Wake Forest®
School of Medicine

Department of Internal Medicine/Section on Nephrology

AN OPEN LABEL STUDY OF THE EFFECT OF ERGOCALCIFEROL ON PLASMA AND URINARY MUCIN-1 LEVELS IN HEALTHY INDIVIDUALS AND INDIVIDUALS WITH AUTOSOMAL DOMINANT TUBULO-INTERSTITIAL KIDNEY DISEASE DUE TO MUC1 MUTATIONS (ADTKD-MUC1)

Informed Consent Form to Participate in Research
Anthony J. Bleyer, MD, MS, Principal Investigator

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you are a healthy individual or have been diagnosed with mucin-1 kidney disease. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to find out if a high dose of Vitamin D (ergocalciferol) will lower blood levels of a specific protein called mucin-1. We are studying this protein due its involvement in a disease called autosomal dominant tubulointerstitial kidney disease due to mucin-1 mutations (ADTKD-MUC1). You are invited to be in the study because you are a healthy individual or have been diagnosed with the kidney disease caused by mucin-1.

We want to study the effects of ergocalciferol on mucin-1 levels found in blood and urine. Individuals with inherited kidney disease due to mucin-1 develop slowly progressive kidney failure. There are no other symptoms associated with this disease except the loss of kidney function over time. Ergocalciferol has been shown in the lab to decrease mucin-1 levels found in the blood and urine and therefore, might be effective in treating mucin-1 kidney disease. Ergocaliferol, an over-the-counter vitamin, has been approved by the US Food and Drug Administration (FDA) to treat low levels of Vitamin D, but it has not been approved for use in this manner.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

Approximately eighty (80) people will be enrolled.

WHAT IS INVOLVED IN THE STUDY?

Participation in this study will involve providing consent and having blood and urine specimens drawn to see if you are eligible. If you take part in this study, you take a one-time dose of ergocalciferol and have blood and urine specimens collected during several study visits to understand what changes might occur in blood and urine mucin-1 levels in healthy individuals

and in individuals with ADTKD-MUC1.

For study participants who are local to Winston-Salem, NC, the study visits will be in-person at Wake Forest Baptist Medical Center. Blood specimens will be drawn by study staff at the time of the visit along with an urine specimen collected and processed at Wake Forest. For study participants who are not local to Winston-Salem, NC, the study visits will be conducted over the phone, and arrangements will be made to have the blood specimens drawn at an outside certified laboratory. The study participant will also collect an urine specimen on the day of the blood specimen draw, and blood and urine specimens will be mailed overnight to Wake Forest. A one-time genetic test will be done for a gene that affects mucin1 levels.

1st Screening Visit:

You will review and sign the study consent with a research team member, and demographic information and a medical history will be obtained. Medications that you are currently taking will also be reviewed. For females of child-bearing potential, a urine pregnancy test will be performed. Once completed, you will have blood and urine specimens collected. The amount of blood collected will equal approximately 2 tablespoons.

On Study Visit:

On Day 0, you will take by mouth four (4) pills containing 50,000 units of ergocalciferol, totaling 200,000 units, as a one-time dose. You will then have blood and urine specimens collected. The amount of blood collected will equal approximately 1½ teaspoons.

Monitoring Visits:

On Day 3 after taking ergocalciferol, you will have blood and urine specimens collected. The amount of blood collected will equal approximately 2½ teaspoons

On Day 7 after taking ergocalciferol, you will have blood and urine specimens collected. The amount of blood collected will equal approximately 1½ tablespoons. For women of child-bearing potential, a urine pregnancy test will be performed.

On Days 10 and 14 after taking ergocalciferol, you will have blood and urine specimens collected. The amount of blood collected will equal approximately 1½ teaspoons.

Observation Visit:

On Day 28 after taking ergocalciferol, you will also have blood and urine specimens collected. The amount of blood collected will equal approximately 1 tablespoon.

During the study, you will have approximately 7 tablespoons of blood drawn over 7 study visits.

De-identified blood and urine specimens will be sent to the Broad Institute of Harvard Medical School, the Massachusetts Institute of Technology, Cambridge, MA, the University of Pittsburgh, Pittsburgh, PA and to the laboratory of Dr. Stanislav Kmoch, Ph.D. of the First Faculty of Medicine, Charles University, Prague, Czech Republic for further evaluation and analysis.

Biospecimens will only be stored if private identifiers (your name, address, date of birth, etc.) is removed. When the identifying information is removed, your private information or biospecimen may be used for future research studies or given to other research investigators without getting additional informed consent from you or your legally authorized representative.

We can send copies of your test results to your personal physician. This would include the blood chemistry and hemotology results. Even if you do not wish to have any of your medical information sent to your physician, you can still participate in this research study.

Do you request that we send important medical findings from your study tests/exams to your personal physician?

[ ] Yes [ ] No _____ Initials

Storage of Biological Tissue

If you agree to participate in this study, we will store blood and urine specimens that may be used for future research. These samples will be kept and may be used in future research to learn more about other diseases. Your sample will be obtained the Section on Nephrology at Wake Forest University Baptist Medical Center. The sample will be stored in Dr. Bleyer's laboratory at Wake Forest School of Medicine, Winston-Salem, NC, and it will be given only to researchers approved by Dr. Anthony Bleyer. 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 this sample for future research.

Your blood and urine samples will be stored with a unique identifier and will not include any identifiable information about you such as your name, address, telephone number, social security number, medical record number or any of the identifiers outlined in the HIPAA Privacy Rule. The unique identifier will be a randomly assigned number and only the principal investigator will have access to the code that links the unique identifier to you. Your name, address, social security number, etc., will never be disclosed to future researchers and neither will the code that links your identifiers to the sample.

The research that may be performed with your blood 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 will not be given to you or your doctor. The results will not be put in your medical record. The research using your blood and urine samples will not affect your care.

Your blood and urine samples 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.

In the future, people who do research may need to know more about your health. While the study investigator may give reports about your health, he/she will NOT be given your name, address, phone number, or any other identifying information about who you are, unless you agree to be contacted in the future.

____YES, you may contact me for future research studies.
____NO, I do not want to be contacted regarding future research studies.

HOW LONG WILL I BE IN THE STUDY?

You will be in the study for up to 6 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 to learn about any potential health or safety consequences.

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.

Ergocalciferol is a synthetic plant-based vitamin that is given to increase Vitamin D levels. A common dose of ergocalciferol in Vitamin D deficiency is 50,000 units orally once a week x 4 weeks and then 50,000 units once a month. We identified 19 studies that gave a one-time dose of at least 200,000 units of ergocalciferol. These studies showed no clinically significant changes in blood levels of common chemicals like calcium, and the increase in Vitamin D levels was within a safe range (ie, not to a toxic level). No serious adverse events were reported except for a slightly increased risk of hip fracture in elderly patients in the year after ergocalciferol administration. Two studies in chronic kidney disease patients found that high doses of Vitamin D was well tolerated.

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other side effects 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.

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.

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).

Reproductive Risks and other Issues to Participating in Research

You should not take any cholecalciferol, ergocalciferol, or other products containing more than -500 units of Vitamin D (contained in a daily multi-vitamin) for six months after participating in this study unless your physician finds that your Vitamin D level is low.

Contraceptive Measures for Females

Due to the lack of large studies of Vitamin D in pregnant women and the unknown risks and potential harm to the unborn fetus, sexually active women of childbearing potential must use a reliable method of birth control while participating in this study. Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, intrauterine device (IUD), DepoProvera, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and spermicidal foam or gel and/or a cervical cap or sponge. We encourage you to discuss this issue further with your physicians if you have any questions.

Pregnant women are excluded from participation in this study. If you are a sexually active woman of childbearing potential, a urine pregnancy test will be administered no later than 2 weeks and no earlier than 1 week prior to the administration of ergocalciferol. A follow-up pregnancy test will also be administered on Day 7 after taking ergocalciferol.

Contraceptive Measures for Males

Due to the lack of any studies in this area, it is not possible to tell if your participation in this research study might damage your sperm, which could cause harm to a child that you may father while on this study. Such harm may be currently unforeseeable. If you are sexually active, you must agree to use a medically acceptable form of birth control in order to be in this study from the time of enrollment until 45 days after the end of the study. Medically acceptable contraceptives include: (1) surgical sterilization (such as a vasectomy), or (2) a condom used with a spermicide. Contraceptive measures such as Plan B (TM), sold for emergency use after unprotected sex, are not acceptable methods for routine use. You should inform your partner of the potential for harm to an unborn child. She should know that if pregnancy occurs, you will need to report it to the study doctor, and she should also promptly notify her doctor.

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 option is not to participate in the clinical trial.

WHAT ARE THE COSTS?

All study costs, including any study medications and 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 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.

The purpose of this research study is to obtain data or information on the safety or effectiveness of ergocalciferol. The results will be provided to Wake Forest School of Medicine, Section on Nephrology, the Food and Drug Administration and other federal and regulatory agencies as required.

WILL YOU BE PAID FOR PARTICIPATING?

You will be paid $210.00 if you complete all the scheduled 7 study visits. If you withdraw for any reason from the study before completion you will be paid $30 for each complete study visit.

To receive payment, you must provide your social security number, name and address so that we can comply with IRS (Internal Revenue Service) reporting requirements. When payments are reported to the IRS we do not let them know what the payment is for, only that you have been paid. If you do not wish to provide this information you can still take part in this study but you will not be paid.

The findings from this research may result in the future development of products that are of commercial value. There are no plans to provide you with financial compensation or for you to share in any profits if this should occur.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by Wake Forest University Health Science, Section on Nephrology. The researchers do not hold a direct financial interest in the product being studied.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional

information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call [redacted]

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**:** your name, demographic information (address, phone #, email address), date of birth, most recent laboratory results, and mucin-1 kidney disease status.

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 Medical Center operations. 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 North Carolina Baptist Hospital; 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.

Monitors, auditors, IRB or other regulatory agencies will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

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. 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 Dr. Anthony J. Bleyer 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:

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.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

A description of this clinical trial will be available on http://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 Web site at any time

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 new information becomes available, you had an unexpected reaction or it is in your best medical interest

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

This study may be enrolling students from the Wake Forest University and/or Wake Forest University Medical Center. In addition to your rights as a research participant noted in the previous section, as a student, you are under no obligation to participate in this study. You may refuse to participate or withdraw from the study at any time and for any reason without affecting your grades, performance evaluations, or assignments. You will not be pressured into participating in this research study by any statements or implied statements that your grades, performance evaluations or assignments will be affected by your willingness to enroll in the study. Your medical records/information will not be used by the faculty, administration or study staff to make decisions regarding the status of your medical benefits. If you have questions regarding your enrollment in the study and your status as a medical student, please contact the Office of Student Services for additional information.

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, Dr. Anthony Bleyer 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