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University of Minnesota
Department of Pediatrics

CONSENT TO PARTICIPATE IN RESEARCH

Study of Epidermal Grafting Using the CelluTome® Epidermal Harvesting System for the Treatment of Individual Lesions in Persons with Epidermolysis Bullosa (EB)

Principal Investigator:
Christen Ebens, MD, MPH

You are invited to participate in this study because you had a stem cell transplant for Epidermolysis Bullosa (EB) which was successful but you still have areas of blistering skin that have not healed. This study is testing a method to heal these remaining areas of skin breakdown.

Taking part in any clinical research involves risks and may provide some benefits. You need to understand these risks and benefits to make an informed decision about whether or not to be in this study.

This form is called a consent form. The intent of this form is to let you know the purpose of this study and the possible risks and benefits of participation. If you wish to take part in this study, you will be asked to sign this consent form.

Research studies only include people who want to take part. Please take time to make your decision. We encourage you to discuss your decision with your doctors, family, and friends.

This study is being conducted at the University of Minnesota. Christen Ebens, MD, MPH in the Department of Pediatrics is the principal investigator (physician in charge) of this study.

Introduction

Areas of blistering (wounds) often remain even after a successful transplant. This study treats such areas by using covering the blistered area with a square of surgical tape (similar to 3M's Tegaderm® transparent dressing) that has been loaded with skin cells collected from the same donor as your transplant. The surgical tape is left on for 3-4 weeks to give the donor skin cells a chance to take hold and promote wound healing. It is like doing a skin graft, but only taking the top most layer of skin cells (the epidermis). The process is done in the out-patient clinic and is non-invasive and bloodless for both the person donating the skin cells and for the person receiving them. A summary of the donor collection process is attached at the end of this consent form.

The device used to collect the donor cells is the CelluTome Epidermal Harvesting System manufactured by KCI (an Acelity company). It was approved by the Food and Drug Administration in 2013 and is used for the treatment of chronic wounds including diabetic ulcers and bed sores. This study is unique in that it uses the donor from your original transplant to provide healthy skin cells. This is possible because donor cells from your original transplant are still present in your body as measured by blood and bone marrow chimerism (genetic profiles).

Study Purpose

The primary goal of this study is to have partial to complete wound healing by 3 months after the epidermal cell graft in each of the treated areas. Secondary goals of the study include the appearance and health of the grafted skin 1 year later and to measure changes in quality of life (QOL) through a questionnaire created specifically for EB called iscorEB.

It is expected up to 60 people will be enrolled in this study with 40 of them using the donor from their previous transplant as the source of the skin cells (Arm A). The other 20 will have a patch of healthy skin as the source of the skin cells (Arm B) and will serve as their own donor.

Study Procedures

To be considered for this study you must be at least 6 months out from transplant and meet all eligibility criteria as stated in the study. The person who served as your transplant donor must also be available and willing to provide skin cells. The donor (or

parent/guardian if younger than 18 years) will be presented with a separate consent form which will be reviewed and written consent obtained if she/he agrees to be the skin cell donor for this study.

If you and the donor are eligible and agree to take part in this study, the following will occur.

You will have a brief physical exam (standard of care) and up to 3 areas of blistering will be identified for treatment (grafting) and an equal number areas will be identified but not treated at this time. The untreated areas are considered "controls." Photographs will be taken of each identified area.

The skin cells will be collected (harvested) from your donor according to the process summarized at the end of this consent. A different collection site will be used for each wound to be treated. Each harvest from the donor takes 30 to 40 minutes. At the end of each collection period, the harvested cells will be transferred onto a surgical tape patch.

The surgical tape then will be placed on one of the areas of blistering that were selected to be treated. Up to 3 donor skin cell transfers will be done during one clinic appointment with a separate surgical tape used for each. The surgical tape will be kept in place for 3 to 4 weeks to permit healing of heathy skin.

Photographs of each of the identified blistering areas will be taken once a week until your first follow-up appointment 6 weeks later. The photos will be done either in clinic or at home using a digital camera (such as a cell phone, iPad or camera) with the images sent to the University of Minnesota electronically by email or other photo sharing method.

Six weeks after the skin cell graft you and the donor may return to the University of Minnesota/or have a remote visit via phone call to have the collection sites (donor) and treated/control wounds (you) examined for healing. You will be asked to complete some brief questionnaires regarding your quality of life including pain and itch levels at each visit, also for research. Then, 12 weeks after the skin cell graft, you and the donor will return to the University of Minnesota/or have a remote visit via phone call to have the collection sites (donor) and treated/control wounds (you) examined for healing . You will be asked to complete another brief questionnaire regarding your quality of life including pain and itch, also for research. A final study visit occurs 1 year after the skin cell graft

to see how well the treated areas have held up. This will include a physical exam and photographs of the sites.

While you are on this study you will also continue your previously planned post-transplant follow-up. Visits for both studies will be overlapped so you are not making separate visits for each study.

Opportunity for Treatment of Additional Areas of Blistering:
If at the 12 week (3 month) follow-up visit, the blister areas are healing well and your donor is willing, you may be offered treatment of the "control" wounds and/or other areas of blistering. This is optional and does allow for additional information to be collected for the study. You may have up to 3 sessions total with up to 3 blistering treated each time (9 wounds total). A new session must be at least 3 months from the previous session. As with the 1st treatment you will need to provide weekly photographs, but the 6 and 12 weeks clinic visits may be arranged at a medical facility closer to your home/or by a remote visit via phone call with the results sent to the University.

Optional Skin Biopsy
If you agree, we would like to take 3 additional samples of your skin, at a time when you are having a biopsy completed for clinical care purposes. These would be used for research tests that help determine whether the donor cells have "taken." Additionally, we would like to save any leftover cells for future research on EB. At the end of this document, you may opt in or opt out of having these samples collected and saved.

Length of Study Participation

For the purpose of the study's research component, participation ends 1 year after the first treatment; however if you have additional skin collection sessions, information will continue to be collected until 1 year after the last session.

Risks of Study Participation

There is a small amount of risk from participation in this study. If the donor cells do not take (non-engraftment) the cells will slough off because of low grade infection, inadequate blood supply or ongoing EB related fibrosis. If this occurs it may be accompanied by local inflammation and possibly fever (sign of a whole body reaction), although neither are expected to be serious.

In theory there is a risk of non-engraftment because the skin cells are being collected from a different person; however, since the skin cells come from the same donor as your transplant, you are essentially using your own cells since you share your donor's immune system.

The completion of the **iscorEB questionnaire** may remind you of the unpleasant aspects of your diagnosis. You may refuse to answer any questions that make you uncomfortable.

Risks associated with a skin biopsy:
Skin biopsy may cause pain, bleeding or bruising at the spot where the skin is taken. There may also be a small scar. Rare side effects include infection at the biopsy site, allergic reactions to the numbing medicine, and excessive scarring.

Benefits of Study Participation

The intent is to provide long term healing of persistent areas of blistering although this is not known and the reason this study is being done. It is hoped that the findings in this study will improve the management of chronic areas of blistering for EB patients.

Alternatives to Study Participation

You may choose to not participate in this study and continue with your current skin management plan.

Study Costs

You are responsible for the costs of the procedures on this study, including the cost of the donor skin cell collection, the transfer of the donor cells to your areas of blistering, tests and physical examinations before and over the 1 year follow-up. Your insurance provider may not cover all or part of these costs. Preauthorization will be requested by a patient financial representative who will work with you and your nurse coordinator should your insurance company deny coverage. You should work with your patient financial representative as reimbursement – methods such as 3rd party reimbursement, charitable funds, self pay - must be confirmed prior to enrollment on this study. You will be responsible for any deductibles or co-pays.

You will receive no payment or compensation for taking part in this study.

Research Related Injury

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company.

It is important that you tell your study doctor or another member of the study staff if you feel that you have been injured because of taking part in this study. Dr. Ebens may be reached at 612-626-2961.

Confidentiality

The records of this study will be kept private. Information will be kept in your electronic medical record, paper research chart and in study case report forms. Information gained from this study will be used for research and educational purposes. 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:

- Departments at the University of Minnesota with appropriate regulatory oversight
- The Food and Drug Administration (FDA) and other governmental agencies involved in keeping research safe for people

To this extent, confidentiality is not absolute.

If you decide to participate in this study, some private health information about you will be stored in a computer database at the Masonic Cancer Center within the University of Minnesota. EB is not a cancer, but this database also stores information for non-cancer bone marrow transplants. This information will include your name and medical record number, date of birth, diagnosis, race/ethnicity, and information about your participation in this study. The purpose of storing this information is to assist the Cancer Center in creating reports about research and in making sure that research studies are being done correctly. Your information will not be used for any other purpose. There are no plans to erase information from the database. It will be stored indefinitely at the Masonic Cancer Center at the University of Minnesota.

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 could identify you. At most, the website will include a summary of the results. You may search this website at any time.

Protected Health Information (PHI)

Your PHI created or received for the purposes of this study is protected under the federal regulation known as HIPAA. Refer to the attached HIPAA authorization for details concerning the use of this information.

Voluntary Participation

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 withdraw your consent at any time by contacting a member of the research staff. Any information obtained up to the time of withdrawal will continue to be used in the study's analysis.

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 still may receive medical care from this institution.

New Information

You will be told about new information or changes in the study that may affect your health or your willingness to continue in the study.

Contacts and Questions

The physicians involved in your care are available to answer any questions you may have concerning this study at any time. Please ask any questions you have; we want you to understand the treatment and the study. If you have additional questions later concerning this study you are encouraged to call the study's Principal Investigator (lead physician) Dr. Christen Ebens at 612-626-2961.

Whom do I contact if I have questions, concerns or feedback about my experience?
This research has been reviewed and approved by an IRB within the Human Research Protections Program (HRPP). To share feedback privately with the HRPP about your research experience, call the Research Participants' Advocate Line at 612-625-1650 (Toll Free: 1-888-224-8636) or go to z.umn.edu/participants.. You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

Will I have a chance to provide feedback after the study is over?
The HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous.

If you are not asked to complete a survey, but you would like to share feedback, please contact the study team or the HRPP. See the "Investigator Contact Information" of this form for study team contact information and "Whom do I contact if I have questions, concerns or feedback about my experience?" of this form for HRPP contact information.

Signature

I agree	I disagree	
_____	_____	The research may take two additional skin biopsies during a standard clinical biopsies in order to determine whether the donated cells are growing.
_____	_____	With your permission, specimens left over after research tests listed above have been completed may be stored and used for future research purposes that have not yet been determined. Samples collected during the study may be stored at the University of Minnesota indefinitely. These samples may be used to develop new assay methods for testing samples from other subjects. In the event the samples are used for tests outside the scope of this study, they will be relabeled in an anonymous manner, so that you cannot be identified in any way. The scientific, diagnostic and/or medical significance of the research to be done is not known. Therefore, neither you nor your doctors will be informed of your individual results, and they will not affect your treatment in any way. Some of this research may result in new inventions or discoveries that may be of potential commercial value and may be patented and licensed for the development of new products. Donors of skin do not retain any property rights to the materials. Therefore, you would not share in any money or other benefits that any entity might receive for these inventions or discoveries. Your decision not to allow storage or future use of your tissue specimens will not affect your ability to participate in this study.

I have read it or it has been read to me. I have had my questions answered. I agree to take part in this study. You will be provided a copy of this signed document.

Signature Block for Capable Adult:

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

_____ _____
Signature of Participant Date

_____
Printed Name of Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent

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Signature Block for Witness:

WITNESS STATEMENT:

The participant was unable to read or sign this consent form because of the following reason:

☐ The participant is unable to read the information

☐ The participant is visually impaired

☐ The participant is non-English speaking

☐ The participant is physically unable to sign the consent form. Please describe:

_____

☐ Other *(please specify)*:

_____

For the Consent of Non-English Speaking Participants when an Interpreter is Used:

A**s** someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

_____ _____

Signature of Interpreter Date

_____

Printed Name of Interpreter

OR:

Statement from a Non-Interpreter:

As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

_____ _____

Signature of Individual Date

_____

Printed Name of Individual

Signature Block for Adult Unable to Consent:

Your signature documents your permission for the named participant to take part in this research.

_____

Printed Name of Participant

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Signature of Legally Authorized Representative	Date
Printed Name of Legally Authorized Representative	Date
Signature of Person Obtaining Consent	Date
Printed Name of Person Obtaining Consent	Date