Partners HealthCare System
Research Consent Form

Subject Identification

General Template
Version Date: August 2016

Protocol Title: Zoledronic Acid to Prevent High-Turnover Bone Loss after Bariatric Surgery

Principal Investigator: Elaine Yu, MD.

Site Principal Investigator:

Description of Subject Population: Obese Adults undergoing bariatric surgery

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 have previously shown that Roux-en-Y Gastric Bypass (RYGB) and sleeve gastrectomy (SG) have negative effects on skeletal health, including bone loss and higher risk of fractures. The purpose of this study is to prevent the bone loss that is occurring in adults who have chosen to undergo these surgeries. We are evaluating the ability of a single dose of zoledronic acid given before gastric bypass or sleeve gastrectomy to improve bone outcomes after the surgery. Zoledronic acid is currently FDA-approved for the treatment of osteoporosis (low bone density), but this study is the first to test its use in the prevention of bone loss after gastric bypass and sleeve gastrectomy.

We are asking you to take part in this research study because you are planning to undergo RYGB or SG and might be at higher risk of bone loss. We hope to enroll 10 subjects in this research study at the Massachusetts General Hospital (MGH).

How long will I take part in this research study?

It will take you about 7 months to complete this research study. During this time, we will ask you to make 5 study visits to the MGH. You will make two visits to the MGH prior to your surgery. After surgery, you will make 3 visits to the MGH over the course of 6 months.

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 complete any study procedures.

Baseline Visit
This visit will take about 5 hours to complete. At this visit, you receive the following laboratory tests, nutrition counseling, and bone density measurements:

- You will have a blood draw. You will need to fast for this visit for 5 hours.
- You will have measurements taken of your height and weight.
- You will receive personalized nutritional counseling. A nutritionist will meet with you to ensure that you receive enough calcium and vitamin D throughout the study. You may be provided with calcium and vitamin D supplements to take at home.
- You will undergo a dual energy x-ray absorptiometry (DXA) bone density scan of your spine, hip, and whole body. During this test, we will ask you to lie on a padded table for a few minutes. The arm-like scanning device will pass over your body as x-ray pictures are taken. You must hold still during the scanning procedure to reduce the possibility of a blurred image.
- You will undergo a quantitative computed tomography (QCT) bone density test of your spine. This test uses x-rays and a computer to determine bone mass (the density of bone tissue in your body). During this test, we will ask you to lie on a moveable table that slides into a large tunnel shaped machine. This table will move forward and backward as the scan is done. You will be asked to lie still during the scan. The test takes about 10 minutes.
- You will receive zoledronic acid through an intravenous catheter (IV). An IV will be placed in your arm, and then you will receive a single dose of either zoledronic acid. This infusion will occur more than one week prior to your bariatric surgery procedure.
- You may be given acetaminophen (the active ingredient in Tylenol) to reduce the possible side effects related to the study drug.

Visits at Weeks 2 and 12

At 2 and 12 weeks after your gastric bypass or sleeve gastrectomy surgery, you will be asked to return to MGH for study visits. You will need to fast for 5 hours for these visits. You will undergo a blood draw, as well as height and weight measurements. You will again meet with a nutritionist for personalized nutritional counseling. The nutritionist will ensure that you are taking enough calcium and vitamin D through supplements and diet. You may be provided with calcium and vitamin D supplements to take at home. These visits will take about 1.5 hours.

Week 24 Visit

At your final visit, you will have another blood draw. You will need to fast for 5 hours for this visit. Your height and weight will be measured. You will again receive personalized nutritional counseling. We will again perform a number of bone density measurements, including a DXA of the spine, hip, and total body, QCT of the spine. This visit should take about 4 hours to complete.

Stopping your Participation without your Permission

The study doctor may take you out of the study without your permission. This may happen because you have a serious unexpected reaction, you have failed to follow the instructions of the study doctor or staff, or if the study is being stopped for other reasons.

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).

Partners Alert System

Partners has an electronic system that lets your study doctors know if you are admitted to a Partners Hospital, or if you visit a Partners Hospital Emergency Department. We want to make sure the study doctors know about any possible problems or side effects you experience while you are taking part in the study.

Storing Samples at MGH for Future Use

Samples of your blood and urine will be saved and stored to measure factors related to this study that may help explain the change in bone mass. We will also store some of your samples for future research related to bariatric surgery or bone health. The stored samples will be labeled only with the date and time of collection and a code number. No identifying information (name, date of birth) will be on the stored samples. The key to the code connects your name to your health information and samples. The research doctor will keep the key to the code in a password protected computer. The samples will be kept in locked freezers. Only members of the study staff and the laboratory technicians who perform the measurements will have access to your stored samples. We may share your anonymous samples with academic groups participating in

research regarding obesity, bariatric surgery, and bone health. These scientists will not know who you are.

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

You may have side effects while taking part in this study. We will watch you carefully for any side effects. If you have any side effects during the study, you should tell the researchers right away.

Zoledronic Acid
The most common side effects associated with zoledronic acid include flu-like symptoms (e.g., fever, chills, muscle/joint aches) occurring after the infusion. Most of these symptoms occur within the first 3 days following drug administration and usually resolve within 3 days of onset but resolution can take up to 7-14 days. Taking acetaminophen or ibuprofen after the infusion can ease these symptoms. Other common side effects include nausea, tiredness, dizziness, headache, or pain/redness/swelling at the injection site.

Very rarely, more severe side effects may occur that include:
-Harm to the jaw bone (called osteonecrosis of the jaw)
-Fracture of your femur (upper leg bone)
-Kidney failure

Hypocalcemia
A small number of patients experience low blood calcium levels within the first two weeks after zoledronic acid administration. It is possible that RYGB or sleeve gastrectomy patients are at a higher risk for developing hypocalcemia. Symptoms of hypocalcemia include numbness or tingling of the hands or feet and muscle spasms or cramps. To reduce this risk, we will give you personalized nutrition counseling to ensure you are taking enough calcium and vitamin D supplements. We will also monitor your blood calcium levels throughout the study. You may be provided with calcium and vitamin D supplements to take at home.

Calcium and vitamin D supplements
The MGH Weight Center recommends that all bariatric surgery patients take supplemental calcium and vitamin D. These supplements may be provided to you during the trial. In the doses used in this study, calcium and vitamin D have minimal side effects. Some individuals may note constipation or stomach upset with calcium supplements. Very rarely, if an individual is over-supplemented with calcium, a kidney stone could result.

Acetaminophen: Acetaminophen, commonly known by the brand name, Tylenol, is very safe when used appropriately. If appropriate, a single standard dose will be given to you at the time of study drug infusion to decrease the likelihood of uncomfortable side effects. Overdose of acetaminophen may harm the liver. The single dose of acetaminophen at the time of study drug infusion will be withheld if you have any signs of liver disease, if a doctor has ever advised you to avoid acetaminophen, or if you have ever had a bad experience with acetaminophen.

Bone Density Tests (DXA, QCT)

Bone density scans are painless and take 5-15 minutes each. As a result of your taking part in this study you will be exposed to radiation from the x-ray procedures that measure your bone density. Please note that this radiation is not necessarily for your medical care and is for research purposes only.

Over the 6-month study period, you will receive 2 DXA scans of the lumbar spine, hip, and total body, and 2 QCT scans of the spine. One set of scans will be performed at the baseline visit, and the second set of scans will be performed at the 6-month visit. The total amount of radiation for the entire study is ~3.82 milliSieverts (mSv). A mSv is a unit of radiation dose. This amount of radiation is less than the background radiation that one is exposed to from the earth and sky over 15 months.

Scientists disagree on whether radiation doses at these low levels are harmful. A possible effect that could occur at doses used in this study is a slight increase in the risk of developing cancer later in life.

If we see something else on your scans that looks like a medical problem, we will ask a radiologist (a doctor who specializes in x-rays/scans/test results of this sort) to review the results. If the radiologist thinks there might be a problem, we will tell you and help you get follow-up care. If the radiologist thinks that you might have a medical problem, but it turns out that you don't, we may have caused you to worry needlessly about your health.

Intravenous Catheter Placement and Blood Collection

Inserting an intravenous catheter and/or taking blood can cause bruising or pain at the insertion site. Some people faint or feel lightheaded when blood is taken or an IV is placed. If you faint when your blood is collected, you should not take part in this study. There is a small risk of infection, which can be treated.

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

You may experience increases in bone density and/or prevention of bone loss during the course of the study. Information from this study will help us understand if zoledronic acid can prevent the deterioration of skeletal health that occurs after RYGB or sleeve gastrectomy. This knowledge has the potential to reduce the negative skeletal consequences of RYGB and sleeve gastrectomy, which are otherwise the most effective treatments for severe obesity.

What other treatments or procedures are available for my condition?

Currently, there are no other methods that have been studied to prevent bone loss after RYGB or sleeve gastrectomy.

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?

We will pay you $200 if you complete the study. In addition, we will give you a voucher (coupon) to pay for your parking in one of the MGH garages at each visit, or up to $20 to cover your travel expenses.

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, including the bone density scans, blood tests, nutrition counseling, ergocalciferol supplements, calcium and vitamin D supplements, study drug infusion, and all the other tests and procedures that are done only for research. 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, such as your bariatric surgery. 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.

Elaine Yu, MD is the person in charge of this research study. You can call her at 617-643-6353 Monday-Friday 9:00 AM-5:00 PM.

If you need to get in touch with the principal investigator on nights and weekends, call the main hospital at 617-726-2000 and have the operator page Elaine Yu, MD at pager # 13495.

If you have questions about the scheduling of appointments or study visits, call the study coordinator Katherine Lindeman at 617-724-3255.

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

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

Consent of Non-English Speaking Subjects Using the "Short Form" in the Subject's Spoken Language

Statement of Hospital Medical Interpreter

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions.

_____ _____

Hospital Medical Interpreter Date Time

Consent Form Version: 10-18-2018