BETA1-Selective Blockade for Prevention of Postmenopausal Bone Loss: A Multi-center, Double-blinded, Randomized, Placebo-controlled Trial

NCT04905277

November 17, 2023

MAYO CLINIC

Name and Clinic Number

Approval Date: **November 17, 2023**
Not to be used after: **September 6, 2024**

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: BETA1-Selective Blockade for Prevention of Postmenopausal Bone Loss: A Multi-center, Double-blinded, Randomized, Placebo-controlled Trial

IRB#: 18-005725

Principal Investigator: Sundeep Khosla and Colleagues

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide. **Please take the time to read the entire consent form carefully and talk to a member of the research team before making your decision.** You should not sign this form if you have any questions that have not been answered.	
It's Your Choice	This is a research study. Being in this research study is your choice; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits or rights you would normally have if you choose not to take part.
Research Purpose	The purpose of this research is to evaluate whether treatment with a widely used and inexpensive drug called atenolol will prevent bone loss at the lower back and hip in postmenopausal women. You have been asked to take part in this research because you are a healthy postmenopausal woman between 50 and 75 years of age.
What's Involved	This study uses a placebo. A placebo looks exactly like the study drug, but it contains no active ingredient. We use placebos in research studies to learn if the effects seen in research participants are truly from the study drug. Study participation involves a screening visit, lead-in visit and 6 study visits to Mayo Clinic over the course of 24 months. You will have various bone density scans, blood draws, ECG and you will be randomized to either placebo or atenolol for 24 months. It will take you 24 months from the baseline visit to complete this research study.

Key Information	The risks of drawing blood include pain, bruising, lightheadedness, and/or fainting, or rarely, infection at the site of the needle stick. You will be exposed to x-ray radiation during the DXA and HRpQCT bone density scans. The amount of radiation you will be exposed to has a low risk of harmful effects. Side effects of atenolol may include blurred vision, cold hands or feet, confusion, cough and/or difficult or labored breathing, dizziness, faintness or lightheadedness when getting up from a lying or sitting position suddenly, headache, low blood pressure, slow heart rate, shortness of breath, sweating, tightness in chest, unusual tiredness or weakness and wheezing, nausea, depression, diarrhea and sleep disorders. Vitamin D has little risk. Side effects that may occur are abdominal cramping, headache, weight gain, nausea, vomiting, and constipation. For your safety during this study, call the Principal Investigator or study coordinator BEFORE you take any: • New medications prescribed by your doctor • Other medications sold over-the-counter without a prescription • Dietary or herbal supplements As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk. **ECG** - This test uses small sticky pads that are placed on your chest and limbs to measure the electrical activity of your heart. There may be mild discomfort from the sticky pads and a possibility of the skin being irritated by the adhesive on the sticky pads. Chest hair may need to be shaved prior to the placement of the sticky pads
Learn More	If you are interested in learning more about this study, read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A member of our research team will talk with you about taking part in this study before you sign this form. If you have questions at any time, please ask us.

Making Your Decision

Taking part in research is your decision. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep. A copy of this form will be put in your medical record.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

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Contact Information

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator:** Sundeep Khosla **Phone:** (507) 255-6663 **Study Team Contact:** Tammie Volkman, RN **Phone:** (507) 538-6023 **Institution Name and Address:** Mayo Clinic Rochester 200 First Street SW Rochester, MN 55905
▪ Rights of a research participant	**Mayo Clinic Institutional Review Board (IRB)** **Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681
▪ Rights of a research participant ▪ Any research-related concern or complaint ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study	**Research Participant Advocate (RPA)** **(The RPA is independent of the Study Team)** **Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** ResearchParticipantAdvocate@mayo.edu
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

Other Information:
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 are you being asked to take part in this research study?

You are being asked to be in this study because you are a healthy postmenopausal woman between 50 and 75 years of age.

Why is this research study being done?

Although there are several medication options for the treatment of osteoporosis, there remain concerns regarding the potential side effects and costs associated with them. For these reasons, many doctors and patients are reluctant to use these medications to prevent bone loss, leading to concern and anxiety about postmenopausal women having to wait until they develop osteoporosis, or high risk of fracture, to begin drug therapy. Therefore, there is a need for relatively low-risk and low-cost medications to prevent and/or treat osteoporosis.

We are doing this research study to find out whether treatment with a widely used and inexpensive drug called atenolol will prevent bone loss at the lower back and hip in postmenopausal women.

Information you should know

Who is Funding the Study?
The NIH (National Institutes of Health) is funding the study. The NIH will pay the Principal Investigator or the institution to cover costs related to running the study.

How long will you be in this research study?

It will take you 24 months from the baseline visit to complete this research study. During this time, we will ask you to make 8 study visits to Mayo Clinic.

What will happen to you while you are in this research study?

Visit 1 (Screening Visit): You should not take any calcium containing supplements including multivitamins 24 hours before your visit. If you take biotin or a multivitamin containing biotin, you should hold them for seven days as these may affect your blood lab results. You will come to the Clinical Research and Trials Unit (CRTU), Charlton building, 7th floor. You will need to be fasting (nothing to eat or drink after midnight except you may have water). At this time, you will meet with a member of the study team, review the study, have your questions answered, and sign this consent form.
You will then have the following:

- You will be asked questions during this visit about your past and current health and medications (to verify inclusion/exclusion criteria).
- You will have your blood pressure and pulse taken 3 times with a one-minute rest between readings and the average will be documented. **(If your blood pressure and pulse are within the guidelines that have been determined for the study, you will proceed to the next step, if it is not you will not be eligible to continue in the study and you will be dismissed.)**
- Measure your height and weight
- DXA scan of your hip, wrist, total body and three spine scans will be done. For these scans, you will lie on an x-ray table and the scanner will move above you over your entire body. An DXA scan is a low energy x-ray measurement of your bone density. **(The study team will go over the scan results with you to discuss if you choose to continue with the screening visit.)**
- You will have an electrocardiogram to examine the health of your heart. **(If your electrocardiogram is within the guidelines that have been determined for the study, you will proceed to the next step, if it is not you will not be eligible to continue in the study and you will be dismissed.)**
- If you are within the guidelines that have been determined, you will then have the following done:
    - Blood sample (about 2 tablespoons) will be drawn

The Principal Investigator will review the results of these tests and procedures If you are found to have low body stores of Vitamin D as assessed by the serum 25-hydroxyvitamin D of less than 20 ng/ml, you will be given a prescription for 50,000 units/per week of Vitamin D for one month and then have your level rechecked. If the level is still less than 20 ng/ml, we will have you take 50,000 units of Vitamin D for one more month and recheck the level again. If the level is still

less than 20 ng/ml, you will not continue in the study and will be referred to your primary physician for further evaluation. If you are not eligible, we will contact you and you will not continue in the study.

Should any of your laboratory blood work drawn at the screening visit return with lab values outside of the "normal limits', you may be asked to have another blood draw to confirm these results. This would be at the discretion of the Principal Investigator.

Visit 2-(Lead-in visit):
You will come to the Clinical Research and Trials Unit (CRTU), Charlton building, 7th floor. You will come to the CRTU fasting since midnight.

You will then have the following:

- You will be asked questions during this visit in regards to your current health and medications and verify if any new fractures.
- You will be asked questions about your reproductive and social history as well as your birth parents fracture history.
- Vital signs (blood pressure and pulse)
- Go over study questionnaires.
- You will have a 100 mL (less than ½ cup) blood draw.
- You will be given a one-month supply of study medication and Vitamin D (If you are currently taking 800-1000 IU's of Vitamin D you will not need to take any additional Vitamin D)
- You will be given a small notebook to record any side effects that are noted between your appointments. **You will need to bring this notebook with you to each appointment.**

If you are not able to tolerate the study drug during the one month lead-in phase, you will not be randomized and your study participation will be complete.

Visit 3-Baseline Visit (one month after lead-in visit)
You will come to the Clinical Research and Trials Unit (CRTU), Charlton building, 7th floor. You will then have the following:

- Turn in study medication
- You will be asked questions during this visit in regards to your current health and medications and verify if any new fractures.
- Vital signs (blood pressure and pulse) **(If your blood pressure and pulse are within the guidelines that have been determined for the study, you will proceed to the next step, if it is not you will not be eligible to continue in the study and you will be dismissed.)**

- You will then have your bone density measured at different parts of your body: High resolution peripheral quantitative computed tomography (HRpQCT). This machine uses low energy X-rays to measure structure of your bones.
  For the HRpQCT scans, you will sit in a chair with your arm resting on a platform which will then be positioned in the machine and scanned at your wrist. Next, your lower leg will be placed on a platform which will then be positioned in the machine and scanned at two separate ankle sites. These scans will take about 9 to 12 minutes.
  It may be necessary to repeat one of the bone scans before you are dismissed. We will only do this if absolutely necessary due to a machine stopping, movement or need for repositioning. You will have the choice to have a scan repeated.
- Study team member will go through your record book.
- You will be randomized to either the study drug (atenolol) or placebo group.
- You will be given a six-month supply of study medication and Vitamin D.

Visits 4 (one month after baseline):
You will come to the Clinical Research and Trials Unit (CRTU), Charlton building, 7th floor.
You will then have the following:

- You will be asked questions during this visit in regards to your current health and medications and verify if any new fractures.
- Vital signs (blood pressure, and pulse)
- Study team member will go through your record book.

This visit will take approximately 30 minutes.

Visits 5-8 (6, 12, 18, 24 months after baseline or early termination)-
You will return to the CRTU fasting since midnight. You will then have the following:

- You will have a fasting blood sample (50mL or less than 1/4 cup) at months 6, 12, 18 and 24 (or off study). You will be seated for a 5-minute rest followed by blood pressure and heart rate check, before each blood draw.
- Turn in study medication
- Go over study questionnaires.
- Vital signs (blood pressure and pulse)
- Measure your height and weight
- You will be asked questions during this visit in regards to your current health and medications and verify if any new fractures.
- Study team member will go through your record book.

- The DXA scans as described above at Visit 1 (screening visit) will be done at the 6, 12, 18 and 24 month visit, or early termination with the exception of the total body scans as they will only be done at Visit 1 (screening visit) and the 24 month or early termination visit. **You should not take any calcium containing supplements including multivitamins 24 hours before visit.**
- HRpQCT scans as described above at Visit 3 (baseline visit) will be done at 12- and 24-month visit, or early termination.
- You will be given a six-month supply of study medication and Vitamin D. (If you are currently taking 800-1000 IU's of Vitamin D you will not need to take any additional Vitamin D)

A member of the study team will contact you at months 3, 9, 15, and 21 to assess current health, new medications and verify if any new fractures.

This will complete the study. Each of these visits will take approximately 1 ½ hours.

Upon completion of the study (or early withdrawal you will receive a one-week taper of either atenolol or placebo depending on the original treatment assignment, and then off the study drug. During this time we will instruct you to observe for palpitations and/or other cardiac symptoms and contact the study team for further direction, if these unexpected events occur.

While you are in this research study, you should check with the study team before participating in any other research studies and refrain from donating blood for 12 weeks before Visit 1, during the study and for 12 weeks following the final visit.

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

The risks of drawing blood include pain, bruising, lightheadedness, and/or fainting, or rarely, infection at the site of the needle stick.

You will be exposed to x-ray radiation during the DXA and HRpQCT scans. The amount of radiation you will be exposed to has a low risk of harmful effects.

Side effects of atenolol may include blurred vision, cold hands or feet, confusion, cough and/or difficult or labored breathing, dizziness, faintness or lightheadedness when getting up from a lying or sitting position suddenly, headache, low blood pressure, slow heart rate, shortness of breath, sweating, tightness in chest, unusual tiredness or weakness and wheezing, nausea, depression, diarrhea and sleep disorders.

Vitamin D has little risk. Side effects that may occur are abdominal cramping, headache, weight gain, nausea, vomiting, and constipation.

For your safety during this study, call the Principal Investigator or study coordinator BEFORE you take any:

- New medications prescribed by your doctor
- Other medications sold over-the-counter without a prescription
- Dietary or herbal supplements

As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.

ECG - This test uses small sticky pads that are placed on your chest and limbs to measure the electrical activity of your heart. There may be mild discomfort from the sticky pads and a possibility of the skin being irritated by the adhesive on the sticky pads. Chest hair may need to be shaved prior to the placement of the sticky pads.

Are there reasons you might leave this research study early?

Taking part in this research study is voluntary. You may decide to stop at any time. You should tell the researcher if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the researchers or Mayo may stop you from taking part in this study at any time:

- If it is in your best clinical interest,
- If you do not follow the study procedures,
- If the study is stopped.

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may continue to be used. You also may be asked to continue in the study to gather further information.

We will tell you about any new information that may affect your willingness to stay in the research study.

What if you are injured from your participation in this research study?

Where to get help:
If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form.
Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries?
Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. Treatment costs for research-related injuries not covered by your insurance will be paid by Mayo Clinic.

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

This study may not make your health better. However, it is possible that the treatment group may benefit from participating in this study as similar approaches have been shown to be effective for increasing bone mass in animal studies.

If you wish, a copy of the result of the DXA (bone density) scans will be provided to you at the screening and 24 month/early termination visits.

What alternative do you have if you choose not to participate in this research study?

This study is only being done to gather information. You may choose not to take part in this study.

What tests or procedures will you need to pay for if you take part in this research study?

You will not need to pay for tests and procedures which are done just for this research study.

These tests and procedures are:

- Study-related blood tests
- DXA bone scans
- HRpQCT bone scans
- DE-QCT bone scan (quantitative CT hip)
- ECG

However, you and/or your insurance will need to pay for all other tests and procedures that you would have as part of your clinical care, including co-payments and deductibles.

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

Will you be paid for taking part in this research study?

Remuneration will consist of up to $970.00 if you complete the entire study. You will receive remuneration for each visit as follows:

1. Screen $ 25.00
   (you will receive an additional $20 if we need to schedule two appointments for your initial screening visit)
2. Lead-in $ 50.00
3. Baseline $ 50.00
4. Month 1 $ 25.00
5. Month 6 $150.00
6. Month 12 $150.00
7. Month 18 $150.00
8. Month 24 or off study $150.00
9. Study Completion $200.00

As a token of study appreciation, you will receive $200.00 for completing all of the study visits in the 2-year period. In addition, you will receive parking passes or taxi reimbursement for the time involved with completing the study visits or travels to the research center for study visits. You will be directed where to park in order to receive the parking passes.

Payment for participation in research is considered taxable income and reportable to the Internal Revenue Service (IRS). Accounts Payable at Mayo Clinic will be given your name, address and Social Security number in order to issue a check for your study participation. If you receive research payments totaling $600 or more in a calendar year, a tax Form 1099 will be sent to you. For Mayo Clinic employees, research payments are included in your paycheck with applicable taxes withheld and reported on your Form W2 after calendar year-end.

Will your information or samples be used for future research?

We would like to keep your sample for future research. Identifiable information such as your name, Mayo Clinic number, or date of birth will be removed from your information or blood samples collected in this study, allowing the information or samples to be used for future research or shared with other researchers without your additional informed consent.

Other researchers at Mayo Clinic who aren't involved with this study may ask to use your sample for future research. Researchers at other institutions may also ask for a part of your sample for future studies. Your sample will be sent to researchers in a coded format, which protects your identity.

Some future studies may examine your DNA, which is the genetic information you inherited from your parents (genetic testing). The Principal Investigator may contact you if there are findings which may be useful for your health care. You would be given general information on the potential risks, benefits, and costs of choosing to learn about the findings.

Because our research is funded by the U.S. National Institutes of Health (NIH), we are required to submit your genetic and/or clinical data in coded form to one or more databases managed by the NIH. These databases permit only controlled access to the data. Researchers who request access to data must promise that they will protect the data, only share data as permitted by the database rules, report any data breaches, and not seek to identify any individual from the data.

That data may be the combined or individual data of many people. Any data that is submitted will not be labeled with your name or other information that could be used to easily identify you.

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

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies, and group health plans must follow this law.

Be aware that this new Federal law doesn't protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.
You can still take part in this current study even if you don't want your sample used for future research. If you agree to give your sample, it will be the property of Mayo Clinic.

Please read the following statements and mark your choices:

1. I permit my sample to be used for genetic analyses related to my response to the study drug:

☐ Yes ☐ No Please initial here: _____Date: _____

2. I permit my sample to be stored and used in future research of osteoporosis at Mayo Clinic:

☐ Yes ☐ No Please initial here: _____Date: _____

3. I permit my sample to be stored and used in future research at Mayo Clinic to learn about, prevent, or treat any other health problems:

☐ Yes ☐ No Please initial here: _____Date: _____

4. I permit Mayo Clinic to give my sample to researchers at other institutions:

☐ Yes ☐ No Please initial here: _____Date: _____

There is a very small chance that some commercial value may result from the use of your donated sample. If that happens, you won't be offered a share in any profits.

You may request to have your sample destroyed by writing to the Principal Investigator. The address is found in the "Contact Information" section of this consent form.

Because we cannot predict how your sample will be used in the future, we cannot promise that samples can be retrieved and destroyed.

How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study. Research material will be stored in locked cabinets, and data stored on computers will be password-protected. If the results of the research are made public, information that identifies you will not be used.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, 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. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or authorization) to Mayo Clinic.

Your health information may be collected from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

- Mayo Clinic research staff involved in this study.
- Other Mayo Clinic staff involved in your clinical care.

- The sponsor(s) of this study and the people or groups hired by the sponsor(s) to help perform this research.
- The Mayo Clinic Institutional Review Board that oversees the research.
- 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 United States agencies) or government agencies in other countries that oversee or review research.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you, but does not include information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

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If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
201 Building 4-60
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: ResearchParticipantAdvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts forever, unless you cancel it.

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Enrollment and Permission Signatures

Your signature documents your permission to take part in this research.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature