University of Minnesota
Department of Pediatrics
Blood & Marrow Transplant Program

Biochemical Correction of Severe Epidermolysis Bullosa by Allogeneic Cell Transplantation and Serial Donor Mesenchymal Cell Infusions

Principal Investigator: Jakub Tolar, MD, PhD

You have a severe form of Epidermolysis Bullosa (EB) and have completed the screening process for this study.

This study involves a stem cell transplant using bone marrow cells from either a relative (a related donor) or an unrelated donor who is identified through the national match program. If your donor is a relative who has a previously banked umbilical cord blood unit available, we may add some of those cells to their donated marrow. All patients will undergo a stem cell transplant; however, if the donor agrees to the collection of extra bone marrow cells at the time of the collection for the transplant, an additional cell product (mesenchymal cells or MSCs) will be given at 2, 3, and 6 months, and if possible at 8 and 10 months after the transplant. The donor's decision does not affect participation in this study - all treatment, tests and procedures are identical whether or not the MSCs are given.

This consent form provides information on the treatment plan, as well as the expected risks and benefits of the proposed treatment. It also tells you what other choices you have. Once you understand the study, you will be asked to sign this form if you wish to take part.

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.

Please take time to make your decision. We encourage you to discuss your decision with your doctors, family, and friends. You will receive all appropriate medical care whether or not you decide to be in the study.

This study is being conducted by Dr. Jakub Tolar of the Department of Pediatrics at the University of Minnesota.

Background

You have a severe form of Epidermolysis Bullosa (EB), a disease that results in severe blistering throughout the body. EB is the result of a defective gene that is responsible for making a specific type of collagen, laminin, integrin, keratin or plakin. As a result, the outer layer of the skin and lining of the gastrointestinal tract is unable to anchor itself to the body.

Stem cell transplants have been successful in treating patients with a variety of inherited disorders in which the patient is missing a protein needed for the body to function correctly. Stem cells are unspecialized "master" cells that have the ability to grow into a number of specialized cells. The transplant consists of 3 parts: 1) a course of chemotherapy (anti-cancer) drugs to make room in the bone marrow for the donor's cells by wiping out blood and marrow cells; 2) infusion of the donor's marrow cells in a manner similar to a blood transfusion (the transplant); and 3) the post-transplant period waiting for the donor cells to take hold and begin to grow in the patient's bone marrow. This last part ends when the patient's blood counts return to a safe level. The entire process can take up to 2 months.

There are several stem cell populations in marrow, including one referred to as Mesenchymal Stromal Cells (MSCs). These cells can mature into any number of tissues, including those found in the skin. In addition to potentially helping to repair injured skin, there are data to suggest that MSCs may also reduce some of the complications of bone marrow transplantation—specifically rejection of the new marrow and graft-versus-host disease (GVHD), a complication where the donor's immune cells try to reject the patient. While there are multiple trials currently evaluating the effectiveness of MSCs in transplant patients, it is clear that MSCs are safe, having been given to hundreds of patients with no major side effects. In this study, MSCs will be grown in a lab at the University from a sample of the donor's bone marrow collected for the transplant. Once enough MSCs are grown, they are stored frozen until needed. The plan is to give an infusion of the MSCs at 2, 4, and 6; and if possible 8 and 10 months after the transplant during a routine post-transplant follow-up visit. MSCs are considered research and therefore require permission from the donor to collect additional bone marrow cells beyond those needed for the transplant. If your donor consents (agrees) to the extra cell collection you will receive the MSC infusions. If your donor does not consent (does not agree), you will have the transplant as planned but will not have

the MSC infusions.

Purpose of This Study

This study is based on the first EB transplant study done at the University of Minnesota with changes in the treatment plan to make it safer (less severe side effects) with quicker recovery of blood counts (reducing the risk of infection) while improving the skin healing. The purpose of this study is to determine how successful a stem cell transplant with up to five infusions of donor MSCs is for correcting the genetic error in persons with severe Epidermolysis Bullosa (EB).

Up to 69 people will be enrolled in this study.

Procedures

Pre-transplant evaluation:

If you decide to take part in this study and have signed the consent, you will be evaluated to make sure it is safe for you to participate in the study. Before starting treatment in this study, your doctor will check your general health. You will have the following tests and evaluations to find out if you can participate. Some of these tests and procedures will have been done as part of the screening and may not have to be repeated at this time.

- Medical history and physical examination, including height and weight.
- Complete a questionnaire created specifically for persons with EB called iscoreEB to assess your activity level and overall quality of life
- Routine blood tests (requiring approximate 4 tablespoons of blood) including bone marrow, liver and kidney function.
- A pre-transplant viral panel (requiring 2 tablespoons of blood) to check for exposure to viruses, including hepatitis and HIV. If you test positive for hepatitis or HIV, you will not be eligible to take part in this study. It will be recommended that a Blood Bank physician contact your personal physician regarding possible further testing. By law, the Minnesota Department of Health must be notified if you test positive for hepatitis or HIV.
- Urinalysis
- Electrocardiogram (ECG or EKG), a picture of the electrical action of the heart)
- Echocardiogram (a picture of the heart in motion made using ultrasound or sound waves) to evaluate heart function
- CT scans with contrast to look for signs of infection.

- Skin biopsies (5 samples) to assess the amount (if any) of collagen, laminin, integrin, keratin or plakin (specific for your disease) and structures by electron microscopy, fragility by a suction blister test (the ability of the skin to resist blistering using gentle suction)
- Photographs will be taken to document areas of blistering
- Biopsy by endoscopy if you have involvement of the GI (gastrointestinal) tract
- A pregnancy test if you are a female of childbearing potential

If you do not have a central venous catheter, one will be placed before treatment begins. A central venous catheter is an intravenous (IV) line that is placed under the skin in a large vein in the chest. It may remain in place for many months. A central venous catheter is used to draw blood, give drugs, and administer fluids greatly reducing the number of needle sticks.

Treatment Plan Overview:
A note about treatment numbering and transplants: The transplant always occurs on Day 0. Treatment given before the transplant (the preparative regimen) are counted backwards from day 0, using negative number (i.e. Day -1, Day -2, Day -3, etc.). Days after the transplant are indicated by positive numbers, often with a "+" sign (i.e. Day +1, Day +2, etc.).

Preparative Regimen (to prepare the bone marrow to accept the donor cells)	
Day-9	thymoglobulin IV over 6 hours
Day -8	thymoglobulin IV over 4 hours
Day -7	thymoglobulin IV over 4 hours
Day -6	fludarabine IV over 1 hour cyclophosphamide IV over 1 hour
Day -5	fludarabine IV over 1 hour cyclophosphamide IV over 1 hour
Day -4	fludarabine IV over 1 hour
Day -3	fludarabine IV over 1 hour busulfan IV over 3 hours*
Day -2	fludarabine IV over 1 hour busulfan IV over 3 hours*
Day -1	total body irradiation (TBI) given as 2 treatments at least 6 hours apart
Transplant	
Day 0	Hematopoietic Cell Infusion
Post-Transplant	
Day 1	rest
Day 2	rest
Day 3	cyclophosphamide IV over 2 hours
Day 4	cyclophosphamide IV over 2 hours
Day 5	begin drugs to prevent GVHD: tacrolimus* (continue until Day 100) mycophenolic acid mofetil (continue until Day 35)
MSC infusion at the time of routine post-transplant follow-up visits if your donor agreed to the collection of additional BM cells for the production of MSCs	
2 months	MSC Infusion #1
4 months	MSC Infusion #2
6 months	MSC Infusion #3
8 months	MSC Infusion #4
10 months	MSC Infusion #5

*excluded if donor is a full (HLA identical) match

Preparative Regimen:

The preparative regimen is given to clear space in the bone marrow for the donor cells to take hold and to lower the immune system to reduce the risk of rejecting the donor cells. All drugs are given into a vein (IV) and can be administered through a central line. On the day before the transplant, total body irradiation (TBI) is given in two treatments.

In addition to the drugs listed in the table above, drugs will be given to lessen or prevent the expected side effects.

Transplant Day:
On transplant day you will receive the donor stem cells in a manner similar to a blood transfusion through the central line.

Post-Treatment Supportive Care Drug Schedule:
After transplant, you may receive a drug called filgrastim which is used to stimulate the growth of the marrow cells. This drug will continue daily as needed until the blood cell counts recover.

To prevent rejection and graft-versus-host-disease (GVHD) cyclophosphamide is given on day 3 and 4 after the transplant. GVHD is when the donor cells attack the patient's cells and is explained in more detail in the risks of transplant section later in this consent. On the 5th day, you will start tacrolimus and mycophenolate mofetil (also called MMF) to prevent GVHD. Tacrolimus is taken daily for 3 months and MMF is taken daily until approximately 35 days after the transplant. You will not receive tacrolimus if your donor is a full (HLA identical) match to you. Your doctor will tell you if this is the case.

Post-Transplant Follow Up:
When medically safe, you will be discharged from the inpatient bone marrow transplant unit and will be followed in the bone marrow transplant outpatient clinic.

Blood tests will be performed daily or at least twice weekly during the first 100 days after transplant as part of routine transplant care. A formal clinic visit will occur at least monthly and include routine blood tests. You will be asked to complete the iscorEB questionnaire at your 3 month (day 100) visit. Skin biopsies (5 samples) and fragility testing to check for the presence of donor cells and signs of skin repair will be done at 3 month (day 100) visit. Photographs will be taken to document changes in blistering as compared to before the transplant.

After day 100 you will be seen in the clinic at 6 months, then at 1 and 2 years after transplant to assess you response to the transplant and for any late effects of the transplant procedure. You will be asked to complete the iscorEB questionnaire at each

visit. Skin biopsies (5 samples per visit) and fragility testing to check for the presence of donor cells and signs of skin repair will be done at each of these visits. Photographs will be taken to document changes in blistering as compared to before the transplant.

MSC Infusions (for persons whose donor agreed to extra BM collection):

The MSC infusions will be given as a short intravenous infusion at the 2 month (day 60), 4 month (day 120) 6 month (day 180), and, if possible, 8 month (day 240) and 10 month (day 300) clinic visits.

Research Related Studies to Better Understand EB:

The following samples will be collected for research related testing:

- Blood samples (approximately 2 teaspoons per time) for research related testing by Dr. Tolar's laboratory will be collected before the start of the preparative regimen and at 1, 2, 3, 6, 12 and 24 months after the transplant (during routine post-transplant visits).
- Additional samples will be collected for Dr. Tolar's lab anytime a skin or gastrointestinal biopsy is performed as part of your clinical care. You also may be asked to complete the iscorEB questionnaire corresponding with these additional assessments.

The samples will be labeled with an indirect identifier (a unique code assigned to you at study enrollment) so that anyone looking at the sample will not know it belongs to you. A link between the code and your name and other identifying information will be kept in a secure database. The testing will be done in the study's research laboratory at the University Of Minnesota.

After testing directly related to this study is completed and the results confirmed, any leftover samples will be destroyed, unless you agree at the end of this consent for the samples to be saved for future research.

There will be no charge to you or your health plan/insurance for this testing nor will the results influence your treatment or be placed in your medical record.

Risks of Being in This Study

Chemotherapy and TBI prior to bone marrow transplant and the cyclophosphamide, tacrolimus and MMF afterward are standard. However, these treatments are associated

with side effects and significant risks, which can be uncomfortable, and in some cases, dangerous, life-threatening, or even fatal. Based on experience with other diseases, the most common and most important of these side-effects are listed below. Importantly, nothing unusual has been observed to date in patients with EB but the number of patients treated has been limited. Therefore, there could be additional side effects in EB that have not yet been recognized.

Risks of Stem Cell Transplantation
The following problems may occur as a result of the transplantation of bone marrow or blood:

Slow recovery of blood counts. The red blood cells, white blood cells and platelets can be slow to recover after stem cell transplantation. Until your counts recover you will be dependent on blood and platelet transfusions, and will be at risk for bleeding and infection. Although infections can be treated with antibiotics, occasionally they can be very dangerous or fatal.

Failure of the donor cells to grow (engraft). Engraftment is when the donor's blood-forming cells start to grow and make healthy blood stem cells that show up in your blood. Lack of donor engraftment occurs when

1) blood tests show poor blood count recovery (graft failure) or
2) blood counts recover, but they are not from the donor's cells and instead from the patient's own cells (auto recovery)

Both indicate the transplant was not successful and a second transplant will be done whenever possible. If you proceed with a second transplant, any additional MSC doses can be saved and used on the same schedule. A second transplant would be explained using a separate consent form. Past experience suggests this occurs in about 20% of patients.

Graft-Versus-Host Disease (GVHD). This condition results from the transplanted stem cells recognizing your body as foreign and attacking it. GVHD can be treated but it can be severe or fatal. You will be monitored closely for this complication and given specific treatment to prevent and treat it.

There are 2 forms: acute GVHD (occurs in the first 3 months after transplant) and chronic GVHD (after the first 3 months). Acute GVHD may produce skin rash, nausea, vomiting,

diarrhea, abnormalities of liver function and an increased risk of infection. To confirm the diagnosis of acute GVHD, you may be asked to have a skin biopsy and possibly a gut and very rarely a liver biopsy. Chronic GVHD may produce skin rashes, hair loss, thickened skin, dry eyes, dry mouth, liver disease, weight loss, diarrhea and an increased risk of infection.

Other complications that can result from the transplantation procedure not specifically related to one specific drug or the stem cells or this study include:

Damage to the vital organs of the body. This could result in malfunction of any organ in the body such as heart, lungs, liver, gut, kidneys and bladder, brain etc. The lungs and the liver are particularly vulnerable. Some patients will experience severe lung problems due to infections and/or due to a reaction of the lungs to the chemotherapy and radiation. Some patients can suffer veno-occlusive disease of the liver (VOD). This is a complication that may result from high doses of chemotherapy. Patients who have VOD become jaundiced (yellowish skin), have liver function abnormalities, abdominal swelling, and abdominal pain. Although many patients recover completely, these complications may result in organ failure and permanent damage or even death.

Serious infections. Full and complete recovery of your immune system may take many months following the initial recovery of the white cell count. During this time, there is an increased risk of infections. You will be prescribed certain medications to reduce the chance of those infections. However, preventative treatments are not always effective. If you have an infection, you may have to stay in the hospital longer or be re-hospitalized after transplant. Infections can be fatal. It is possible that patients with severe EB will be at higher risk of infection due to the skin and mucosal breakdown that already exists prior to the chemotherapy. It is also possible that the addition of antithymocyte globulin (ATG) may increase the risk that certain viruses, like EBV which causes mononucleosis, will reactivate in those previously exposed to the virus before transplant.

Sterility and future childbearing potential for men and women: Chemotherapy may affect fertility. Male patients may become sterile (unable to produce sperm). Female patients may find that their menstrual cycle becomes irregular or stops permanently. However, this DOES NOT MEAN THAT WOMEN CANNOT BECOME PREGNANT, and, if you are sexually active she/he must use some effective method of birth control. Damage to reproductive tissue may result in birth defects or permanent inability to father a child or

become pregnant. You should discuss these risks and options in detail with your doctor before entering this study.

Central venous catheter: Placement and use of central venous access is routine. The most common complications are clotting and local infection which sometimes leads to a generalized infection in the blood. Clotting may require the catheter to be removed or treatment with a medicine to dissolve blood clots. Infections will be treated with antibiotics, and sometimes, removal of the catheter is required. Occasionally, skin redness at the catheter exit site occurs, this may require antibiotic treatment. There is also a small risk of puncturing the lung at the time of the catheter insertion. If this occurs, placement of a temporary chest tube to re-inflate the lung may be required. There are no long-term effects once the lung puncture has resolved. Importantly, it has been observed a higher than usual rate of the central line being pulled out accidentally in patients with EB because of the inability to tape the line to the skin. Therefore, it is possible that you will need the line replaced multiple times during the therapy.

Risks of Donor MSC Infusion (if given): The infusion of MSCs could result in allergic reactions. You will receive medications to prevent or reduce the severity of an allergic reaction. Long term adverse effects of MSC infusion have not been described to date in patients. However, in one animal study, MSCs cultured in the laboratory for prolonged periods caused a cancer. The MSCs for this study will be culture expanded for only over a short period (3-4 weeks) as has been done for other patients.

It is also possible that the collection may not yield enough cells to infuse, or the cells may not pass our standards for infusion. If that happens, the infusion you receive may not contain a helpful number of cells, or you may not be able to receive the MSC infusion at all. If this occurs, we will discuss the situation with you and review your options.

Risks of Chemotherapy and Supportive Care Drugs

For the risks of the chemotherapy and supportive care drugs, please see Appendix A at the back of this consent.

Risks of completing the iscorEB questionnaire

Completing the questionnaire may remind you of how EB affects your life on a daily basis. This may make you sad or angry. You may refuse to complete any question that makes you feel uncomfortable.

Risks of Skin Tests

Skin biopsy. The most common side effect is slight soreness for several days at the site of the skin biopsy. It may be associated with some discomfort from the placement of the lidocaine, the anesthetic. There may be bleeding and bruising. Rarely, infection may occur. The skin biopsy will leave a small scar.

*Skin fragility test***.** There is mild if any discomfort from the continuous suction used to make the blister. However, the blister site will likely be very sensitive for several days to anything, like clothes that rub the area. The procedure is not likely to leave any scar.

Benefits Of Being In The Study

Benefit cannot be guaranteed. On the basis of results in animal studies and in the first patients with one form of severe EB—called recessive dystrophic EB in which normal collagen type VII is missing—it appears that a reduction in blistering and need for dressings is possible. Rate of improvement and completeness of response may be variable. For patients with other forms of severe EB, it is unknown whether there will be any benefit.

Alternatives To Being In The Study

If you decide that you do not want to be in the study, there may be other options for treatment, potentially including stem cell transplant using bone marrow cells from a related or an unrelated donor. You may wish to continue conventional treatment with skin ointments and/or skin grafts. No treatment may be an option. You can discuss these options with your doctor.

Costs

You and your insurer will not be charged for any of the research tests performed on your blood and biopsy samples or the production of the MSCs (if given).

The costs of the transplant procedure including the preparative regimen, donor cell collection, medications to prevent or reduce side effects, tests and procedures done to assess your health, the hospitalization, and clinic visits will be charged to you and/or your health insurance/health plan. You also will be responsible for any co-payments and deductibles.

Prior to transplant, the Transplant Coordinator will verify your coverage with your insurance company to be sure that you are pre-authorized before beginning any part of

this study. If you have concerns or questions regarding coverage or potential charges, you should contact the patient financial representative at (612) 273-2800.

You will not be paid or compensated 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. If you think that you have suffered a research related injury let the study physicians know right away.

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.

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 data 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. Any images of the skin or biopsy material will not include any information that would make it possible for anyone to identify you.

A panel of experts in transplant medicine and EB will be reviewing information about you. They are required to sign a confidentiality agreement prior to receiving access to your information. All identifying information will be removed. However, information will include photographs of involved areas of your skin, including your face if appropriate. This material will be provided either via a secure password protected website or by private fax machine. These individuals will review the information to assess your response to the treatment.

If you decide to participate in this study, some private health information will be stored in a computer database at the Masonic Cancer Center (which includes all bone marrow transplant patient information at the University of Minnesota, whether or not cancer related). This information will include your name and medical record number, date of birth,

diagnosis, race/ethnicity, and information about 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.

Organizations that may inspect and/or copy your records for quality assurance and data analysis include:

- Departments at the University with appropriate regulatory oversight;
- The Masonic Cancer Center at the University of Minnesota and/or their designee;
- National and international transplant registries including the Center for International Blood and Marrow Transplant Research (CIBMTR) and National Marrow Donor Program (NMDP)
- Government agencies including the Food and Drug Administration (FDA) and the Office for Human Research Protections, (OHRP). These agencies may review the research to see that it is being done safely and correctly.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment. Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

A description of this clinical trial is available on 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 may search this web site at any time.

Voluntary Nature Of The Study

Your participation in this study is voluntary and your decision whether or not to participate in this study will not affect your relations with the University of Minnesota Medical Center, Fairview or with the physicians.

If you decide to participate, you are free to withdraw at any time. However, there are times during this study that it could be dangerous for you to quit; for example, if you have already received the preparative regimen but has not yet received the transplant, your marrow may not recover and the chances of dying would be much higher.

If during the course of the study there are significant findings discovered which might influence your willingness to continue, the researchers will inform you of those developments.

Questions

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. Jakub Tolar at 612-626-2961).

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 or go to https://research.umn.edu/units/hrpp/researchparticipants/questions-concerns.

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.

Optional Consent For Storing Leftover Research Samples

There may be some blood cells, MSCs and or tissue collected for research purposes leftover at the end of the study related testing. With your permission; we would like to store them for up to 15 years after the study ends for future analysis as new research tests become available. These samples will be the property of and under the control of

the Principal Investigator Dr. Jakub Tolar. They will not be used for studies other than ones to learn about epidermolysis bullosa.

The samples will be stored with indirect identifiers. They will be labeled with a unique code number, rather than a name or medical record number, and the samples can only be linked back to the patient using a master list for the study. This master list will be kept in a secured manner and only accessible to persons directly involved with the research.

There will be no cost to you for storing and future testing of the leftover samples. You will not be paid for allowing your samples to be used for future research. Because it is not known how soon these samples will be used, you will not be given the results of the tests.

Fifteen years after the end of the study any remaining samples will be destroyed. However, if you agree to storage now and later change your mind, you may request to have any remaining identifiable samples destroyed by contacting your study doctor or another member of the study staff.

Optional Consent For Skin Grafting Using the CelluTome® Epidermal Harvesting System

If,you still have wounds that have not healed 3 months after transplant and if your original marrow donor agrees to donate skin cells, you will have the option to receive skin grafts to help heal the wounds. The procedure will treat such areas by covering the wounds with a square of surgical tape (similar to 3M's Tegaderm® transparent dressing) that has been loaded with skin cells collected from the donor. The surgical tape is left on for a recommended 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 with minimal loss of blood for both the person donating the skin cells and for the person receiving them.

This graft procedure would be performed up to three times, with sessions about three months apart.

Weekly photographs of the areas treated with the CelluTome device are requested through 12-weeks post-treatment. These can be sent to the University of Minnesota study team via email or other photo-sharing method. Additionally, we would request you follow-

up in clinic at 6 weeks, 12 weeks, and 1-year after the grafting session if possible for photographs and evaluation of the treated wounds.

There is a small amount of risk from receiving donor skin cells. 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 costs of the graft procedure will be billed to your insurance. Preauthorization will be requested by a patient financial representative who will work with you and your nurse coordinator.

Consent for Storage of Leftover Samples for Future Research

☐ YES, I consent (agree) to the storing of any leftover samples for future research to learn about EB.

☐ NO, I do not consent (do not agree) and want any leftover samples destroyed once research directly related to this study is completed.

Consent for Skin Grafting

☐ YES, I consent (agree) to receiving skin grafts.

☐ NO, I do not consent (do not agree) to receiving skin grafts.

YOU WILL BE GIVEN A COPY OF THE SIGNED CONSENT FORM TO KEEP

Statement of Consent

I have read the information in this consent form and have had the study explained to me. My questions have been answered to my satisfaction. I agree to take part in this study.

Signature of Patient	Date
Signature of Person Obtaining Consent	Date

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

APPENDIX A --RISKS OF THE CHEMOTHERAPY:

Anti-Thymocyte Globulin (ATG)		
Common (experienced by >20% or between 20 and 100 out of 100 patients)	**Less Common** (experienced by 5-20% or between 5 and 20 out of 100 patients)	**Rare** (experienced by <5% or fewer than 5 out of 100 patients)
• fever • chills • low white blood cell count with increased risk of infection • low platelet count with increased risk of bleeding • pain • headache • abdominal pain • diarrhea • high blood pressure (hypertension) • nausea • swelling of hands and/or feet (peripheral edema) • shortness of breath (dyspnea) • loss or lack of strength (asthenia) • high levels of potassium in the blood (hyperkalemia) • rapid heartbeat (tachycardia)	• feeling poorly (malaise) • dizziness	• severe allergic reaction (anaphylaxis)

Fludarabine		
Common (experienced by >20% or between 20 and 100 out of 100 patients)	**Less Common** (experienced by 5-20% or between 5 and 20 out of 100 patients)	**Rare** (experienced by <5% or fewer than 5 out of 100 patients)
• low white blood cell count with increased risk of infection • low platelet count with increased risk of bleeding • low red blood cell count (anemia) with tiredness and weakness • tiredness (fatigue) • nausea • vomiting	• pneumonia • diarrhea • loss of appetite • weakness • pain	• numbness and tingling in hands and/or feet related to irritation of nerves • changes in vision • agitation • confusion • clumsiness • seizures • coma • cough • trouble breathing

Fludarabine		
Common (experienced by >20% or between 20 and 100 out of 100 patients)	**Less Common** (experienced by 5-20% or between 5 and 20 out of 100 patients)	**Rare** (experienced by <5% or fewer than 5 out of 100 patients)
• fever and chills • infection		• intestinal bleeding • weakness • death due to effects on the brain, infection, bleeding, severe anemia, skin blistering, or other causes

Cyclophosphamide		
Common (experienced by >20% or between 20 and 100 out of 100 patients)	**Less Common** (experienced by 5-20% or between 5 and 20 out of 100 patients)	**Rare** (experienced by <5% or fewer than 5 out of 100 patients)
• low white blood cell count with increased risk of infection • low platelet count with increased risk of bleeding • low red blood cell count (anemia) with tiredness and weakness • nausea/vomiting • mucositis (sores in the mouth and esophagus, which may be painful and cause difficulty swallowing) • inability to have children • diarrhea • fluid weight gain/edema • hair loss	• hemorrhagic cystitis (inflammation of the bladder with severe bleeding)	• cardiomyopathy (heart muscle becomes damaged and the heart doesn't pump properly) • skin rash • SIADH (Syndrome of Inappropriate Anti-diuretic Hormone)

A drug called Mesna will be given to reduce the risk of damage to the bladder with severe bleeding (hemorrhagic cystitis). The most common risks of Mesna include: nausea, vomiting, tiredness, headache, pains in your legs and arms and an unpleasant taste in your mouth.

Total Body Irradiation		
Common (experienced by >20% or between 20 and 100 out of 100 patients)	**Less Common** (experienced by 5-20% or between 5 and 20 out of 100 patients)	**Rare** (experienced by <5% or fewer than 5 out of 100 patients)
• nausea and vomiting • diarrhea • cataracts • sterility • endocrinopathies including hyperthyroidism (may cause fatigue, weight loss, rapid heartbeat, sweating, trouble with heat, nervousness) or hypothyroidism (may cause fatigue, weight gain, fluid retention, feeling cold, decreased cognitive function) • growth failure • intestinal cramps • mucositis (sores in the mouth and esophagus, which may be painful and cause difficulty swallowing)	• parotitis (painful swelling under the jaw) • interstitial pneumonitis- a lung disorder that may make moving air in and out of the lungs difficult • generalized mild erythema (redness of the skin) • veno-occlusive disease (explained under risks of transplant – damage to vital organs	• dysphagia (difficulty swallowing) • vertebral deformities • kidney damage • risk of malignancy years later (when given along with chemotherapy)

Busulfan– excluded if your donor is a full (HLA identical) match to you		
Common (experienced by >20% or between 20 and 100 out of 100 patients)	**Less Common** (experienced by 5-20% or between 5 and 20 out of 100 patients)	**Rare** (experienced by <5% or fewer than 5 out of 100 patients)
• Nausea/vomiting • mucositis (sores in the mouth and esophagus, which may be painful and cause difficulty swallowing) • Rash • low white blood cell count with increased risk of infection • low platelet count with increased risk of bleeding • low red blood cell count	• veno-occlusive disease (explained under risks of transplant – damage to vital organs • Difficulty breathing and lung disease including pneumonia, hemorrhage and/or tissue build up	• Seizures • liver failure

Busulfan– excluded if your donor is a full (HLA identical) match to you		
Common (experienced by >20% or between 20 and 100 out of 100 patients)	**Less Common** (experienced by 5-20% or between 5 and 20 out of 100 patients)	**Rare** (experienced by <5% or fewer than 5 out of 100 patients)
(anemia) with tiredness and weakness • Diarrhea • Fluid weight gain • Hair loss • Skin discoloration •		

To check the level of busulfan in your body, we will take a little less than a teaspoon of blood right after each busulfan infusion, 15 minutes after each busulfan infusion, 1 hour after each busulfan infusion, 3 hours after each busulfan infusion, 5 hours after each busulfan infusion, 7 hours after each busulfan infusion, and right before the second busulfan infusion. The blood will be taken from your line.

Supportive Care Drugs

Mycophenolate mofetil (MMF)		
Common (experienced by >20% or between 20 and 100 out of 100 patients)	**Less Common** (experienced by 5-20% or between 5 and 20 out of 100 patients)	**Rare** (experienced by <5% or fewer than 5 out of 100 patients)
• miscarriage • birth defects • diarrhea • damage to unborn baby • limited effectiveness of birth control • stomach pain • upset stomach • vomiting • headache • tremors • low white blood cell count with increased risk of infection	• anemia • rash • difficulty falling asleep or staying asleep • dizziness • uncontrollable hand shakes	• difficulty breathing • unusual bruising • fast heartbeat • excessive tiredness • weakness • blood in stool • bloody vomit • change in vision • cancers, such as lymphoproliferative disease or lymphoma • progressive multifocal leukoencephalopathy – a disorder of the brain with a variety of symptoms including

Mycophenolate mofetil (MMF)		
Common (experienced by >20% or between 20 and 100 out of 100 patients)	**Less Common** (experienced by 5-20% or between 5 and 20 out of 100 patients)	**Rare** (experienced by <5% or fewer than 5 out of 100 patients)
• increased blood cholesterols • swelling of the hands, feet, ankles or lower legs		muscle weakness, difficulty with speaking and/or movements

Addendum for Females taking MMF:

1. MMF could be damaging to an unborn baby if you are pregnant or become pregnant while receiving the drug.

2. MMF can limit the effectiveness of birth control pills and thus increase your chances of becoming pregnant while taking it.

Tacrolimus - excluded if your donor is a full (HLA identical) match to you		
Common (experienced by >20% or between 20 and 100 out of 100 patients)	**Less Common** (experienced by 5-20% or between 5 and 20 out of 100 patients)	**Rare** (experienced by <5% or fewer than 5 out of 100 patients)
▪ kidney problems ▪ loss of magnesium, calcium, potassium ▪ high blood pressure ▪ tremors ▪ increases in cholesterol and triglyceride	▪ nausea ▪ vomiting ▪ liver problems ▪ changes in how clearly one can think ▪ insomnia ▪ unwanted hair growth ▪ confusion	▪ seizures ▪ changes in vision ▪ dizziness ▪ red blood cell destruction

It is very important that grapefruit or drinks with grapefruit juice are not consumed while taking Tacrolimus. Grapefruit has an ingredient called bergamottin, which can affect some of the treatment drugs used in this study**.** Common soft drinks that have bergamottin are *Fresca*, *Squirt*, and *Sunny Delight*.

G-CSF (Filgrastim)		
Common (experienced by >20% or between 20 and 100 out of 100 patients)	**Less Common** (experienced by 5-20% or between 5 and 20 out of 100 patients)	**Rare** (experienced by <5% or fewer than 5 out of 100 patients)
• ache or pain inside the bones	▪ local irritation at injection site ▪ increased levels of liver enzymes and uric acid in the blood, low number of platelets in the blood ▪ fever	▪ allergic reaction, low fever ▪ enlargement of the spleen and even splenic rupture (rare) ▪ worsening of pre-existing skin rashes, ▪ hair loss ▪ inflammation of a blood vessel in the skin