RUBI: Romosozumab Use to Build Skeletal Integrity

NCT05058976

17DEC2024

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CONSENT TO ACT AS A SUBJECT IN A RESEARCH STUDY

Title:
RUBI Study: Romosozumab Use to Build skeletal Integrity

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SOURCE OF SUPPORT: National Institutes of Health (NIH) Grant #R01 AG066825

Key Information Sheet

General Information	You are being asked to participate in a randomized controlled research study. Research studies include only people who choose to take part. The study team members will explain the study to you and will answer any questions you might have. You should take your time to make your decision.
Purpose	The purpose of this research study is to find out if a combination of romosozumab (Evenity®), an injection given in your arm under the skin every month, and zoledronic acid (Reclast®), an intravenous (IV) drug works to treat bone loss and prevent it from worsening in postmenopausal women who have osteoporosis and reside in long-term care (LTC) facilities
Duration & Visits	If you are eligible to take part in this research study, it will involve 15 more study visits over the next 2 years.
Overview of Procedures	You will complete questionnaires, answer questions regarding medical history and report falls. Tests will include your grip strength, balance and physical ability and ability to do routine daily tasks. You will also complete dual-energy X-ray absorptiometry (DXA) scans and provide blood samples. The DXA machine

	has a table that you will lay on, where two X-ray beams will be aimed at your bones to obtain images. You will receive monthly study treatment injections for the first year and an additional study drug injection at month 12.
Risks	There are risks and side effects related to the procedures, intervention and study drug. Likely risks: • Pain, feeling lightheaded or fainting, and the possibility of bruising or soreness at the site of the blood draw. • Minimal radiation exposure with DXA scans. • Constipation with Calcium & Vitamin D supplements. • Soreness at injection site of Romosozumab or placebo. • Pain with IV line placement. • Fever, bone pain, joint pain, muscle pain, pain in arms and legs and headache with Intravenous Zoledronic Acid. • Itchiness or rash, constipation, nausea and vomiting with acetaminophen. Less likely risks: • Pain, discomfort, falling while completing tests with Walking & Balance tests. • Bone loss due to not receiving the study drug with placebo. • Infection, inflammation of the vein (phlebitis), and IV fluid accidentally entering the surrounding tissue (infiltration) with IV line placement. • Flu-like symptoms (fever, chills, bone pain, joint pain, muscle pain, fatigue, nausea, vomiting and diarrhea) with Intravenous Zoledronic Acid. Rare, but serious risks: • Infection at the site of the blood draws. • Allergic reactions, such as low blood pressure; trouble breathing; throat tightness; swelling of your face, lips, or tongue; rash, itching or hives. • Low blood calcium levels (hypocalcemia).

	• Severe jaw bone problems (osteonecrosis). • Unusual thigh bone fractures. • Major Adverse Cardiac Events (MACE), such as a heart attack or a stroke, with Romosozumab injections. • eye inflammation. • Severe kidney problems with Intravenous Zoledronic Acid. • • Liver failure with acetaminophen use. Risks are detailed further throughout this document.
Benefits	Some direct benefits from taking part in this research study are that you will also be given calcium and vitamin D supplements, therapies that have been shown to help prevent bone loss and broken bones. However, there is no guarantee that you will receive a direct benefit. You will know the mineral content of your bones from your DXA results and the composition of your body in terms of percentage of muscle and fat. The knowledge gained from your part in this study may help people who have osteoporosis in the future, particularly LTC residents.
Alternatives	Evaluations and treatments for osteoporosis are available outside of this study.

Who is being asked to take part in this research study?

You are being asked to participate in this study because you are a female LTC resident, age 65 or older, and have osteoporosis. Up to 600 LTC residents will be screened in order to find up to 200 women who are eligible to take part in the research study. **Participants will be randomly assigned (by chance, a 50-50 chance such as with flipping a coin) to either romosozumab or placebo (an injection containing no study drug).** Of the 200 participants, approximately 100 will receive the study drug and approximately 100 will the receive placebo. **All participants will receive zoledronic acid 5 mg IV in the second year of the research**

study. All participants will receive calcium and vitamin D supplements.

What procedures will be done for research purposes?

If you decide to take part in this research study, the study visits will be done at your facility where you will go through some procedures that are not part of your standard medical care. The screening visit that you already had done determined that you are eligible to take part in this research study which **will involve 15 more study visits over the next 2 years.** We will **obtain your written informed consent** before any research study procedures are done. If you think you would like to take part but are not able to make decisions alone, we will obtain written informed consent from your legal guardian (the person legally responsible for your care) with your agreement.

Baseline / Randomization Visit

This visit will take a total of approximately 1 hour of your time and will involve the following procedures which may occur over several days:

1. **Brief physical exam** (blood pressure, pulse, oxygen saturation, respiratory rate, temperature).
2. You will be asked about changes in your health since the screening visit and if you have had any broken bones or falls since then.
3. Approximately 2 teaspoons of **blood will be drawn** from your arm for tests that measure your bone health. A sample of your blood will be frozen and saved for later testing and for possible future tests which may include research on aging, function, bone and muscle health, inflammation and overall health.
4. **You will receive an injection of the study drug (romosozumab 210 mg or placebo).** This injection, which is given in your arm under the skin, will be performed by a nurse or other qualified health care professional who is a member of the research team. This injection is given every month for 12 months (at baseline, Month 1, Month 2,

Month 3, Month 4, Month 5, Month 6, Month 7, Month 8, Month 9, Month 10, and Month 11).

5. You will receive calcium and vitamin D supplements as needed based on your dietary calcium questionnaire to achieve the Institute of Medicine and National Osteoporosis Foundation recommended calcium of approximately 1200 mg/daily (divided dose from diet and/or supplement) taken at meals and vitamin D (at least 800 IU/daily).

Months 1, 2, 3, 4, and 5

Visits at Months 1, 2, 3, 4, and 5 will take a total of approximately 30 minutes of your time and will involve the following procedures:

1. You will be asked about changes in your health since the previous visit and if you have had any broken bones or falls since then.
2. **Brief physical exam** (blood pressure, pulse, oxygen saturation, respiratory rate, temperature).
3. **You will receive study drug (romosozumab or placebo).** This monthly injection, which is given in your arm under the skin, will be performed by a nurse or other qualified health care professional who is a member of the research team.
4. You will receive calcium and vitamin D supplements as needed based on your dietary calcium questionnaire to achieve the Institute of Medicine and National Osteoporosis Foundation recommended calcium of approximately 1200 mg/daily (divided dose from diet and/or supplement) taken at meals and vitamin D (at least 800 IU/daily).

Month 6

Visits at Month 6 will take approximately 3-4 hours of your time and will involve the following procedures which may occur over several days:

1. **Brief physical exam** (blood pressure, pulse, oxygen saturation, respiratory rate, height, weight, temperature).
2. You will be asked about changes in your health since your previous visit and if you have had any broken bones or falls since then.

3. You will have **blood drawn**. Blood will be saved and frozen for tests of bone health and for possible future testing which may include research on aging, function, bone and muscle health, inflammation, and overall health. Approximately 2 teaspoons of blood will be drawn at this study visit.
4. Bone density test of your spine (front and side, and trabecular bone score [TBS] which is an indicator of bone strength, and Texture Research Investigational Platform [TRIP] software to analyze bone microarchitecture), hip (total hip) forearm, and total body. This bone density test, known as a **DXA scan**, uses a special low-radiation x-ray machine. This will inform us about your bone health and the amount of muscle and fat in your body, and it will also include vertebral fracture assessment (VFA) to show if any of the small bones in your spine are broken. For the DXA procedure, you will be asked to go outside to the mobile unit and lie on a padded table for a total of approximately 50 minutes. You will need to lie still for several minutes at a time while the arm of the machine passes over these body regions to measure the thickness of your bones.
5. You will be asked some questions about your **daily activities**, **energy level**, your **ability to do physical tasks**, and about your **thinking ability** (remembering words, identifying objects, following instructions), **mood, outlook** and **recent falls**. This information will be gathered using questionnaires.
6. We will **test your grip strength, balance and physical ability and your ability to do routine daily tasks such putting on a sweater.** You may be asked to do things like get up from a chair or walk down a hallway.
7. **You will receive study drug (romosozumab or placebo).** This monthly injection, which is given in your arm under the skin, will be performed by a nurse or other qualified health care professional who is a member of the research team.
8. You will receive calcium and vitamin D supplements as needed based on your dietary calcium questionnaire to achieve the Institute of Medicine and National Osteoporosis Foundation recommended calcium of approximately 1200 mg/daily (divided dose from diet

and/or supplement) taken at meals and vitamin D (at least 800 IU/daily).

Months 7, 8, 9, 10, and 11

Visits at Months 7, 8, 9, 10, and 11 will each take a total of approximately 30 minutes of your time and will involve the following procedures:

1. You will be asked about changes in your health since the screening visit and if you have had any broken bones or falls since then.
2. **Brief physical exam** (blood pressure, pulse, oxygen saturation, respiratory rate, temperature).
3. **You will receive study drug (romosozumab or placebo).** This monthly injection, which is given in your arm under the skin, will be performed by a nurse or other qualified health care professional who is a member of the research team.
4. You will receive calcium and vitamin D supplements as needed based on your dietary calcium questionnaire to achieve the Institute of Medicine and National Osteoporosis Foundation recommended calcium of approximately 1200 mg/daily (divided dose from diet and/or supplement) taken at meals and vitamin D (at least 800 IU/daily).

Month 12

Visits at Month 12 will take approximately 3-4 hours of your time and will involve the following procedures which may occur over several days:

1. **Brief physical exam** (blood pressure, pulse, oxygen saturation, respiratory rate, height, weight, temperature).
2. You will be asked about changes in your health since your previous visit and if you have had any broken bones or falls since then.
3. You will have **blood tests** for safety checks. Blood will also be saved and frozen for tests of bone health and for possible future testing which may include research on aging, function, bone health, and overall health, including blood for immune response measures at the 6 month visit. No more than approximately 4 teaspoons of blood will be drawn at this study visit**.**

4. Bone density test of your spine (front and side, and trabecular bone score [TBS] which is an indicator of bone strength, and Texture Research Investigational Platform [TRIP] software to analyze bone microarchitecture), hip (total hip) forearm, and total body. This bone density test, known as a **DXA scan**, uses a special low-radiation x-ray machine. This will inform us about your bone health and the amount of muscle and fat in your body, and it will also include vertebral fracture assessment (VFA) to show if any of the small bones in your spine are broken. For the DXA procedure, you will be asked to go outside to the mobile unit and lie on a padded table for a total of approximately 50 minutes. You will need to lie still for several minutes at a time while the arm of the machine passes over these body regions to measure the thickness of your bones.
5. **You will receive zoledronic acid 5 mg IV (Relcast®).** The zoledronic acid infusion will be given by a nurse or other qualified health care professional who is a member of the research team. This requires a small catheter (a thin tube) be placed in a vein in your arm using a needle. The study drug IV solution will be given through the IV catheter. There is approximately ½ cup of solution which will be given over approximately 60 minutes. After the infusion is complete, the IV catheter will be removed. You will be given acetaminophen (Tylenol) to take the day of the infusion and for several days after if needed.
6. You will be asked some questions about your **daily activities**, **energy level**, your **ability to do physical tasks**, and about your **thinking ability** (remembering words, identifying objects, following instructions), **mood, outlook** and **recent falls**. This information will be gathered using questionnaires.
7. We will **test your grip strength, balance and physical ability and your ability to do routine daily tasks such putting on a sweater.** You may be asked to do things like get up from a chair or walk down a hallway.
8. You will receive calcium and vitamin D supplements as needed based on your dietary calcium questionnaire to achieve the Institute of Medicine and National Osteoporosis Foundation recommended

calcium of approximately 1200 mg/daily (divided dose from diet and/or supplement) taken at meals and vitamin D (at least 800 IU/daily).

Monitoring/Follow-up Procedures

Procedures done for your safety and to check how well the zoledronic acid works and whether or not you have any side effects are called “monitoring” or “follow-up” procedures. You will have **brief safety checks done up to 2 days prior to receiving the Month 12 zoledronic acid 5 mg IV (Reclast®) and 1-3 days after.** A member of the research team will visit you to do a safety check up to 2 days prior to the infusion when **samples of blood** (approximately 2 tsp.) will be drawn from your arm for safety measures. Another safety check will be done 1-3 days after the study drug infusion, when a member of the research team will make a telephone call to check on how you are feeling.

Month 18

Visits at Month 18 will take approximately 3-4 hours of your time and will involve the following procedures which may occur over several days:

1. **Brief physical exam** (blood pressure, pulse, oxygen saturation, respiratory rate, height, weight, temperature).
2. You will be asked about changes in your health since your previous visit and if you have had any broken bones or falls since then.
3. You will have **blood drawn**. Blood will be saved and frozen for tests of bone health and for possible future testing which may include research on aging, function, bone and muscle health, inflammation and overall health. Approximately 2 teaspoons of blood will be drawn at this study visit.
4. Bone density test of your spine (front and side, and trabecular bone score [TBS] which is an indicator of bone strength, and Texture Research Investigational Platform [TRIP] software to analyze bone microarchitecture), hip (total hip) forearm, and total body. This bone density test, known as a **DXA scan**, uses a special low-radiation x-ray machine. This will inform us about your bone health and the amount of muscle and fat in your body, and it will also include

vertebral fracture assessment (VFA) to show if any of the small bones in your spine are broken. For the DXA procedure, you will be asked to go outside to the mobile unit and lie on a padded table for a total of approximately 50 minutes. You will need to lie still for several minutes at a time while the arm of the machine passes over these body regions to measure the thickness of your bones.

5. You will be asked some questions about your **daily activities**, **energy level**, your **ability to do physical tasks**, and about your **thinking ability** (remembering words, identifying objects, following instructions), **mood, outlook** and **recent falls**. This information will be gathered using questionnaires.
6. We will **test your grip strength, balance and physical ability and your ability to do routine daily tasks such putting on a sweater.** You may be asked to do things like get up from a chair or walk down a hallway.
7. You will receive calcium and vitamin D supplements as needed based on your dietary calcium questionnaire to achieve the Institute of Medicine and National Osteoporosis Foundation recommended calcium of approximately 1200 mg/daily (divided dose from diet and/or supplement) taken at meals and vitamin D (at least 800 IU/daily).

Month 24

Visits at Month 24 will each take a total of approximately 3-4 hours of your time and will involve the following procedures which may occur over several days:

1. **Brief physical exam** (blood pressure, pulse, oxygen saturation, respiratory rate, height, weight, temperature).
2. You will be asked about changes in your health since your previous visit and if you have had any broken bones or falls since then.
3. You will have **blood drawn**. Blood will be saved and frozen for tests of bone health and for possible future testing which may include research on aging, function, bone and muscle health, inflammation,

and overall health. Approximately 3 teaspoons of blood will be drawn at this study visit.

4. Bone density test of your spine (front and side, and trabecular bone score [TBS] which is an indicator of bone strength, and Texture Research Investigational Platform [TRIP] software to analyze bone microarchitecture), hip (total hip) forearm, and total body. This bone density test, known as a **DXA scan**, uses a special low-radiation x-ray machine. This will inform us about your bone health and the amount of muscle and fat in your body, and it will also include vertebral fracture assessment (VFA) to show if any of the small bones in your spine are broken. For the DXA procedure, you will be asked to go outside to the mobile unit and lie on a padded table for a total of approximately 50 minutes. You will need to lie still for several minutes at a time while the arm of the machine passes over these body regions to measure the thickness of your bones.
5. You will be asked some questions about your **daily activities**, **energy level**, your **ability to do physical tasks**, and about your **thinking ability** (remembering words, identifying objects, following instructions), **mood, outlook** and **recent falls**. This information will be gathered using questionnaires.
6. We will **test your grip strength, balance and physical ability and your ability to do routine daily tasks such putting on a sweater.** You may be asked to do things like get up from a chair or walk down a hallway.

Possible Repeat Tests

It is possible that the blood tests performed as part of the research study procedures may need to be repeated. Due to the fragile nature of the samples, which must be transported back to the UPMC Clinical Laboratory for processing, the specimens may deteriorate or become damaged despite the best precautions. These repeat blood tests would be done at your LTC facility by the research staff as soon as possible after the need for retesting becomes known. The risks remain the same as outlined in the risks section of this consent form; however, repeat testing would increase the total amount of blood drawn for that study visit's tests. If blood tests

need to be repeated, the total amount of blood drawn for each visit would increase to the following:

- Randomization / Baseline – Approximately 4 teaspoons
- Month 6 – Approximately 4 teaspoons
- Month 12 – Approximately 8 teaspoons
- Month 18 – Approximately 4 teaspoons
- Month 24 – Approximately 6 teaspoons

What will happen to your blood samples?

Your blood samples and any components of your cells not used for the tests listed above may be frozen and stored indefinitely for possible future research, which may include research on aging, function, bone or muscle health, inflammation and overall health. It is possible that secondary investigators not listed on the consent form may have access to de-identified frozen samples collected for possible future research. These samples will be labeled with a unique code to de-identify them. Future testing may include research on aging, function, bone and muscle health, inflammation, immune response measures, and overall health.

Participants in this research study may experience the following risks:

- Risks of the Study Drug. As with any drug, there may be adverse events or side effects that are currently unknown, and it possible that certain of these unknown risks could be permanent, serious, or life-threatening.

Romosozumab (Evenity®):

The most common side effects are joint pain and headache.

Other side effects:

- Allergic reactions may occur. Symptoms of a serious allergic reaction may include low blood pressure; trouble breathing; throat tightness; swelling of your face, lips, or tongue; rash, itching, or hives. Tell your study doctor if any allergic reactions occur.
- Low calcium levels in your blood (hypocalcemia). The study doctor may prescribe calcium and vitamin D to help prevent low calcium

levels in your blood while you take romosozumab. Take the calcium and vitamin D as your study doctor tells you to do.

Rare side effects:

- Severe jaw bone problems (osteonecrosis). You should let your study doctor know if you are scheduled for a tooth extraction before receiving the study drug. It is important for you to practice good mouth care during treatment with romosozumab.
- Unusual thigh bone fractures. Tell your study doctor if you have new or unusual pain in your hip, groin, or thigh.
- Major Adverse Cardiac Events (MACE). A heart attack or stroke are examples of a MACE. Romosozumab may increase the risk of heart attack, stroke, or cardiovascular death. You should let your study doctor know if you have had a heart attack or stroke within the past year. If you experience a heart attack or stroke during the first year of this research study, romosozumab or placebo injections will be discontinued. If treatment is discontinued due to an adverse event, the zoledronic acid infusion will be offered. Receiving zoledronic acid infusions in place of romosozumab or placebo can take place at any time after one month or more time has passed since your last romosozumab or placebo injection. If zoledronic acid infusions are given prior to Month 12, you will not receive a zoledronic acid infusion at Month 12.

Placebo: Subjects in the placebo group will have the same risks as described in this risks section except for those associated with romosozumab as described above. There is a potential risk for bone loss in not receiving the study drug; however, you will receive calcium and vitamin D supplements which have been shown to reduce bone loss. If we find that you have significant bone loss during the study, you will be informed and appropriate treatment options will be discussed with you. You will be allowed to continue in the study for follow-up visits on a therapy chosen by your physician.

Zoledronic Acid (Reclast®):

The most common side effects are fever; pain in your bones, joints or muscles; pain in your arms and legs, and headache.

Other side effects:

- Flu-like symptoms, such as fever chills, bone, joint, or muscle pain, fatigue, nausea, vomiting, and diarrhea. The majority of flu-like symptoms occur within 3 days following the dose of Reclast® and usually last about 3 days but can last up to 7-14 days. These temporary fever and flu-like symptoms can be treated with acetaminophen (Tylenol) to be taken every 6 hours, as needed, for 72 hours following the IV zoledronic acid, for participants who are able to take acetaminophen.
- Allergic reactions, such as hives, swelling of your face, lips, tongue, or throat may occur.

Serious and rare side effects:

- Eye inflammation (iritis, uveitis, episcleritis, conjunctivitis). Tell your study doctor if you experience any unusual symptoms with your eyes or vision.
- Low calcium levels in your blood (hypocalcemia). The study doctor may prescribe calcium and vitamin D to help prevent low calcium levels in your blood while you take Reclast®. Take the calcium and vitamin D as your study doctor tells you to do.
- Severe kidney problems. You should drink at least 2 glasses of fluid a few hours before receiving Reclast® to reduce the risk of kidney problems.
- Severe jaw bone problems (osteonecrosis). You should let your study doctor know if you are scheduled for a tooth extraction before receiving the study drug. It is important for you to practice good mouth care during treatment with Reclast®.
- Unusual thigh bone fractures. Tell your study doctor if you have new or unusual pain in your hip, groin, or thigh.

You should not receive Reclast® if you are already receiving Zometa® because both Reclast® and Zometa® contain zoledronic acid. Do not take Reclast® if you have low levels of calcium in your blood, have kidney problems, or have a history of allergic reaction to bisphosphonates (such as Fosamax® and Actonel®).

Intravenous (IV) line placement: The risks of IV insertion may include pain, infection, inflammation of the vein (phlebitis), and IV fluid accidentally entering the surrounding tissue (infiltration).

Acetaminophen: Common side effects include itchiness or rash, constipation, nausea, and vomiting. Serious side effects include liver failure.

Calcium and vitamin D supplements: Mild constipation from the calcium supplement commonly occurs. This may be eliminated by adding fiber to your diet. There are no known side effects for vitamin D when taken within the recommended daily allowance of 800 IU, or up to 4000 IU daily. You will receive calcium and vitamin D supplements as needed based on your dietary calcium questionnaire to achieve at total of approximately 1200 mg calcium daily (dietary plus supplement) and 800-1000 IU vitamin D daily (dietary plus supplement).

Participation in this research study will involve radiation exposure from the dual-energy x-ray absorptiometry (DXA) scans. You will have DXA scans of your spine (front and side, and TBS which is a measure of bone strength, and Texture Research Investigational Platform [TRIP] software to analyze bone microarchitecture), vertebral fracture assessment (VFA), hip (total hip), forearm, and total body. If you complete all the DXA scans for the study as outlined above, the amount of radiation exposure that you will receive from these procedures is equivalent to a uniform whole body dose of 15.24 mrem (an mrem is a unit of radiation). The radiation dose from DXA scans of your spine will be about 13.2 mrem. The radiation dose from DXA scans of your hip will be about 0.8 mrem. The radiation dose from DXA scans of your wrist will be about 0.04 mrem, and the radiation dose from DXA scans of your total body will be about 1.2 mrem. For comparison, these radiation doses are a very small fraction of the maximum annual whole body radiation dose (5000 mrems) permitted by federal regulation to adult radiation workers. There is no known minimum level of radiation

exposure that is recognized as being totally free of the risk of causing genetic defects (cellular abnormalities) or cancer. However, the risk associated with the amount of radiation exposure from participation in this study is considered to be low and comparable to everyday risks.

Blood draws: The risks and discomforts of having blood drawn may commonly include pain, feeling lightheaded or fainting, and the possibility of bruising or soreness at the site of the blood draw. In rare instances, infection at the site of the blood draw may occur.

Collection and storage of personal health information and biospecimens: The risks of collecting and storing your personal health information and storing your samples long-term is breach of confidentiality.

Walking and Balance tests: There is a risk of falling or of discomfort (pain) while doing the walking and balance tests. The study coordinator is trained to intervene to prevent a fall from happening. You can decline to do any of the balance or walking tests that you do not want to do or that you feel is too painful. To protect your privacy, these tests will be done in a private room except for the walking test, which may be done in a cleared hallway.

There are possible benefits from taking part in this research study:
Some direct benefits from taking part in this research study are that you will also be given calcium and vitamin D supplements, therapies that have been shown to help prevent bone loss and broken bones. However, there is no guarantee that you will receive such a benefit. This study involves a placebo group and participants assigned to the placebo group are expected to receive no direct benefit from the subcutaneous placebo injection. All participants will receive zoledronic acid (Reclast®), a medication for treatment of osteoporosis, during the second year of study participation. You will also know the mineral content of your bones from your DXA results and the composition of your body in terms of percentage of muscle and fat. The knowledge gained from your part in this study may help people who have osteoporosis in the future, particularly LTC residents.

What treatments or procedures are available if you decide not to take part in this study?

You may choose not to participate in this research study and either continue your current health treatment plan or discuss other therapies with your physician. Evaluations and treatments for osteoporosis are available outside of this study.

None of the tests or procedures done for research study purposes will be billed to you or your health insurance (blood tests, DXA scans, calcium and vitamin D supplements, physical assessments and questionnaires, study drug). If you receive a bill or believe your health insurance has been billed for something that is part of the research study, notify the study coordinator as soon as possible.

Other tests and procedures that would normally be done as part of your conventional care will be your responsibility and charged to you or your health insurance, in the standard manner, for services and procedures that are done as part of your routine care. Any deductible or copayments that are part of your insurance coverage will apply.

Are participants paid for taking part in this study?

You will not be paid for participating in this research study. You will receive a study lap blanket, reusable bag, or flashlight as a thank you gift after your randomization visit has been completed.

If you believe that the research study procedures have resulted in an injury to you, immediately contact the Principal Investigator or Study Coordinator (see first page for contact info). Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of these costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of follow-up care. At this time, there is no plan for any additional financial compensation.

Will this research study involve the use or disclosure of my identifiable medical information?

This research study will result in identifiable information that will be placed into your medical records held at UPMC and at the Osteoporosis Prevention and Treatment Center. The nature of the identifiable information resulting from your participation that may be recorded in your medical record includes DXA scan reports, past medical history, medications, lab values, physical exam, X-rays, dental exam reports, demographic information, questionnaires, physician order sheets, and progress notes performed for research purposes and information related to any adverse events you may experience related to the study procedures.

This research study will also involve the recording of past, current and/or future identifiable medical information from your hospital and/or other health care provider (e.g. physician office) records. Information that may be recorded from your medical records for research purposes includes medical history, medications, lab values, X-rays, dental exam reports, hospitalizations, physical exam reports, physician order sheets, progress notes, and information related to any adverse events experienced.

To protect your privacy and maintain the confidentiality of information we obtain from you and from your medical records, we will keep all information about you in a secure location.

All paper records that could identify you will be stored in a locked file cabinet, and all electronic records will be stored in password-protected files. Your identity on these records will be indicated by a case number rather than your name, and the code linking your name to this number will be maintained separately with very limited access by research team members.

Although we will do everything in our power to protect your privacy and the confidentiality of your records, just as with the use of your medical information for health care purposes, we cannot guarantee the

confidentiality of your research records, including information that we obtained from your medical records.

Your research information and data may be shared with investigators conducting other research. This information will be de-identified.

In addition to the investigators listed on the first page of this consent document and their research team, the following individuals may have access to your identifiable medical information related to this research study:

- UPMC hospitals may have access to identifiable information only for the purposes of (1) filling orders made by the researchers for hospital and health care services (e.g. laboratory tests) associated with the study, (2) addressing correct payment for tests and procedures ordered by the researchers, and/or (3) for internal hospital operations (e.g. quality assurance).
- Authorized representatives of the University of Pittsburgh Office of Research Protectionsmay review your identifiable research information for the purpose of monitoring the appropriate conduct of this research study.
- Authorized representatives of the sponsor(s) of this research study (see page 2), such as outside laboratories assaying blood samples, may review and/or obtain identifiable information related to your participation in this study for the purposes of monitoring the accuracy and completeness of the research data and for performing requires scientific analyses of the research data.
- In unusual cases, the investigators may be required to release identifiable information related to your participation in this research study in response to an order from a court of law. If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform the appropriate agencies as required by law.

Your data or specimens used in this research study may contribute to a new discovery or treatment. In some instances, these discoveries or treatments may be of commercial value and may be sold, patented, or licensed by the investigators and the University of Pittsburgh for use in other research or the development of new products. You will not retain any property rights, nor will you share in any money that the investigators, the University of Pittsburgh, or outside agencies may receive.

According to University of Pittsburgh policy, **all research records must be maintained for at least 7 years following the final reporting or publication of a project.**

Your doctor may be involved as an investigator in this research study, but you are not under any obligation to participate in any research study offered by your doctor. As both your doctor and a research investigator, s/he is interested both in your medical care and the conduct of the research study. Before agreeing to participate in this research study, or at any time thereafter, you may wish to discuss participation with another health professional that is not associated with the research.

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.

Your participation in this research study is completely voluntary.

You may want to discuss this research study with your family and friends and your personal physician before agreeing to participate. If there are any words you do not understand, feel free to ask us. The investigators will be available to answer your current or future questions. Whether or not you participate will have no effect on your current or future relationship with the University of Pittsburgh, UPMC, or its affiliated health care providers or health insurance providers.

You will be notified of any results that might affect your personal health or decisions. You will be promptly notified if any new information we learn during this research study may cause you to change your mind about continuing to participate in the study.

If you decide you no longer wish to participate after you have signed the consent form, you should contact the principal investigator or the research coordinator (contact info on page 1). **To formally withdraw your consent for participation, you should provide a written and dated notice of this decision to the principal investigator** listed on the first page of this form. You may also withdraw, at any time, your authorization to allow the research team to review your medical records, but if you do so, you will no longer be able to participate in this research study. Any information obtained from you up to that point, however, will continue to be used by the research team (including blood samples already collected during the study). Your decision to withdraw from this research study will have no effect on your current or future relationship with the University of Pittsburgh or with UPMC or its affiliated health care and insurance operations.

The investigators may withdraw you from the research study if they feel that you cannot complete the study requirements safely (for example, if you need other treatment, cannot undergo the study procedures, do not follow the investigators' instructions, experience adverse events).

You might also be removed from the research study for other medical or administrative reasons (for example, the research resources are no longer available or no longer funded by the research sponsor). We will notify you should this arise and advise you if there are available alternatives that may be of benefit at the time.

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Certificate of Confidentiality

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for examples, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable disease) but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings; if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

VOLUNTARY CONSENT

The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that any future questions, concerns, or complaints will be answered by a qualified member of the research team listed on the first page of this consent document at the telephone numbers given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator. At any time I may also contact the Human Subjects Protection Advocate at the IRB Office, University of Pittsburgh (toll-free at 1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations in the event that the research team is unavailable. **By signing this form I agree to participate in this research study and allow the use and disclosure of my medical record information for the purposes described above.** A copy of this consent form will be given to me.

_____ _____

Participant's Signature Date

_____

Participant's Name (Print)

The above-named individual is unable to provide direct consent for study participation because

_____

Therefore, by signing this form, I give my consent for participation in this research study.

_____	_____
Representative's Name (Print)	Representative's Relationship to Participant
_____	_____
Representative's Signature	Date
_____	_____
Witness's Signature	Date

VERIFICATION OF EXPLANATION:
I certify that I have carefully explained the purpose and nature of this research study to the above-named participant in appropriate language. He/she has had an opportunity to discuss it with me in detail. I have answered all his/her questions and he/she has provided affirmative agreement (i.e., assent) to participate in this study.

_____	_____
Investigator's Signature	Date (Time if placed in medical record)

_____ _____

Participant's Signature Date

CERTIFICATION OF INFORMED CONSENT:

I certify that I have explained the nature and purpose of this research to the above individual and/or their proxy representative, and I have discussed the potential benefits and possible risks of study participation.

Any questions the individual has about this study have been answered, and we will always be available to address future questions as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____ _____

Printed Name of Person Obtaining Consent

Role in Research Study

_____ _____

Signature of Person Obtaining Consent

Date