Partners HealthCare System
Research Consent Form

Subject Identification

General Template - Drug Clinical Trial
Version Date: August 2016

Protocol Title: Efficacy and Safety Of 0.25% Timolol Gel In Enhancing Full Thickness Skin Grafts Healing and Cosmetic Outcomes. A Randomized-Controlled Trial

Principal Investigator: Chrysalyne D. Schmults, MD, MSCE

Site Principal Investigator:

Description of Subject Population: 18+ years old needing a full-thickness skin graft

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

Partners HealthCare System is made up of Partners hospitals, health care providers, and researchers. In the rest of this consent form, we refer to the Partners system simply as "Partners."

If you have any questions about the research or about this form, please ask us. Taking part in this research study is up to you. If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

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.

Why is this research study being done?

We are doing this research study to find out if 0.25% timolol gel can help with full-thickness skin graft receiving site wound healing. We also want to confirm that 0.25% timolol gel is safe to use without causing too many side effects.

0.25% timolol gel is a betablocker that, based on previous studies and our experience, we think might help significantly with the wound healing process of surgical wounds, making them heal faster and better cosmetically.

0.25% timolol gel is approved by the U.S. Food and Drug Administration (FDA) to treat eye problems, but 0.25% timolol gel is not approved by the FDA to treat wound healing.

We are asking you to take part in this research study because you are receiving a full-thickness skin graft (FTSG) to close your wound. A full-thickness skin graft is a skin graft including the epidermis (top layer of skin) and the dermis (layer below the top layer). Its thickness depends on the donor site and your needs for wound healing. FTSG are frequently used in dermatologic surgery as they can cover surgical defects with better long term cosmetic outcome than split-thickness skin grafts.

About 58 subjects will take part in this research study at the Brigham and Women's Hospital (BWH).

How long will I take part in this research study?

It will take you about one week to complete this research study.

What will happen in this research study?

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures. The study visits may coincide with your regular dermatology appointments.

Screening Visit (Visit 1)

The Screening Visit will take about 15 minutes. At this visit, we will do some procedures to see if you qualify to take part in this research study. The study doctor will review the results of these procedures. If you don't qualify, the study doctor will tell you why.

At this visit, we will:

- Ask you about your medical history
- Do a physical exam

These activities are done as part of your clinical care and the information collected may be incorporated into this research study.

- Ask you to do a urine pregnancy test, if you are a woman able to become pregnant

- Take pictures of your surgical wound (these pictures will not include identifying features, such as your face, tattoos, etc.; however, if they do, you will have the option to 'opt out' of having photos taken)

If you still qualify for the study, we will assign you by chance (like a coin toss) to the timolol group or to the standard of care (Vaseline) group. You and the study doctor cannot choose your study group. You will have an equal chance of being assigned to the 0.25% timolol gel group or the standard of care (Vaseline) group.

Before signing this consent form, you and the study doctor won't know which study group you are in. However, after you sign it, you and the physician will know which treatment you will be receiving.
The physician assessing the pictures and your pain scores will not know which treatment did you receive.

This research study will compare 0.25% timolol gel to standard of care (Vaseline). During this study, you may get Vaseline instead of 0.25% timolol gel. Vaseline is used in this research study to see if the results are due to the study drug or due to other reasons.

Using the Study Drug

You will be followed up for 7 days post-surgery. Standardized pictures will be taken. Your wound surface area will be assessed by a computer scan; we will also look at the percentage of successful graft uptake, as well assessing any infections or need for reoperation. This will be done by a physician who does not know which study group you are in.

You and the study doctor will record any side effects occurring during the study period.

Timolol Group (0.25% timolol Gel)
On the receiving site of the FTSG, which will be dressed with 0.25% timolol and gauze during surgery, starting 7 days after surgery: You will apply daily dressings with Vaseline directly over the wound and cover with a bandage. This will be done for 4 weeks as per the standard of care.

Standard Care Group (Vaseline)
On the receiving site of the FTSG, which will be dressed with Vaseline and gauze during surgery, starting 7 days after surgery: You will apply daily dressings with Vaseline directly over the wound and cover with a bandage. This will be done for 4 weeks as per the standard of care.

Study Phase (Visit 2)

As part of the clinical care you are receiving, you will come in for a follow up visit at 7 days post-surgery. This visit will take about 20-30 minutes
At this visit we will:

- Perform a physical exam, as part of your clinical care and the information collected may be incorporated into this research study.
- Examine the receiving graft site
- Take standardized photos (these will not include identifying features, such as your face, tattoos, etc.; however, if they do, you will have the option to 'opt out' of having photos taken)
- Assess the wound surface area by a computer scan for the receiving site of a FTSG
- Assess rate of successful graft for the receiving site (a doctor will do this using a standardized score)
- Assess wound infection rate and reoperation rate which will be assessed by a doctor at each follow up visit
- Record your "Pain perception Analogue Scale" for the receiving site of the FTSG
- Have you and a study doctor assess any side effects occurring during the study period

Follow-up Phase
After your visit at 7 days, you will apply Vaseline to your wound whether you were initially assigned the Timolol or the Vaseline. We will not ask you to do any study-specific activities. If you happen to continue to follow up on your wound with the principal investigator or the co-investigators, we will review your medical records that only relates to this wound.

After You Complete the Study
After you complete the study, the treating surgeon will decide depending on your clinical progress when to refer you back to your own doctor for your ongoing medical care.

Stopping the Study Early

If you decide to stop taking part in the study for any reason, we will ask you to make a final study visit, which can be done in person, phone or secure email. The final study visit will take about 20 minutes. At this visit, we will:

- Do a physical exam
- Ask you about any side effects or health problems since your last visit
- Take standardized photos
- Assess the wound surface area by a computer scan for donor sites

- Assess rate of successful graft for the receiving site (a doctor will do this using a standardized score)
- Assess wound infection rate and reoperation rate which will be assessed by a doctor at each follow up visit
- Use a "Visual scar scale" by a blinded physician
- Record your "Pain perception Analogue Scale" for both donor and receiving site
- Record your "Scar satisfaction Visual Analogue Scale" for both donor and receiving site

Also, the study doctor may take you out of the study without your permission. This may happen because:

- The study doctor thinks it is best for you to stop using the study drug
- You can't make the required study visits
- We stop doing the study for other reasons

If this happens, the study doctor will explain why you need to stop taking part in the study. We will ask you to come in for a final study visit as described above.

Study Information Included in Your Electronic Medical Record
A notation that you are taking part in this research study may be made in your electronic medical record. Information from the research that relates to your general medical care may be included in the record (for example: list of allergies, results of standard blood tests done at the hospital labs).

Please ask your study doctor if you have any questions about what information will be included in your electronic medical record.

What are the risks and possible discomforts from being in this research study?

Risks of Taking 0.25% timolol gel

Taking 0.25% timolol gel may cause you to have one or more of the side effects listed below.

Common side effects:

- Erythema (reddening of the skin)

- Itching

Less common side effects:

- Pain
- Irritant or allergic contact dermatitis in case of patient sensitization
- Headache, weakness, drowsiness
- Numbness, tingling, or cold feeling in your hands or feet
- Ringing in your ears
- Dry mouth
- Nausea, diarrhea, loss of appetite, upset stomach
- Skin rash or worsening psoriasis
- Sleep problems (insomnia)
- Cough, stuffy nose

Uncommon side effects:

- Depressed mood, confusion, hallucinations, unusual thoughts or behavior
- Wheezing, gasping, or other breathing problems
- Swelling, rapid weight gain
- Chest pain, slow or uneven heart rate
- Feeling short of breath, even with mild exertion.

There may be other risks of 0.25% timolol gel that are currently unknown.

As with any drug, an allergic reaction can occur. Allergic reactions can be mild or more serious, and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing. If you think you are having an allergic reaction, call the study doctor right away. If you are having trouble breathing, call 911 immediately.

Risks of NOT using the Vaseline (for those assigned to the Timolol Group)
If you are assigned to the Timolol Group, you might incur in an increased risk of wound infection because you will not use Vaseline, which protects the wound against infection and/or other contaminants, while maintaining moisture.

Risks to an Embryo or Fetus, or to a Breastfeeding Infant

The effect of 0.25% timolol gel on an embryo or fetus (developing baby still in the womb), or on a breastfeeding infant, is unknown and may be harmful. This drug can pass through breastmilk. Because of these unknown risks, women cannot take part in this study if they are:

- Pregnant
- Trying to become pregnant
- Breastfeeding

If you are a menopausal woman and have not had a menstrual period for the past 12 months or more, you will not need to have a pregnancy test. Also, if you have had any well-documented method of surgical sterilization, you will not need to have a pregnancy test. Methods of surgical sterilization include having had a hysterectomy (removal of the uterus), bilateral oophorectomy (removal of both ovaries), a tubal ligation (having your tubes tied), and transvaginal occlusion (plugging the opening of the tubes with a coil). All other female subjects must have a negative pregnancy test before starting the study drug.

If you are sexually active and able to become pregnant, you must agree to use one of the birth control methods listed below. You must use birth control for the entire study and for at least 30 days after your last dose of study drug.

Acceptable birth control methods for use in this study are:

- hormonal methods, such as birth control pills, patches, injections, vaginal rings, or implants
- barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- intrauterine device (IUD)
- abstinence (no sex)

If you miss a period, or think you might be pregnant during the study, you must tell the study doctor immediately. If you become pregnant, you must stop taking the study drug and stop taking part in the study. The study doctor may ask for your permission to collect information about the outcome of your pregnancy and the condition of your newborn.

Risks of Taking 0.25% timolol gel with Other Medications

Do not start taking medications such as clonidine, quinidine, reserpine, digitalis, acetazolamide, dichlorphenamide, methazolamide, calcium channel blockers, or antidepressants while you are in the study. Taking these drugs and 0.25% timolol gel together may cause serious side effects. If you are already taking any of these medications, please tell the study doctor immediately.

For your safety during this study, call your study doctor BEFORE you take any:

- new medications prescribed by your own doctor
- other medications sold over-the-counter without a prescription
- dietary or herbal supplements

What are the possible benefits from being in this research study?

You may not benefit from taking part in this research study. If you receive 0.25% timolol gel, it is possible that your full-thickness skin graft wound will improve while you are taking it, but this is not guaranteed.

What other treatments or procedures are available for my condition?

You do not have to take part in this research study to be treated for full-thickness skin graft wound healing. The standard of care to treat full-thickness skin graft wound healing include: The receiving site is dressed with Vaseline and gauze during surgery, which is left in place for 7 days before wound inspection. After 7 days daily Vaseline is applied for 15-20 days.

Talk with the study doctor if you have questions about any of these treatments or procedures.

Can I still get medical care within Partners if I don't take part in this research study, or if I stop taking part?

Yes. Your decision won't change the medical care you get within Partners now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should I do if I want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will I be paid to take part in this research study?

You will not be paid for participation in the study.
Patients will only be receiving a single in-office application of timolol so will not require reimbursement.
Study funds will pay for study visits that are done only for research.

What will I have to pay for if I take part in this research study?

Study funds will pay for certain study-related items and services. We may bill your health insurer for, among other things, routine items and services you would have received even if you did not take part in the research. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff. If necessary, we will arrange for you to speak with someone in Patient Financial Services about these costs.

What happens if I am injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the next section of this consent form.

If I have questions or concerns about this research study, whom can I call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Chrysalyne D. Schmults, MD, MSCE is the person in charge of this research study. You can call her at (617) 983-4626 M-F 8-4:30. You can also call our Mohs coordinator M-F 8-4:30 at (617) 983-7207 with questions about this research study.

If you have questions about the scheduling of appointments or study visits, call the Mohs and Dermatologic Surgery Center at (617) 983-4626.

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at 857-282-1900.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research

Also, if you feel pressured to take part in this research study, or to continue with it, they want to know and can help.

If I take part in this research study, how will you protect my privacy?

During this research, identifiable information about your health will be collected. In the rest of this section, we refer to this information simply as "health information." In general, under federal law, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so.

In this study, we may collect health information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable health information and why they may need to do so:

- Partners research staff involved in this study
- The sponsor(s) of this study, and the people or groups it hires to help perform this research
- Other researchers and medical centers that are part of this study and their ethics boards
- A group that oversees the data (study information) and safety of this research
- Non-research staff within Partners who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- The Partners ethics board that oversees the research and the Partners research quality improvement programs.
- People from organizations that provide independent accreditation and oversight of hospitals and research
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Federal and state agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health, and other US or foreign government bodies that oversee or review research)
- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)
- Other:

Some people or groups who get your health information might not have to follow the same privacy rules that we follow and might use or share your health information without your permission in ways that are not described in this form. For example, we understand that the sponsor of this study may use your health information to perform additional research on various products or conditions, to obtain regulatory approval of its products, to propose new products, and to oversee and improve its products' performance. We share your health information only when we must, and we ask anyone who receives it from us to take measures to protect your privacy. The sponsor has agreed that it will not contact you without your permission and will not use or share your information for any mailing or marketing list. However, once your information is shared outside Partners, we cannot control all the ways that others use or share it and cannot promise that it will remain private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifying information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others.

You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my health information to be used and shared as described above.

_____	_____	_____
Subject	Date	Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

_____	_____	_____
Study Doctor or Person Obtaining Consent	Date	Time (optional)

Consent Form Version: 01/21/2020