utmb Health

IRB #19-0298

The University of Texas Medical Branch at Galveston

Protocol Title: Growth Hormone Therapy for Muscle Regeneration in Severely Burned Patients

IRB Number: 19-0298

Principal Investigator: Ludwik K. Branski, M.D., M.M.S,
Shriners Burns Hospital, 815 Market St, Galveston, TX 77550,
(409)770-6741, Fax (409) 770-6919

Why am I being asked to take part in this research study?

You are being asked to take part in this study because you have a severe burn injury over 30% or more of your total body surface. Your participation in this study is completely voluntary. You may refuse to participate or stop your participation in this research study at any time without penalty or loss of benefits and without jeopardizing your medical care at UTMB.

Study Summary:
The following things you should know about this research study:

- The purpose of the study is to investigate the long-term effects of growth hormone in severely burned adult patients, including side effects, and determine if growth hormone can improve quality of life by preventing height, weight and muscle loss in burned patients.
- If you choose to participate, you will be asked to take human growth hormone injections or placebo (injection of saline, a salt solution, that does not contain any drug) daily until 9 months after burn injury. You will participate in the study until about 24 months (2 years) after your burn injury. Your total length of participation in this study depends on when you were discharged from the Burn Unit, meaning how many months after your burn injury you were discharged from the hospital. For example, if you were discharged 3 months after your burn injury then you will be participating in the study longer than someone who was discharged from the hospital 6 months after their burn injury. The study team will try to conduct all study-related procedures at the same time you come back for routine clinic appointments, specifically 6 months, 12 months, 18 months and 24 months after your burn injury. The required procedures and frequency are summarized below in a chart.
- Risks or discomforts from this research may include slight pain during injections or hypertrophic scarring (thick, raised and often red-colored scars). Long-term use of growth hormone may increase calcium and glucose levels in your blood which may require you to temporarily or completely stop giving yourself the study drug. High calcium levels may increase your risk of developing a kidney stone. Other common side effects that may occur include numbness, tingling, carpal tunnel syndrome, stiffness in arms or legs, joint pain, muscle pain, retaining fluids (swelling), upper respiratory infection, fatigue or back pain. Additional less common side effects are listed below in the "Risks" section. In addition, some of the study procedures have their own risks.
- The study may or may not be of direct benefit to you. Potential direct benefit may include the prevention of height loss, weight loss, muscle loss or loss of strength which may help you to do things sooner, such as returning to work. We hope the information learned from this study will benefit other severely burned adults in the future.
- Taking part in this research study is voluntary. You do not have to participate, and you can stop at any time.
- The US Department of Defense is providing funding for this study.

Please take your time to read the entire form and ask questions before deciding if you want to take part in this research project.

Detailed Consent Information:

What is the purpose of this research study?
Severe burn causes the loss of muscle and bone. Muscle and bone loss are associated with a longer need for rehabilitation. The purpose of this study is to investigate the long-term effects of growth hormone in severely burned adult patients, including side effects, and determine if growth hormone can improve quality of life by preventing height, weight and muscle loss.

How many people will take part in this study?
About 62 people will take part in this study at UTMB.

Group Assignment/Randomization/Study Drug:
If you consent to participate in this study, you will be randomly assigned (like flipping a coin) to either receive the recombinant human growth hormone (GH) or placebo. Neither you or the doctor and study team will know whether you are receiving GH or placebo [both GH and placebo will be referred to as "study drug" in the remainder of the consent form]. You will begin receiving the study drug (GH or placebo) within 2 ½ weeks before your planned discharge from the Blocker Burn Unit. The group receiving GH will start with a lower dose that will be increased throughout the week. If you are in the group that receives GH, the dose will be calculated based on your weight, but will not exceed the maximum dose of 5 milligrams (mg) per day if your between 18 – 64 years old or 3.5 mg if you are between 65 – 85 years old. The study drug dose will be prepared by the investigational pharmacy so that the study doctor, study team and you will not know if you are receiving GH or placebo. The study drug (GH or placebo) is taken by injection in your fat tissue, usually in your stomach, but it may depend on what areas of your body that you were burned. You will be taught to give the study drug injection to yourself by a nurse. As you learn to give yourself the injection, a nurse will be present to assist, answer questions and make sure you are doing it correctly. Once you are discharged from the burn unit you will be responsible for self-injecting the study drug in your fat tissue once every day until you are 9 months post burn injury. In the event you are not physically able to give yourself an injection, for example limited use of your fingers or an amputation, your caregiver, if s/he agrees, can be trained to give it to you.

What procedures are involved as part of this research study?
If you agree to take part, you will be asked to sign this consent form and have the following tests and procedures done. If you participate, you will be asked to come back about every 6 months until 24 months (2 years) after your burn injury. The study team will try to coordinate these study visits to occur on the same day you come for your routine clinic appointments to minimize the amount of travel to and from the burn unit. The number of times you come for a study visit will vary based on how many months post-burn you are at the time of your discharge. You may have between 2 to 7 study visits until 2 years after your burn injury.

Study Procedures:
We will review your medical history, including the care you received for your burn, and all medications including over the counter medications that you are taking.

All of the following activities and tests will be performed for **<u>research</u>** purposes at your **baseline, 6, 12, 18 and 24 month post burn injury study visits**, unless otherwise noted:

- Medical History, including the care you received for your burn *(baseline only)*

- Review current medications and health changes
- Ask if you have had any change in your health or side effects *(6, 12,18 and 24 month post burn injury only)*
- Quality of Life Questionnaire (QOL) – You will answer questions about your physical abilities and how your burn injury interferes with work and daily activities.
- Dual-Energy X-ray Absorptiometry (DEXA) Scan – You will lie still on an open X-ray table for a few minutes as the scanner passes over your body to measure muscle, fat and bone density. This will help us see any changes in your muscles and bones over time.
- Bruce Treadmill Test – You will be asked to exercise on treadmill.
- Biodex Isokinetic Dynamometer – You will be in a seated position and asked to flex and extend your leg several times to test the strength of your leg, if you are physically able to do so.
- Hand Dynamometer – If you are physically able to, we will ask you will squeeze a device that will measure the strength of your hand grip three times.
- Indirect Calorimetry – You will breathe in and out of a mouthpiece to measure how much energy your body needs.
- Echocardiogram – You will lie down while gel is placed on your chest and a transducer (handheld device that emits sound waves) is slowly moved over the gel to obtain images of your heart.
- Electrocardiogram (ECG) – Patches are placed on your chest, arms and ankles where electrodes are attached to record your heartbeat.
- Six-Minute Walk Test – You will be asked to safely walk for six minutes on a flat surface so the distance can be measured.
- Pulmonary Function Test – You will be asked to breathe deeply and then breathe out as hard as you can into a tube (spirometer) that is attached to a computer screen. This helps to measure the health of your lungs.
- Doubly Labeled Water Study – You will be asked not to eat anything for 6 hours before drinking a special preparation of water that contains isotopes. These isotopes are eliminated from your body in urine. You will collect your urine samples seven times over two weeks to measure the isotopes and measure how efficiently your body uses energy. You will be sent home with supplies to collect and send back the urine samples.
- Scar Measurements – We would like to measure the development of your scars over time by using photography and performing an analysis of the scar development, as well as a scar perfusion test that is pain free, radiation free and non-invasive and is based on the Doppler Technique, and scar quality measurements that assess the softness of the scar (pliability) and general scar quality.
- Lab tests - As part of the study, about 22 ml (about 1 ½ tablespoons) of blood will be collected from your vein with a needle to perform IGF-1, lactic acid, A1C, glucose, and calcium levels at both your routine clinic visits and scheduled study visits.

  FEMALES will provide either a urine or blood sample to test for pregnancy. If you become pregnant during the course of the study you will be removed from the study.

  The total amount of blood collected for research during the entire study will vary based on the number of routine clinic appointments you have. We estimate that over 2 years it will be between 6 ½ oz (195 ml) to 14 oz (415 ml).

What are the possible risks for choosing to participate in this research study?
While on this study, you may be at risk for possible side effects. Most of them are listed in this form, but they will vary from person to person. You should discuss these with the researchers and your regular health care provider. The research related procedures may also involve risks that cannot be predicted at this time.

Treatment with Growth Hormone (GH)
Common side effects (likely to occur in fewer than 1 in 10 patients):

- Numbness or tingling
- Pain or burning sensation in the hands or forearms (known as Carpal Tunnel Syndrome)
- Stiffness in the arms and legs
- Joint pain
- Muscle pain
- Retaining fluids (swelling)
- Upper Respiratory Infection
- Fatigue
- Back Pain

Uncommon side effects (likely to occur in fewer than 1 in 100 patients):

- Increased heart rate
- Increased calcium in the blood that may increase your risk of developing a kidney stone

Rare side effects (likely to occur in fewer than 1 in 1,000 patients):

- Type 2 diabetes
- Intracranial hypertension (increased pressure in the skull due to swelling of the brain) which causes symptoms such as a strong headache that will not go away, vision problems, nausea or vomiting*. Call Dr. Branski if you have any of these symptoms.*
- Rash
- Itching
- Raise itchy bumps on the skin
- High blood pressure
- Tumor formation
- Hypertrophic scarring (thick, raised and often red-colored scars)

Very rare side effects (likely to occur in fewer than 1 in 10,000 patients)

- Leukemia

These risks are minimized by restricting the GH dose based on your weight and age. Lab tests will be done to test your glucose (blood sugar) and calcium and we will treat high levels according to the standard of care. If you have uncontrollably high calcium or sugar levels, the GH dose will be lowered or may be completely stopped by the study doctor.

Dual-energy x-ray absorptiometry (DEXA)
This research study involves exposure to radiation from DEXA procedures. This radiation exposure is not necessary for your medical care and is for research purposes only. The total amount of radiation that you will receive in this study is estimated to be 0.125 mSv or 12.5 mrem, which is approximately equivalent to a uniform whole body exposure of 15.2

days of the average annual natural background radiation (300 mrem). This use involves minimal risk and is necessary to obtain the research information desired.

Bruce Treadmill Test
You may feel uncomfortable while walking on the treadmill and breathing into a tube. If you let us know that you feel uncomfortable, we will stop the test immediately.

Biodex Isokinetic Dynamometer (leg strength), hand dynamometer (grip strength) or 6-Minute Walk Test (walking ability)
You may feel very tired or dizzy during these tests. If so, please stop immediately and we will monitor you.

Pulmonary Function Test
You may experience small discomfort as you are breathing in and out of the tube for this test. We will stop as soon as you let us know that you feel uncomfortable. We will monitor you very carefully to make sure that there are no problems as you are breathing in and out of the tube.

Blood Samples
You may experience minimal discomfort and/or pain when the needle enters the vein during blood draws. We will draw an approximate total of 195 mLs (6 ½ oz or 14tablespoons) to 415 mLs (14 oz or 28 tablespoons) over a 2-year period. This amount of blood drawn is minimal and does not increase your risk for anemia. Although very rare, infection, excess bleeding, clotting, and fainting are possible.

Indirect Calorimetry, Echocardiogram and EKG readings
There are no known risks from indirect calorimetry, echocardiogram, and EKG readings.

Scar Development Monitoring
There are no known risks associated with the tests we will use to measure your scar development such as the Vancouver scar scale and the laser Doppler, or with the equipment we will use to measure your scars such as the durometer and the pneumotonometer.

Quality of Life (QOL) Questionnaires
Although it is unlikely, you may feel uncomfortable answering some of the questions in the questionnaire. You may refuse to answer any of the questions, take a break or stop your participation in this study at any time.

Loss of Confidentiality
Any time information is collected; there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

Risks to Sperm, Embryo, Fetus or Breast-fed Infant
Males: Being in this research may damage your sperm, which could cause harm to a child that you may father while on this study. If you take part in this study and are sexually active, you must agree to use a medically acceptable form of birth control. Medically acceptable forms of birth control include:

(1) Surgical sterilization (vasectomy), or
(2) A condom used with a spermicide (a substance that kills sperm).

Females: If you are part of this study while pregnant or breast-feeding an infant, it is possible that you may expose the unborn child or infant to risks. For that reason, pregnant and breast-feeding females cannot participate in the study. If you are able to become pregnant, a pregnancy test will be done with either urine or blood and it must be negative before you participate in this study. If you take part in this study and you are sexually active, you and any person that you have sex with must use medically acceptable birth control (contraceptives) during the study. Medically acceptable birth control (contraceptives) includes:

(1) Surgical sterilization (such as hysterectomy or "tubes tied"),

(2) Approved hormonal contraceptives (such as birth control pills, patch or ring; Depo-Provera, Implanon),

(3) Barrier methods (such as condom or diaphragm) used with a spermicide (a substance that kills sperm), or

(4) An intrauterine device (IUD).

If you do become pregnant during this study, you must tell the researchers immediately. The research treatment or procedures may involve risks to the embryos or fetus that are not known at this time, therefore, if you become pregnant you will be withdrawn from the study.

Pregnancy tests performed during the early stages of pregnancy do not always reveal pregnancy. Therefore, radiation exposure that includes the reproductive organs will be limited to the first ten days after a woman who can become pregnant has begun her most recent menstrual period. This is standard policy in clinics and hospitals within UTMB. This policy applies unless there is an important medical reason requiring radiation outside this period.

What are the potential benefits for participating in this research study?
If you agree to take part in this study, there may or may not be direct benefits to you. We hope the information learned from this study will benefit others severely burned in the future. Potential direct benefit may include the prevention of height loss, weight loss, muscle loss or loss of strength which may help you to do things such as returning to work sooner. We hope the information learned from this study will benefit other severely burned adults in the future.

Will I be paid for participating in this research study?
There are no funds available to pay for parking expenses, transportation to and from the Blocker Burn Unit, lost time away from work and other activities, lost wages, or childcare expenses.

Is there an alternative treatment/procedure?
You do not have to participate in this research to receive care for your medical problem. Instead of being in this study, you have the following options:

- There is no alternative treatment. The alternative is to not participate in the study. Please note that you will receive all treatment relevant to your burn care whether you choose to participate in this study or not.

Please talk to the researchers or your personal doctor about these options.

If I agree to take part in this research study, can I be removed from the study without my consent?
Yes. The researchers may decide to take you off this study if:

- Your medical problem remains unchanged or becomes worse.
- The researchers believe that participation in the research is no longer safe for you.
- The researchers believe that other treatment may be more helpful.
- The sponsor or the FDA stops the research for the safety of the participants.
- The sponsor cancels the research.
- You are unable to keep appointments or to follow the researcher's instructions.

Will my insurance provider or I be charged for the costs of any part of this research study?
No. Neither you, nor your insurance provider, will be charged for anything done only for this research study (i.e., Study Drug, or Monitoring/Follow-up Procedures described above).

However, the standard medical care for your condition (care you would have received whether or not you were in this study) is your responsibility (or the responsibility of your insurance provider or governmental program). You will be charged, in the standard manner, for any procedures performed for your standard medical care.

What will happen if I am harmed as a result of taking part in this study?
It is important that you report any illness or injury to the research team listed at the top of this form immediately.

Compensation for an injury resulting from your participation in this research is not available from the University of Texas Medical Branch at Galveston.

You or your insurance company or health care plan, will be billed and you will be responsible for any charges.

You will be responsible for paying any costs related to illnesses and medical events not associated with being in the study. There are no plans to provide other forms of compensation. However, you are not waiving any of your legal rights by participating in this study.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?
Yes. You will be told if any new information becomes available during the study that could cause you to change your mind about continuing to participate or that is important to your health or safety.

How will my information be protected?
All results obtained in this study will be kept confidential and only available to the research study team. Your individual information will not be reported, only the results of all participants as a group.

Data or specimens collected in this research might be de-identified and used for future research or distributed to another investigator for future research without your consent.

You will be assigned a unique subject ID (such as 001, 002) that will be used when information and blood samples are collected for research. Only the study team will have access to the key that links the subject ID to your identity. Blood samples that are collected and sent to the UTMB lab for testing, such as calcium and glucose levels, will have your name on them, however, the results recorded in your study record will be listed with your subject ID.

Clinicaltrials.gov Registration Information
A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

How will my privacy be protected?
We have rules to protect information about you. Federal and state laws and the federal medical Privacy Rule also protect your privacy. By signing this form, you provide your permission, called your “authorization,” for the use and disclosure of information protected by the Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records. This could include information about HIV and genetic testing, or treatment for drug or alcohol abuse or mental health problems.

The research team will know your identity and that you are in the research study. Other people at UTMB, particularly your doctors, may also see or give out your information. We make this information available to your doctors for your safety. If you think this study might affect your clinical care, please inform your doctor.

People outside of UTMB may need to see or receive your information for this study. Examples include government agencies (such as the Food and Drug Administration and Department of Defense), safety monitors, other sites in the study and companies that sponsor the study.

The Department of Defense (DOD) is authorized to review and have access to research records as part of their responsibility to protect human volunteers in research.

We cannot do this study without your authorization to use and give out your information. You do not have to give us this authorization. If you do not, then you may not join this study.

We will use and disclose your information only as described in this form; however, people outside UTMB who receive your information may not be covered by this promise or by the federal Privacy Rule. We try to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee that your information will not be re-disclosed.

The use and disclosure of your information has no time limit. You may revoke (cancel) your permission to use and disclose your information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, phone and information are on page one of this consent form.

If you do cancel your authorization to use and disclose your information, your part in this study will end and no further information about you will be collected. Your revocation (cancellation) would not affect information already collected in the study, or information we disclosed before you wrote to the Principal Investigator to cancel your authorization.

Finally, please specifically authorize the use of your private health information relating to substance abuse, psychiatric information, or HIV/AIDS, if applicable, for the above-described purposes.

Initial: _____

Whom can I contact with questions about this Research study?

If you have any questions, concerns or complaints before, during or after the research study, or if you need to report a research related injury or bad side effect, you should immediately contact Ludwik K. Branski, M.D., M.M.S. at (409) 770-6742 or, if after normal office hours, page Dr. Branski at 409-643-0797.

This study has been approved by the Institutional Review Board. If you have any complaints, concerns, input or questions regarding your rights as a subject participating in this research study or you would like more information about the protection of human subjects in research, you may contact the Institutional Review Board Office, at (409) 266-9400 or irb@utmb.edu.

CONSENT TO PARTICIPATE:
The purpose of this research study, procedures to be followed, risks and benefits have been explained to you. You have been given the opportunity to ask questions, and your questions have been answered to your satisfaction. You have been told who to contact if you have additional questions. By signing this form, you are confirming that you have read this consent form and voluntarily agree to participate as a subject in this study.

_____
Printed Name of Subject

_____ _____
Signature of Subject Date and Time

Using language that is understandable and appropriate, I have discussed this project and the items listed above with the subject

_____
Printed Name of Person Obtaining Consent

_____ _____
Signature of Person Obtaining Consent Date and Time Consent Obtained