Official Title: WFBCCC 74121: Oral Aromatase Inhibitors Modify the Gut Microbiome
NCT05030038
IRB-Approved Date: 03/13/2026

Department/Section of *Hematology and Oncology*

ORAL AROMATASE INHIBITORS MODIFY THE GUT MICROBIOME EFFECTING ESTROGEN BIOAVAILABILITY

Informed Consent Form to Participate in Research
Katherine Ansley, MD, Principal Investigator
WFBCCC 74121

SUMMARY

You are invited to participate in a research study. The purpose of this research is to study the bacteria in your gut before you receive a medicine called an aromatase inhibitor for your breast cancer and after you receive medicine for your breast cancer. Aromatase inhibitors (AI) stop the production of estrogen in postmenopausal women. You would receive this drug, whether or not you participate in this study. Your participation in this research will involve 2 visits (which is already part of your routine visit) and last about 12 weeks.

Participation in this study will involve donating a sample of stool and donating a blood sample for analysis in a lab. All research studies involve some risks. A risk to this study that you should be aware of is the risk of breach of confidentiality and risk of the blood draw. You will not benefit from participation in this study.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. There may be other choices available to you. Some other choices may include participating in another study or not participating in a study at all. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. The person in charge of this study is Katherine Ansley, MD. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study her contact information is: [redacted].

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at [redacted] or the Research Subject Advocate at Wake Forest at [redacted]

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INTRODUCTION

You are invited to participate in a research study. The purpose of this research is to study the bacteria in your gut before you receive a medicine called an aromatase inhibitor for your breast cancer and after you receive medicine for your breast cancer. Aromatase inhibitors (AI) stop the production of estrogen in postmenopausal women. You would receive this drug, whether or not you participate in this study. Your participation in this research will involve 2 visits (which is part of your routine visit) and last about 12 weeks.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to study the bacteria in your gut before and after receiving the AI drug. Researchers hope to learn about the differences in the bacteria before and after the drug has been taken.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

Twenty-five people at *one* research site will take part in this study.

WHAT IS INVOLVED IN THE STUDY?

Study Schedule

	Pre-Study Visit	**Baseline**	**Week 4 Stool Collection**	**Week 12 Follow Up Visit**
Informed consent	X			
Demographics	X			
History and Physical	X			
Concurrent meds	X			X
Vital signs	X			X
Height, Weight, M^2	X			X
Blood draw		X		X
Stool swab		X	X	X
Monitoring phone call			X	
Probiotic Use	X			X
Adverse event evaluation			X	X
Diet Questionnaire	X			X

PRESTUDY ASSESSMENTS

After you have agreed to be in this study, you will need to undergo the following tests or procedures to find out if you can be in the study. Some of these tests or procedures may be part of your regular medical care and may be done even if you do not take part in the study. If some of these were completed recently, they may not need to be repeated.

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- Discussion of this study, and review and signing of this Informed Consent Form.
- Recording of your demographic information, including your age, sex, and race/ethnicity
- A quick review of your level of mobility, your capability to care for yourself, and ability to work.
- Review of your medical and surgical history-This review will include previous cancer treatments and any medications, including herbal or dietary supplements that you are taking or have taken within the last 7 days.
- Complete physical examination that will include the recording of your height and weight
- Measurement of your vital signs (blood pressure, pulse, body temperature, and respiratory or breathing rate)
- You will be asked about your use of Probiotics (things such as yogurt, kim chi, sauerkraut, etc.)
- You will complete a questionnaire about your diet.

BASELINE

At the baseline visit, the following procedures will be performed:

- You will provide a stool sample, using a kit provided by the study team prior to starting your endocrine therapy This will be collected at home.
- You will have approximately 1 teaspoon of blood withdrawn from a vein, for research.

Stool Sample-Please refer to Stool Collection Handout at the end of this document.

WEEK 4 Stool Sample

At week 4, you will perform the following at home:

- You will receive a phone call from the study team to remind you to submit your stool sample. You will be asked about any symptoms you are having.

Stool Sample- Please refer to the Stool Collection Handout at the end of this document.

WEEK 12 FOLLOW UP VISIT

At the 12 Week follow up visit you will have the following procedures performed:

- Review of your medical and surgical history: This review will include any medications, including herbal or dietary supplements that you are taking or have taken within the last 7 days.
- Complete physical examination that will include the recording of your height and weight
- Measurement of your vital signs (blood pressure, pulse, body temperature, and respiratory or breathing rate)
- You will have approximately 1 teaspoon of blood withdrawn from a vein, for research.
- You will complete a questionnaire about your diet.

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Stool Sample- Please refer to the Stool Collection Handout at the end of this document.

BIOLOGICAL SAMPLES

If you agree to participate in this study, we will draw 2 teaspoons of blood and a fecal sample to use for future research. These samples will be kept and may be used in future research to learn more about other diseases. Your blood sample will be obtained in the Wake Forest Baptist Comprehensive Cancer Center, at the main campus or one of the satellite clinics; your fecal sample will be collected at home. The blood sample will be stored at the Cook Lab at BioTech Place and it will be given only to researchers approved by Katherine Ansley, MD. Your fecal sample will be stored at CosmosID and it will be given only to researchers approved by Katherine Ansley, MD. An Institutional Review Board (IRB) must also approve any future research study using your tissue sample. In order to participate in this study, you must be willing to provide these samples for future research.

The research that may be performed with your blood and fecal sample is not designed to help you specifically. There is no personal benefit to you from taking part in this aspect of the research study. It might help people who have diseases at some point in the future, but it is not known if this will happen. The results of the research performed with your blood /fecal sample will not be given to you or your doctor. The results will not be put in your medical record. The research using your blood/fecal sample will not affect your care.

Your blood/fecal sample will be used only for research and will not be sold. The findings from this research may result in the future development of products that are of commercial value. There are no plans to share any of the profits with you which may occur as a result of the research.

HOW LONG WILL I BE IN THE STUDY?

You will be in the study for about 12 weeks. You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first.

WHAT ARE THE RISKS OF THE STUDY?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. Risks and side effects related to the procedures we are studying include:

You may experience discomfort, bruising and/or bleeding where the needle is inserted. Occasionally some people become dizzy lightheaded or feel faint. Infection may occur on rare occasions. Frequent donation of blood can result in low iron in your blood (iron deficient anemia).

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect

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your confidential information. There also may be other risks that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

The risk of harm or discomfort that may happen as a result of taking part in this research study is not expected to be more than in daily life or from routine physical or psychological examinations or tests. You should discuss the risk of being in this study with the study staff.

Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

You are not expected to receive any direct benefit from taking part in this research study. We hope the information learned from this study will benefit other people in the future.

WHAT OTHER CHOICES ARE THERE?

This is not a treatment study. Your alternative is to not participate in this study.

WHAT ARE THE COSTS?

All study costs, including procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required or permitted by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified**.**

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

TEXT MESSAGE COMMUNICATION. I give permission to Atrium Health, Wake Forest University Health Sciences, and their respective affiliated entities and representatives (including third-party agents if applicable) to contact me by text message at the number I provided to send information, reminders, and to communicate with me about the research study. I understand that

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I am responsible for the standard text message rate of my carrier. I also understand that text messaging is not a secure form of communication and I accept the risk that individuals not involved in the research study may be able to access the text messages. I also understand that texting is not to be used for emergency situations.

EMAIL COMMUNICATION. By providing my email address, I give permission for Atrium Health, Wake Forest University Health Sciences, and their respective affiliated entities and representatives (including third-party agents if applicable) to send me information, reminders, and messages about the research study by email. I understand that these email messages may not be encrypted, and I understand and accept the risks that individuals not involved in the research study may be able to access unencrypted email messages. I also understand that email is not to be used for emergency situations.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

There are some important things that you need to know. The Certificate DOES NOT stop reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate CANNOT BE USED to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate DOES NOT stop disclosures required by the federal Food and Drug Administration (FDA). The Certificate also DOES NOT prevent your information from being used for other research if allowed by federal regulations.
Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information**.**

WILL YOU BE PAID FOR PARTICIPATING?

You will not be paid for participating in this study. However, you will receive validation of your parking ticket.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by the Wake Forest Baptist Comprehensive Cancer Center. The sponsor is providing money or other support to the researchers to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor.

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WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and/or information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**: name, medical record number, information about your cancer treatment and medical visits.**

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study may be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with the health care operations of Atrium Health, Wake Forest University Health Sciences, and their respective affiliated entities.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and Atrium Health Facilities ; representatives from government agencies such as the Food and Drug Administration (FDA) or the Office of Human Research Protections (OHRP), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for an indeterminate period of time. This authorization does not expire.

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Any research information entered into your medical record will be kept for as long as your medical record is kept by the Medical Center. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Katherine Ansley, MD that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Katherine Ansley, MD
[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

Laboratory test results and other clinically relevant medical reports created as a result of your participation in the research study may be entered into the computer systems of Atrium Health, Wake Forest University Health Sciences, and/or their respective affiliated entities. These results and reports will be kept secure, with permission to access this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A medical record will be created for all study participants seen on-site and if a medical record doesn't already exist. Information about your participation in the study will be placed in the medical record, along with any routine medical test results that were obtained as part of this study.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because, it is in your best medical interest, your condition worsened, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped. Information that identifies you may be removed from the data or specimens that are collected as part of this study and could be used

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for future research or shared with others without additional consent.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, *Katherine Ansley, MD at* [redacted]

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted] or the Research Subject Advocate at [redacted]

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm

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Stool Collection Instructions

GENERAL INFORMATION

We would like a stool sample BEFORE you start taking your medicine for your cancer treatment. **After the stool sample is collected or if you are unable to provide a sample within 4 days**, you may begin dosing as instructed.

Please collect a sample that is solid or somewhat solid. If you think you will have diarrhea, skip that sample and wait for the next one.

When the stool sample is collected, please contact the study team. Contact information will be given to you at the time of consent.

If we do not hear from you within 4 days of your first study visit, someone from the study team will call you.

Your kit contains: an instruction card, 2 paper feces catchers, 1 long-handled brush, 1 pipette (elongated eyedropper), 1 collection tube, 1 orange biohazard bag, 1 prepaid padded envelope for mailing

Detailed Instructions

1. When you are ready to pass your stool, wash your hands thoroughly with soap and water.
2. Prepare the paper Feces Catcher.
   a. There are 2 fecal catchers in your kit. They look like booklets or pamphlets.
   b. You only need to use 1 of the fecal catchers. If your attempt at a stool sample is a failure for any reason, use the second fecal catcher for your next bowel movement.
   c. Use the arrows to guide you, and open the paper Feces Catcher.
   d. Place the Fecal Catcher, sticky ends down, toward the back of the toilet seat. This will keep it in place while you pass the stool.
3. Sit on the toilet seat over the fecal catcher, and pass the stool so that the stool rests on the paper Feces Catcher.

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4. Unwrap the brush and remove the collection tube from the baggie. Unscrew the cap on the tube and set it aside, taking care not to let the inside of the lid touch any surfaces. Do not spill the liquid from the tube; set the tube aside.
5. Use the brush to stab your fecal sample 5-10 times in different places so that the bristles on the brush collect some fecal matter.
6. Insert the dirty brush into the tube with the clear fluid preservative. Whisk the brush into the liquid for about 10 seconds, so that the collected fecal sample goes into the liquid.
7. Tighten the cap on the collection tube and invert the tube about 10 times to mix the contents.
8. Place the collection tube into the orange biohazard specimen bag and seal the bag.
9. Place the orange biohazard specimen bag into the padded envelope and mail it. Postage is pre-paid, so it is ready for the postman.
10. Release the Feces Catcher and remaining stool into the toilet water, and let it get soggy for about 1 minute. Then it can be flushed away!
11. Discard what remains of your collection kit.
12. Wash your hands thoroughly with soap and water.
13. Contact the study team as instructed at the top of these guidelines. Please contact the study team using the contact information you have been provided. If you have lost this information, you can leave a message by calling the clinic at [redacted] and a study team member will return your call.

If you would like additional detailed instructions, please read the provided COSMOSID handout or see the feces catcher instructional video at https://www.fecesvanger.nl/en_GB/c-2863379/how-it-works

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