OFFICIAL TITLE:

Effect of Intensive Medical Treatment on Quantified Coronary Artery Plaque Components with Serial Coronary CTA in Women with NonObstructive CAD

NCT NUMBER:

NCT05035056

DOCUMENT DATE:

06-16-2022

CONSENT FORM FOR RESEARCH

Study title: Effect of Intensive Medical Treatment on Quantified Coronary Artery Plaque Components with Serial Coronary CTA in Women with NonObstructive CAD: A WARRIOR Ancillary Study

Sponsor: National Institute of Health (NIH)

Cedars-Sinai Principal Investigator: Damini Dey, PhD

Study contact phone number at Cedars-Sinai: 310-423-3763

After-hours emergency contact (24 hours): Rebekah Park 310-423-3763

1. Key Information

We are asking for your consent to take part in this research study. This section provides key information about the study. The rest of this form has more detailed information.

- **Voluntary:** Taking part in this research study is your choice. You can also stop taking part at any time. You will not lose any services, benefits or rights you would normally have if you choose not to take part or stop taking part.

- **Purpose:** The purpose of this study is to measure and evaluate the results of coronary CT angiogram (CCTA) to determine if intensive medical therapy (IMT) had greater reduction in type of cholesterol plaque compared to usual medical care (UC).

- **Procedures:** The main procedures of this trial include a CCTA scan approximately 3 years after the CCTA you had for the Warrior Trial, and a blood draw to evaluate inflammatory biomarkers, including high sensitivity C-reactive protein (hs-CRP).

- **Duration:** If you choose to take part in this study, you will participate in a one-day visit that will include imaging and blood draw.

- **Risks:** All research studies involve some risk. Risks or discomforts from this study may be risks of CT Angiogram with contrast (CCTA); side effects from Beta Blocker, Calcium Channel Blocker and Nitroglycerin if used during CT Angiogram; and bleeding or bruising as result of drawing blood

- **Benefits:** You are not likely to be helped from taking part in this research study. But the information learned from this study may help others in the future.

- **Alternatives:** You can choose not to take part. Please talk about these choices with the study team.

Please take time to read this entire form. You should ask questions before deciding whether to take part in this study. You can talk with family, friends and/or healthcare providers before you decide.

During the study, we may find out new information about this research study. We will tell you about any important changes or new findings that may impact whether you want to continue taking part in the study.

2. Purpose of the Study

The purpose of this study is to evaluate Coronary Computed Tomography (CT) imaging data to determine if women who were treated with intensive medical therapy had a greater reduction in the amount and type of plaque (fat, cholesterol and calcium in the blood which can harden and lessen blood flow) compared to women receiving usual medical care, and to see if this resulted in favorable changes in clinical symptoms.

You are being invited to take part in this research study because you had a coronary CT angiogram (CCTA) scan as a participant in the Women's Ischemia Trial to Reduce Events in Non-Obstructive CAD (WARRIOR) Trial. This study will review the results of previous clinical and image data taken during the WARRIOR Trial, and compare it to the follow-up CCTA being done as part of this study.

The study will enroll up to 400 people in total.

3. Main Study Procedures

This section talks about what will happen in this study. When you read this section, also read the flowchart of procedures. The flowchart is given with this consent form.

The flowchart of procedures shows a timeline of the study. It shows which study procedures are research-related and which are standard of care (routine). **Research-related procedures** are procedures done only for the research study. They would not be performed for your routine care outside of the study. **Standard of care (routine) procedures** would be performed as part of your routine care even if you did not take part in this study. This study includes only research-related procedures

Description of main research procedures:

- CCTA approximately 3 years after the CCTA you had for the WARRIOR Trial
- Blood draw to evaluate functional changes that may accompany coronary artery disease

- Transfer of data from the WARRIOR Trial and the ancillary study to Cedars-Sinai Medical Center, Los Angeles, CA for research analysis

Coronary CT Angiogram:
CCTA is an imaging method that uses a computed tomography (CT) scanner to look at the structures and blood vessels of the heart. You will be given a gown to wear during the procedure. The technologist will clean three small areas of your chest and place electrodes (small, sticky discs) on these areas. The electrodes are attached to an electrocardiograph (ECG) monitor, which shows your heart's electrical activity during the test. A nurse will insert an intravenous (IV) line into a vein in your arm to administer contrast material (dye) during your procedure. You'll lie on a long table that slides through a short, tunnel-like machine. During the scan you'll need to stay still and hold your breath so as not to blur the images. A technician will operate the machine from a room that's separated from your exam room by a glass window. There will be an intercom system that allows you and the technician to communicate with each other. Although the actual scanning portion of the test takes as few as five seconds, it may take up to an hour for the whole process.

How long will you be in the study?
This study includes one imaging visit at the facility where your initial WARRIOR scan took place. Your direct participation will end after that visit, although your data and specimen(s) may be studied for many years.

4. Possible Risks and Discomforts of the Main Research Procedures

This section talks about the possible risks and/or discomforts of the study procedures.

Risks of Coronary CT Angiogram

Radiation risk:
CT images involve the use of radiation. The estimated radiation dose you will be exposed to from the coronary CT scan is 1,690 millirads (mrads) to the skin of your back. A millirad is a unit of measurement for radiation. No amount of radiation is considered safe. In comparison, other estimated doses of medical radiation are: chest x-ray (25 mrads), set of dental x-rays (750 mrads) and barium enema x-ray (2,000 mrads). Non-medical doses are: natural radiation exposure living at sea level (about 360 mrads per year) and watching TV 1 hour per day (1 mrad per year). The maximal amount of radiation you could receive from this study is less than that which is considered acceptable on a yearly basis for individuals who are exposed to radiation because of their work.

Risks of Omnipaque:
We'll follow the clinical standard of care procedure protocol to perform CCTA, including the total amount of the contrast Omnipaque administered up to the max clinical dose. Sometimes repeat dosing may be needed if a repeat scan is needed (for better imaging quality.) Renal failure has been reported in diabetic patients with diabetic nephropathy and in susceptible non-diabetic patients with preexisting renal disease, particularly in the setting of dehydration. Serious allergic reactions may occur in patients with or without a known history

of iodine-contrast allergy. Most adverse reactions appear within 1 to 3 minutes after the start of injection, but delayed reactions may occur.

Very Likely	Rare, but not Serious	Rare, but Serious
• Sensation of warmth, flushing and discomfort • Premature heart beats (PACs, PVCs) • Headache • Nausea • Blurred vision • Chest pain • Taste abnormality	• Transient (temporary) low blood pressure • Vomiting • Skin hives • Itchiness • Shortness of breath • Coughing	• Fainting (syncope) • Heart Failure • Stroke • Anaphylaxis (allergic shock) • Renal Failure

IV iodine contrast:
Giving contrast during the CT exam has some risks. Often people will feel a sensation of warmth and mild discomfort during the injection. Other possible risks that occur infrequently (occur in about 3 in 100 people) include irregular heart rhythms, chest pain, low blood pressure, dizziness, temporary vision changes, headache, nausea and vomiting, itching, hives or flushing.

Severe reactions to contrast dye are uncommon and occur in less than 1 in 1000 people. Serious reactions can include difficulty breathing and anaphylactic shock (low blood pressure and severe problems with breathing). Anaphylactic shock is extremely rare but can result in death. To minimize this risk, you will not be allowed to join this study if you have a known allergy to CT contrast dye. In the event that you experience an allergic reaction to CT contrast, a physician will be present during the scan to give you medical treatment.

There is also a small risk of kidney damage occurring as a result of the contrast dye. Such damage is also rare and is usually, but not always, reversible. Since the risk of kidney damage is higher among persons with abnormal kidney function, the study doctor will review the result of the blood test of your kidney function to determine if it is safe for you to undergo a CT with contrast. To reduce the risk of kidney damage, you will be asked to drink one liter of water the night before your CT scan to prevent dehydration.

Less common risk includes extravasations or “leaking” of the X-ray contrast material outside the vein during injection. This may result in painful soft tissue (skin or just under the skin) swelling and bruising.

Beta-blocker (metoprolol):
Beta-blocker medication (metoprolol) may be necessary if you undergo a coronary CT angiogram, and there is a need to lower your heart rate. Side effects from beta-blockers used for CT scans are rare, and may include abnormally low heart rates, low blood pressure, dizziness, breathing problems, or an allergic reaction. We will observe you closely for any of these effects. If you have a history of severe lung or breathing problems or asthma, we will not give you a beta-blocker medication.

Calcium channel blocker (Diltiazem):
If your heart rate is not slow enough with the beta-blocker medication or you are not able to take beta blocker medications, you might receive a calcium channel blocker medication called diltiazem, which also slows the heart rate but is less likely to cause breathing problems in people with lung disease. Side effects of diltiazem include slow heart rate and rarely dizziness.

Nitroglycerin:
Nitroglycerin may be given if you have a coronary CT angiogram. Nitroglycerin dilates (widens) the heart arteries. Nitroglycerin can sometimes cause a headache or low blood pressure, but if either of these occurs, it is usually brief in duration. Again, we will observe you closely for any of these effects.

Intravenous (IV) Insertion:
An IV catheter (tube) will be inserted into a vein in your arm for the coronary CT angiogram. There is a risk of discomfort at the site where the needle is placed. There is also a risk for infection, bruising, swelling, and bleeding at site the catheter is inserted. When any IV drug or material is given, there is always a chance that the catheter inserted into a vein may infiltrate (become blocked or puncture the wall of the vein) causing temporary swelling, bruising, and/or pain. Should this occur, the study staff would remove the IV and insert a new catheter into another vein. In order to reduce these risks, study staff will follow standard procedures for the safe insertion of IV catheters.

Reproductive Risks:
You should not be pregnant while undergoing the coronary CT angiogram because the radiation can affect an unborn baby.

Unknown Risks
There may be other side effects or risks that we cannot predict. Many side effects may go away shortly after the study medication or procedure is stopped. However, in some cases they can be serious, long-lasting, permanent, and/or fatal.

5. Common Medical Procedures Performed for Research Purposes and Risks

The procedures listed below are often part of routine care for a person with your condition. They are not experimental procedures. The procedures and their risks are research-related. This means they are being *repeated* or performed *more frequently* for this study. These common procedures and their risks should be the same as when performed outside this study.

Study Procedure	Related Risks
Demographic Information: We will ask you about demographics, which may include your age, gender identity, sexual orientation, race and ethnicity.	This does not have any physical risks.
Blood Draw: A needle is placed in the vein in your arm to draw blood. We will draw	Blood drawing may cause some pain. There is a small risk of bleeding, bruising or infection at the site of the blood draw. There is also a small risk of fainting.

about 2 tubes (less than 30cc's) of blood one time only.	
Physical Exam: Includes height, weight, vital signs (heart rate and blood pressure)	There are no physical risks associated with these procedures
Concomitant Medications: You will be asked about your previous and current medications that you take.	There are no physical risks associated with these procedures.
Pregnancy Test: People who can become pregnant will have a pregnancy test. Urinesamples will be used to do the pregnancy test.	You will be told about any positive test result. At that point, you should talk about your available options with your primary care doctor.
Electrocardiogram (ECG): This test is often called an ECG or EKG. This test measures the electrical activity of the heartbeat. It does this by using electrodes (disposable, sticky adhesive discs). The discs are placed on the skin of your chest.	Removing the disposable sticky discs from your skin may cause minor skin discomfort or irritation. This includes pulling on the skin/hair during removal of the patches.
Infusion/Intravenous (IV) Lines: An IV line is small tube inserted by a needle into a vein, usually in your arm or hand. It can stay in place for a long time, allowing drugs or other fluids to be put into the body.	Most people do not experience any issues from IV lines. Complications are rare but can include bruising, swelling of the vein and infection. There is also a small risk of feeling lightheaded and fainting. The IV may come out accidentally or blood may leak around the line. If the IV is not in the vein, medication or fluid can enter the surrounding soft tissues. This can cause swelling, discomfort, bruising and irritation. Rarely, a clot can develop in the IV line itself. If this happens, the staff may remove the old IV line and start a new IV line.

6. Benefits From Taking Part in the Study

You should not expect to benefit from taking part in this research study.

7. Whether Research Results Will Be Shared

The imaging procedure(s) in this study are being done for research purposes. However, they will be done following standard clinical imaging techniques. The imaging results may be shared with you. They may be placed in your Cedars-Sinai medical record.

Unanticipated Incidental Findings

We will contact you using the last contact information you gave if, unexpectedly, we find results that suggest potentially clinically relevant medical information. We may suggest you talk with your treating physician about possible additional clinical testing to further evaluate the research finding. You and/or your insurance would pay for any additional testing and any related treatment.

8. Reasons Participation May Be Stopped

Your participation in this study may be stopped at any time. The researcher or the sponsor can stop your participation without your consent for any reason. Some reasons for stopping your participation include:

- The study is stopped or suspended.
- Funding for the study is reduced, stopped or withdrawn.
- It is in your best interest.
- You do not follow the study procedures.

9. Choosing to Take Part and Other Options

Taking part in research is voluntary. You have the right to choose not to take part. You can stop taking part in this research study at any time. You can do this without any penalty or loss of benefits to which you would be entitled outside of the study. Your choice not to take part or to stop taking part will not affect the care you get at Cedars-Sinai.

If you decide to stop taking part, we will keep any data collected on you up to the time you choose to stop. Also, if you stop taking part, the study team may ask you whether you want to give further data from your routine medical care.

10. Confidentiality Protections

We will do our best to keep your personal information collected as part of this study private. But we cannot guarantee total privacy. We may put a copy of your research consent and authorization forms in your electronic medical record at Cedars-Sinai. Your personal information may be given out if required by law. Publications or presentations about this study at scientific meetings will not use your name and other identifiable personal information.

Organizations that may look at and/or copy your medical records for research oversight, quality assurance and data analysis include:

1. Accrediting agencies (agencies that grant official certifications to educational institutions)
2. Government and regulatory groups, such as the Food and Drug Administration (FDA) and Office for Human Research Protections (OHRP)
3. The Institutional Review Board (IRB), which reviews research to protect people taking part in studies
4. Safety monitors, which monitors the safety of individual participants and the overall safety of the study

5. Companies that sponsor the study and authorized representatives of the sponsor

Attached to this consent form is an Authorization Form. It outlines with whom your information may be shared for this research and under what circumstances.

We might share your information and/or research samples collected in this study. It might be shared with other researchers at Cedars-Sinai, other academic institutions or third-party commercial entities for future research without additional informed consent from you. Information that identifies you will be removed and will not be shared with other researchers or anyone outside of Cedars-Sinai.

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

11. Research-Related Illness or Injury

Contact your study doctor at once if you feel that you are ill or have been injured because of taking part in this study. If it is a medical emergency, call 911 or go to an emergency room. Promptly notify your study doctor of your situation at the phone number listed on page 1 of this consent form.

12. Financial Considerations

Costs of Participation
You and your insurance company will not be charged for your participation in this research study. The Study Sponsor will cover the cost of all items, drugs and services required by this study. This includes any procedures required by the study that may be standard of care.

Payment

You will be paid $100 for participating in the research study.

You will be paid back for parking or receive a parking voucher if you park in approved parking facilities.

You may have to fill out a W-9 form to get paid. Our accounting department at Cedars-Sinai will keep the W-9 form. Any amount of payment may be reportable to the IRS. If you receive $600 or more from Cedars-Sinai in a calendar year, a 1099 form will be filed with the IRS in accordance with federal tax law. Check with a tax professional if you have questions.

Payment will be managed by an outside company. They will give you a debit card. Your payment for taking part in the research will be loaded onto the card. The money will generally be available within 4 weeks after you finish each study visit. You will need to share

your name, address, social security number and birthdate with the outside company to get this debit card. Your information will be stored in a protected fashion. Your information will be removed from the debit card system once the study is finished and the money on the card has been used. The outside company will not share your information with any other third parties.

Financial Interest in the Research
The principal investigator and institution have no potential financial conflict of interest with this study.

13. Contact for Questions or Problems

Please contact the investigator for questions, problems or concerns about the research. Their contact information is on page 1 of this form.

You might have feedback, questions, problems, concerns or want to obtain more information about this study. If so, you can talk with someone who is not part of this study by contacting:

Cedars-Sinai Human Research Protection Program (HRPP)
Phone: 310-423-3783
Email: ResearchConcerns@cshs.org
Website: cedars-sinai.org/research/administration/office-of-research-compliance/review-board.html

The Cedars-Sinai HRPP protects the rights and welfare of research participants.

Experimental Subject's Bill of Rights

In accordance with California Health and Safety Code 24172, any person who is required to consent to participate as a subject in a research study involving a medical experiment or who is requested to consent on behalf of another has the right to:

1. Be informed of the nature and purpose of the experiment.

2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.

3. Be given a description of any attendant discomforts and risks to the subject reasonably to be expected from the experiment.

4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

5. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.

6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.

7. Be given an opportunity to ask any questions concerning the experiment or the procedure involved.

8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.

9. Be given a copy of any signed and dated written consent form used in relation to the experiment.

10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

AUTHORIZATION FOR USE AND DISCLOSURE OF IDENTIFIABLE HEALTH INFORMATION FOR RESEARCH

1. USE AND DISCLOSURE OF HEALTH INFORMATION

If you agree to this Authorization, you give permission to the Sponsor, Principal Investigator, other investigators and their research team described in the Consent Form for Research ("Research Team") to use or disclose your identifiable health information ("private information") for the research study titled "Effect of Intensive Medical Treatment on Quantified Coronary Artery Plaque Components with Serial Coronary CTA in Women with NonObstructive CAD: A WARRIOR Ancillary Study" which is described in the Consent Form for Research ("Consent Form") to which this Authorization is attached. In particular, you authorize the research team acting under the direction of the Principal Investigator to review your medical records and collect your private information from the following sources:

☒ Laboratory tests
☒ Pathology reports
☒ Imaging reports (e.g., x-rays or scans)
☐ Photographs or videos of your image
☒ Doctor/clinic records
☒ Hospital/medical records
☐ Mental health records
☐ Billing records

☒ Demographics, which may include age, gender identity, race, ethnicity, and/or sexual orientation

☐ Other tests or other types of medical information: N/A

2. WHO WILL HAVE ACCESS TO YOUR PRIVATE INFORMATION?

Your private information will be used by and/or shared with the Research Team.

In addition to the research team, if applicable, the following parties may receive your private information and inspect your records:

- The reviewing Institutional Review Boards and Cedars-Sinai offices with authority to oversee research compliance.
- U.S. government agencies, such as the Food and Drug Administration and the Department of Health and Human Services.
- Researchers at other organizations who are participating in this research study.

- The Study Sponsor, its business partners, and Cedars-Sinai's business partners for matters related to research study oversight, conduct of the research, data analysis, use of research results in product development, and payment or reimbursement.
- Representatives from regulatory agencies in other countries may join in the review of your research records, including research-related medical reports and information, with the Sponsor and/or the FDA.

Cedars-Sinai takes steps to protect your private information when sharing it with the recipients described above. Though these steps and applicable law are meant to protect your private information, there is a risk that a recipient could share your private information without your permission.

3. WHEN WILL MY AUTHORIZATION EXPIRE?

By signing this document, you authorize the use and sharing of your private information until the end of the research study and any related optional sub-study you choose to participate in.

4. REVOKING AUTHORIZATION

You may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, the research team may still use or disclose private information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this Authorization, you must write to the Principal Investigator of the research study by writing to the Office of Research Compliance and Quality Improvement, 6500 Wilshire Blvd, Suite 1800, Los Angeles, Calif. 90048 and/or emailing to ResearchConcerns@cshs.org.

5. NOTICE OF RIGHTS AND OTHER INFORMATION

You do not have to agree to this Authorization, but if you do not agree, you may not participate in the research study. Cedars-Sinai may not condition (withhold or refuse) the provision of standard of care treatment for you on whether you agree to this Authorization.

If you agree to this Authorization, please sign on the appropriate signature line on the Signature Page. You will receive a copy of this Authorization.

Signature Page

Consent Form for Research and Authorization for Use and Disclosure of Identifiable Health Information (Research)

If you agree to take part in this study, you should sign and date on the signature lines below. You will be given a signed and dated copy of this form. This includes the "Experimental Subject's Bill of Rights," "Authorization for Use and Disclosure of Identifiable Health Information (Research)" and any optional sub-study descriptions, when applicable.

Signature by the Participant
I agree to take part in the research study described to me during the informed consent process and described in this informed consent form. My questions have been answered to my satisfaction.

You will be given a signed and dated copy of this form.

Participant name (please print)	Signature	Date

Authorization for Use and Disclosure of Identifiable Health Information (Research): *I hereby agree that my identifiable health information may be used and/or disclosed in accordance with the "Authorization for Use and Disclosure of Identifiable Health Information (Research)."*

Participant name (please print)	Signature	Date

Signature by the Investigator
I attest that all the elements of informed consent described in this form have been discussed fully in non-technical terms with the participant. I further attest that all questions asked by the participant were answered to the best of my knowledge.

Investigator name (please print)	Signature	Date

Signature by the Interpreter/Witness
(Signature of an interpreter is only required when enrolling a non-English-speaking subject with the assistance of an interpreter and IRB-approved "short form" consent processes. The witness may be any person who is conversant in both English and the

language of the non-English-speaking subject, such as a certified hospital interpreter, study staff, a family member or other person. The witness signs the consent forms to confirm that the oral interpretation occurred.

Signature of a witness is required when an English-speaking subjects who has been determined to have capacity to consent is unable to read or physically sign the consent form, but choses to indicate via a "mark" or verbally that he/she agrees to participate. The witness signs the consent form to confirm that an oral consent process occurred and that the individual verbally consented to participate in the research.)

Interpreter/Witness name (please print)	Signature	Date

To be marked at time of signature:
Consent obtained:
☐ *From non-English speaking individual with assistance of interpreter*
☐ *From English speaking individual who is not physically able to sign the consent document*