hours after Visit #3).	Average 5 min	Average 5 min.
If uterine lining <7mm, cycle will be canceled. If lining ≥7mm, will start progesterone and FET day will be scheduled		
Frozen embryo transfer (FET)	Standard procedure	Same as standard care

Asherman's Syndrome

Asherman's Syndrome treatment	Standard care	Study Treatment
Initial visit with	Standard clinical	Same as standard

diagnosis of Asherman's syndrome	approach	care
Hysteroscopic resection of intrauterine adhesions	Standard procedure to resect adhesions under sedation. Intrauterine balloon will be placed at the end of procedure and estrogen treatment initiated same day	Same as standard care
Blood draw during surgery	none	Additional blood draw about 2 tablespoons (30ml)
Intrauterine PRP infusion during or postop day 1 after surgery	none	#1 Intrauterine PRP infusion 0.5ml
Clinic visit 5-7 days after surgery	5-10 min. Intrauterine balloon removal.	5-10 min. Intrauterine balloon removal.
Monitoring #1 by ultrasound in 2 weeks after surgery	Appointment will be scheduled at patient convenience and will take approximately 5-10 minutes.	Appointment will be scheduled at patient convenience and will take approximately 5-10 minutes. If lining <7mm, will get second treatment same day
Blood draw during monitoring #1 visit	none	Blood draw of about 2 tablespoons (30ml)
Intrauterine PRP infusion during monitoring #1 visit	none	#2 Intrauterine PRP infusion 0.5ml in the office
Monitoring #2 by ultrasound in 4 weeks after surgery	Appointment will be scheduled at patient convenience and will take approximately 5-10 minutes.	Appointment will be scheduled at patient convenience and will take approximately 5-10 minutes.
Second look hysteroscopy to assess for re-scarring in 4 weeks after 1st surgery	Standard procedure in REI clinic under sedation	Standard procedure in REI clinic under sedation

Management of FET cycle or Asherman's Syndrome treatment will be done by your primary doctor based on their knowledge, expertise, and established standard of care guidelines. You will

continue to come to the clinic for transvaginal ultrasound visit as part of your routine care until you are ready for embryo transfer or otherwise meet the goal of your initial visit.

Along with the standard of care labs your doctor has ordered, you will have one additional blood draw for isolation of PRP. You will also take a survey about how you are feeling after the PRP infusion.

When you have completed your treatment cycle

You will be scheduled for a follow up visit with your treating physician to discuss the outcome. This visit is a standard of care procedures for all IVF patients. Your nurse will be able to schedule this with you.

Study Location

All study procedures will take place at the UCSF Center for Reproductive Health IVF clinics at 499 Illinois Street, San Francisco, California.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop your participation safely.

It is important to tell the study doctor why you are thinking about stopping so that your doctor can evaluate any risks or side-effects from the study treatment group and discuss that with you. The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from being in the study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. Side effects may be mild or severe and serious. They can be the result of the standard treatment or the PRP infusion. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking drugs. In some cases, side effects can be serious, long lasting, or may never go away.

Before you begin your hormonal medication for the FET cycle or as a postoperative treatment for Asherman's Syndrome, you will be given additional details about the possible side effects of these drugs by talking to your doctor or nurse. Typical side effects of hormonal treatments include bloating, breast tenderness, mood changes, and fatigue

If you elect to receive the PRP intrauterine infusion (the study treatment), there is no additional health risk expected based on multiple studies done in the areas of orthopedic surgery, sports medicine, dentistry, dermatology, cosmetics and cardiology.

However, prior to the current study, the intra-uterine infusion has only been done in 5 people and there is a possibility that a potential risk will not be known until after the study has started and the data is analyzed. We will be closely monitoring you for any unexpected side effects that you experience in the study.

The procedure (intrauterine infusion of PRP) is similar to a pap smear, intrauterine insemination (IUI) or embryo transfer (ET) if you have had one. You may experience some discomfort, but it is very unlikely to be painful. For the procedure, you will lie on a table with your feet in stirrups as you would for a gynecologic exam. A speculum is placed in the vagina, and cervix is cleaned with an antiseptic solution. A small caliber plastic catheter about 3mm in diameter (usually used for IUI) is passed through the vagina and cervix and inserted into the uterus. There is a syringe attached to the operator's end of the catheter with 0.5-1ml of PRP, and gentle pressure on the plunger will release the PRP inside of the uterus. We anticipate none-to-mild uterine cramping, equivalent to mild menstrual cramps, usually lasting no longer than the duration of the procedure and about 1-2 minutes thereafter. You will be advised to lie down for 5-10 minutes. You may leave the office shortly after the procedure is finished.

Other risks in this study:

1. Blood drawing (venipuncture) risks: Drawing blood may cause temporary discomfort from the needle stick, bruising, and infection.
2. Transvaginal ultrasound risks: The ultrasound procedure has no known short or long-term risks. A small number of women find it uncomfortable and rarely, women complain of pain exceeding simple discomfort. The test mainly directed to identify thickness of uterine lining and ovarian follicular activity. As with any pelvic examination, this may involve some loss of privacy.
3 Hysteroscopy surgical procedure (for patients with Asherman's Syndrome): this will be discussed in great details with you by your doctor at your preoperative visit and also on the day of surgery. The risks of the procedure include infection, bleeding, pain and uterine perforation (hole in the uterus) during the dissection of the adhesions
For more information about risks, benefits and alternatives talk to your treatment doctor and your study doctor.

Are there benefits to taking part in the study?

Taking part in this study may or may not make your health better. While it has been tested only in few patients, doctors hope that using PRP will improve the endometrial (uterine) lining, and thus increase your chance of pregnancy. However, there is no proof of these benefits yet. Information gained will help improve the infertility treatment process for the future patients.

What other choices do I have if I do not take part in this study?

If you decide not to participate on the study, you will continue to proceed with standard FET protocol and standard surgical and postoperative treatment for Asherman's Syndrome.

Please talk to your doctor about your choices before deciding if you will take part in this study.

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record is kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- University of California
- Food and Drug Administration (FDA)

Participation in research may involve a loss of privacy, but information about you will be handled as confidentially as possible. A medical record will be created because of your participation in this study. Your consent form and some of your research test results will be included in this record.

Therefore, your other doctors may become aware of your participation. Hospital regulations require that all health care providers treat information in medical records confidentially.

What are the costs of taking part in this study?

There is no extra cost to you by participating on the study. All patients participating in the study will not be charged for the extra blood draw, PRP isolation kit and isolation procedure, PRP infusion procedure and extra ultrasounds.

The costs of all routine standard visits, treatments (including surgery), and tests described above for the FET cycle or Asherman's Syndrome treatment will be billed to you or your insurance carrier. Insurance companies and other carriers sometimes refuse to pay the costs of treatment when individuals are undergoing fertility treatment. If this happens in your case, you will be billed for the care your insurance will not cover.

Financial counselors are available through the hospital accounting department to discuss this with you.

Will I be paid for taking part in this study?

You will not be paid for taking part in this study.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctors, Heather Huddleston, M.D. and Lusine Aghajanova, M.D, Ph.D., if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at 415-353-7475.

Treatment and Compensation for Injury: If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California, depending on a number of factors.

The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at 415-476-1814.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits.

Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study doctor about any questions, concerns, or complaints you have about this study. Contact your study doctors, Heather Huddleston, M.D. and Lusine Aghajanova, M.D, Ph.D., at 415-353-7475.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the Office of the Committee on Human Research at 415-476-1814.

ClinicalTrials.gov is a website that provides information about clinical trials. 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

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

Date _____ _____
Participant's Signature for Consent

Date _____ _____
Signature of Person Obtaining Consent

VOID