CONSENT FORM

Safety and Efficacy of Avmacol ES in Chronic Kidney Disease: First Phase

Principal Investigator: Thu H. Le, MD

This consent form describes a research study, what you may expect if you decide to take part and important information to help you make your decision. Please read this form carefully and ask questions about anything that is not clear before you agree to participate. You may take this consent form home to think about and discuss with family or friends.

Key Information

- Being in this research study is voluntary – it is your choice.
- You are being asked to take part in this study because you are an adult who have been clinically diagnosed with chronic kidney disease for which there is no cure, and you may or may not progress to end stage kidney disease.
- The purpose of this study is to determine dosage, safety, and adverse events related to the investigational drug Avmacol Extra Strength (ES) being studied in patients with chronic kidney disease (CKD). The drug is being studied to determine if it can decrease kidney disease progression rate and improve levels of antioxidants and inflammation in patient with chronic kidney disease (CKD).
- Your participation in this study will last for 7 days or less if you develop serious side effects or have side effects to Avmacol ES that cannot be helped by reducing the dose.
- Study procedures will include two in-person study visits. The first visit will last about one hour and include a cheek swab to extract DNA, receive questionnaires, and obtaining the study drug to be taken at home over a 7-day period. The second visit (day 7) will last for 8 hours and involve collection of urine and blood samples at different time intervals during the 8-hour period. This visit will take place at Strong Memorial Hospital with food and beverage provided. Outside of the in-person study visits you take the study drug (tablets) at home as instructed and complete questionnaire. Additionally, information from your medical record will be obtained for the study.
- There are risks from participating.
  - The most common risks with the study drug Avmacol ES, are side effects of headache and gastrointestinal, including nausea and indigestion, which are lessened or prevented when taken with food.
  - The most serious risk for Avmacol ES is the possibility of allergic reaction. See the “Risks of Participation” section in this consent form for more information. You should discuss these risks in detail with the study team.

- You might not benefit from being in this research study.

Purpose of Study

The purpose of this study is to test the safety of drug (Avmacol ES) to determine if it can decrease kidney disease progression rate, decrease markers of oxidative stress, and inflammation that is usually high in patients with kidney disease.

The study drug Avmacol ES is a commercially available as a supplement however, it has never been tested in patients with kidney disease. Avmacol has not been approved by the Food and Drug Administration (FDA) for treatment of chronic kidney disease and is therefore investigational for the purpose of this study.

This is a phase 1 drug study which is being done to establish a safe dose for patients with chronic kidney disease based on blood levels of the drug. We will also obtain your DNA to determine if you have a gene (GSTM1) that affects the clearance of the drug; no other genetic testing will be done on your DNA sample. Up to 50 percent of human populations do not express this gene.

If proven to be well tolerated, this phase of the study will determine the best dose for the next study phase.

Description of Study Procedures

Your participation in the study will be 7 days or less if you develop serious side effects or have side effects that cannot be mitigated by dose reduction.

Medical Record Data: A member of the study team will access your medical record to collect information about your age, sex, race, height and weight, medications you are taking, and the results of any laboratory or diagnostic tests. For eligibility purposes, if you are of childbearing potential, you will be asked to complete a urine pregnancy test before taking the study drug.

DNA sample: After you consent, a buccal (cheek) swab will be obtained to extract DNA to determine if you have or don't have the GSTM1 gene that can metabolize the drug. We will only determine whether or not you have the GSTM1 gene that may influence the metabolism of the drug. We will not look at any other gene, such genetic risk for cancer. The result of whether you have the GSTM1 gene will NOT be recorded in your medical record. We will store your DNA sample for 5 years unless we receive your request for us to discard your sample sooner. Your request can be by simple phone call, in person, or by email to our study team.

Visit 1:
This visit may occur at Strong Memorial Hospital AC3 or Highland Hospital and will take about one hour to complete. The following procedures will occur at this visit:

Drug Dosing: You will be randomized (like the flip of a coin) to take either 2 tablets or 4 tablets of the study drug once a day for 7 days.

Questionnaires: You will be provided instructions and 3 paper questionnaires to take home and fill out. Each questionnaire will be completed at Visit 1 and as noted below:

- *General Questionnaire:* Includes questions about how you are feeling, if you experience any new symptoms. Completed daily for the 7-day period.

- *Gastrointestinal Questionnaire*: Includes questions about symptoms. Completed on Day 3 and Day 7.

- *Kansas City Cardiomyopathy Questionnaire:* Includes questions about heart failure symptoms. Completed on Day 3 and Day 7.

Tracker: A chart will be provided to help you track daily study drug intake and questionnaires. This form will also include study drug dosage and 7-day study timeline.

At Home Procedures: At the end of visit 1, you will be given the study drug. questionnaires, and the tracker to take home. You will take the assigned drug dosage once daily as instructed. You will also complete the study questionnaires on the designated day(s), as instructed.

Visit 2:
On day 7, you will come to the Clinical Research Center (CRC) in Strong Memorial Hospital. Visit 2 will take about 8-hours to complete with food and beverage provided during this period.

You will need to bring your last dose of the study drug with the package, along with the all the study questionnaires, and the tracker sent home with you at visit 1. The following procedures will occur with Visit 2:

Drug Dose: You will take your study drug dose with food in front of a study coordinator.

Blood Draw: You will have blood drawn through a vein in your arm or hand at 5 separate intervals; immediately after you take the medication, at 1 hour, 2 hours, 4 hours and 8 hours after. An IV-line will be placed for the blood draws to minimize needle sticks. You

are free to leave in between blood collection times. Approximately 4 mL (just slightly more than a teaspoon) of blood will be obtained each time.

Urine Sample: You will also a urine sample occur immediately after each blood draw. Approximately 1 milliliter of urine will be obtained each time in sterile cup.

Information about your study participation and study results may be included in your electronic health record. If you have concerns about this or to obtain more detail, you should discuss this with the study team.

Number of Subjects:
Approximately 24 subjects with chronic kidney disease will take part in this study.

Risks of Participation

Avmacol ES - Study Drug: While Avmacol has been well-tolerated in other clinical trials such as for autism, chemotherapy drug toxicity, it has not been previously tested in patients with kidney disease. The potential risks are side effects. The most common side effects are headache and gastrointestinal, including nausea and indigestion, which are lessened or prevented when taken with food. Since Avmacol has a short half-life, we expect the side effects would be short-lived when the drug is stopped.

Based on the multiple clinical trials that have been done with Avmacol or the actual sulforaphane compound in other diseases, we do not anticipate any serious risks.

Although not reported in any earlier trial, it is possible that you may have an allergic reaction to the study drug. This reaction may be mild, such as a skin rash, or you may have more severe symptoms like swelling of the throat, low blood pressure, and shortness of breath. In rare cases, a severe reaction could cause death.

Blood Draws: Blood draws may cause pain, redness, bruising or infection at the site of the needle stick. Rarely some people faint. The study team member may apply numbing cream to the area so that the needle stick won't hurt as much.

Buccal (cheek) Swab: The risk associated with this procedure are minimal.

Urine Sample: The risk is minimal. There is risk of spilling urine onto clothes during your collection.

Pregnancy: The effect of sulforaphane on the fetus is not known. If you think you may be pregnant, please immediately stop taking the drug and notify the research team.

Risks of Questionnaires: There are no anticipated risks for you to complete the requested questionnaires other than the time it takes to complete them. If any questions make you uncomfortable, you may skip them or stop any time.

Risks to Social/Emotional Well-Being: We do not anticipate any psychological, social or legal risks beyond those related to participation in a clinical study.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, (NCT05153174) 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 website at any time.

The study team may be notified if you receive other health care services at URMC or its Affiliates (e.g., visit to the emergency room). In addition, the following individuals may know you participated in research and may see results of testing conducted for this study:

- Staff at the University of Rochester Medical Center and its Affiliates (e.g., Strong Memorial Hospital, Highland Hospital, URMC primary care, specialist physician offices) who have a reason to access your electronic health record.
- Health care providers who are involved in your care at a facility that is not part of the University of Rochester Medical Center and its Affiliates and who have reason to access your electronic health record.
- Individuals who request a copy of information from your health record for activities such as treatment or payment (e.g., medical insurance companies, worker's compensation).

Benefits of Participation

You might not benefit from being in this research study. Your participation will enable us to determine the best dose for the next study in patients with chronic kidney disease in which you would also be eligible to participate in.

Compensation for Injury

If you are directly injured by Avmacol ES, or by medical procedures needed because of this study, and you receive medical care for the injury, you may need to pay for that care. You will be reimbursed for reasonable and necessary medical costs for such care, but you might not be reimbursed for care covered and paid for by a third party like your health insurance provider, or costs such as required co-payments or deductibles related to that coverage. No other funds have been set aside to pay for such things as lost wages or expenses due to a current underlying illness or condition.

If your research injury is paid for by the University, we will collect your name, date of birth, gender, and Medicare Health Insurance Claim Number or Social Security Number to determine your Medicare status. This information will be used only in accordance with the law. If you are a Medicare beneficiary, information about the study you are in, and any payments made related to your injury, will be reported to the Centers for Medicare & Medicaid Services (CMS), in accordance with CMS requirements. This information will not be used for any other purpose.

Costs

There will be no cost to you to participate in this study.

Payments

You may be paid up to $100.00 for your participation in the study via a prepaid Visa card:
Visit 1: $50.00
Visit 2: $50.00
Expect up to 4-6 weeks for the prepaid card to be processed and mailed after the completion of each study visit.

Confidentiality of Records and Authorization to Use and Disclose Information for Research Purposes

The University of Rochester makes every effort to keep the information collected from you private. We will not label your data/samples with identifying information about you, such as your name, medical record number or social security number. We will label your data/samples with a unique ID# and store your identifying information linked to the code in a separate document. All data/samples will be stored in a secure manner. Sometimes, however, researchers need to share information that may identify you with people that work for the University, regulators or the study sponsor.

If you have never received a copy of the University of Rochester Medical Center (URMC) and Affiliates Notice of Privacy Practices, please ask the investigator for one.

What information may be used and given to others?

The study doctor will get your personal and medical information. For example:

- Research records
- Records about phone calls made as part of this research
- Records about your study visits
- Past and present medical records related to the study, including records of external providers that are available via your electronic health record at URMC & Affiliates
- Results of medical tests

Who may use and give out information about you?

- The study doctor and the study staff
- URMC and Affiliates

Your information may be given to:

- The Department of Health and Human Services
- The University of Rochester
- University of Virginia, to share de-identified data
- National Institute of Health (NIH) who is the sponsor for this study (they provide funding to conduct the study).
- Nutramax who provides the study drug
- The U.S. Food and Drug Administration (FDA) may also need to inspect study records at some point during the study or even after it has been completed. In the event that this should occur, every effort will be made to keep identifying information about you private.

Why will this information be used and/or given to others?

- To do the research
- To study the results
- To see if the research was done correctly

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

How long will this permission be valid?
This permission will last indefinitely.

May I cancel my permission to use and disclose information?
Yes. You may cancel your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. Upon receiving the written notice, the study team will no longer use or disclose your health information and you will not be able to stay in this study. Information that has already been gathered may need to be used and given to others for the validity of the study.

May I withdraw from the study?

Yes. If you withdraw your permission to be in the study, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
No. There is a risk that your information will be given to others without your permission.

Future Use of Information/Samples
Your information and samples might be distributed or used for future research studies without additional informed consent. All identifiers will be removed before your information and samples are used or distributed. You will be given the option at the end of this consent form to decide if you would like your information or samples used for future research.

Circumstances for Dismissal
You may be withdrawn from the study if you do not keep appointment for study visits or if you cannot complete study activities. You also may be withdrawn from the study if your disease becomes worse or if your doctor feels that participating in the study is harmful to your health, if you become pregnant, or if you have a new diagnosis such as advanced heart failure, cardiovascular event, life threatening infection, or cancer.

Completion of the first phase
To ensure your safety after you have stopped the study drug, our research coordinator will call after about 2 weeks to ask how you are feeling, and whether you have developed any new symptoms.

As noted, this is a phase 1 study being done to establish a safe dose of Avmacol ES for patients with chronic kidney disease. Once you complete this phase of the study, you may be eligible to participate in the next phase (Phase 2) of the study which is expected to last about 6 months.

New Study Information
If we discover any new information that is clinically relevant, we will let you know.

Sponsor Support
The University of Rochester is receiving funding support from the National Institutes of Health (NIH) for conducting this research study.

Commercial Profit
We will use your information and/or samples for research only. However, the results of this research might someday lead to the widespread use of sulforaphane in the treatment of chronic kidney disease. You will not receive money from the sale of

sulforaphane.

Return of Research Results
In general, we will not give you any individual results from your participation in the study. If we find something of urgent medical importance to you, we will inform you, although we expect that this will be a very rare occurrence.

You will not receive your individual results.

Some things you should know about the results:

- While we expect to have an idea of how kidney function level will affect the metabolism of the drug, it is possible the results will difficult to interpret.
- For the genetic part of this study, we will only determine whether or not you have the GSTM1 gene that may influence the metabolism of the drug. We will not look at any other gene.

Certificate of Confidentiality
To help us further protect your privacy, the investigators have a Certificate of Confidentiality from the Department of Health and Human Services (DHHS).

With this Certificate, the investigators cannot be forced (for example, by court subpoena) to disclose or use research information, documents, or samples that may identify you in any Federal, State, or local civil, criminal, administrative, legislative, other proceedings, or be used as evidence. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes, or to other government agencies related to communicable diseases.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your consent to receive research information, then the investigator may not use the Certificate to withhold that information. This means that you and your family must also actively protect your own privacy.

Finally, you should understand that the investigator is not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself or others. Include the following only if applicable: The Certificate of Confidentiality will not be used to prevent disclosure to state or local authorities of child abuse and neglect, or serious harm to the subject or others.

Contact Persons

For more information concerning this research or if you feel that your participation has resulted in any research related injury, emotional or physical discomfort, please contact**:** Dr. Thu Le at 585-275-1554 or the nephrologist on call after regular hours.

Please contact the University of Rochester Research Subjects Review Board at 265 Crittenden Blvd., CU 420628, Rochester, NY 14642, Telephone (585) 276-0005 or (877) 449-4441 for the following reasons:

- You wish to talk to someone other than the research staff about your rights as a research subject;
- To voice concerns about the research;
- To provide input concerning the research process;
- In the event the study staff could not be reached.

Voluntary Participation

Taking part in this study is voluntary. You are free not to take part or to withdraw at any time, for whatever reason. No matter what decision you make, there will be no penalty or loss of benefit to which you are entitled. In the event that you do withdraw from this study, the information you have already provided will be kept in a confidential manner.

This will not affect the care you receive for chronic kidney disease.

CONSENT TO FUTURE USE OF INFORMATION / SAMPLES

May we share your samples, health information, and genotype data with other researchers who study kidney disease?

Yes No

May we share your samples, your GSTM1 data, and health information with other researchers for future research projects related to other topics?

Yes No

CONSENT TO RE-CONTACT

May your study doctor, or someone from the study team, contact you in the future about using your samples or information for research that is not described in this consent form?

Yes No

May your study doctor, or someone from the study team, contact you in the future to see if you would like to participate in other research?

Yes No

SIGNATURES/DATES

After reading and discussing the information in this consent form you should understand:

- Why this study is being done;
- What will happen during the study;
- Any possible risks and benefits to you;
- Other options you may have instead of being in the study;
- How your personal information will be protected;
- What to do if you have problems or questions about this study.

Subject Consent

I have read (or have had read to me) the contents of this consent form and have been encouraged to ask questions. I have received answers to my questions. I agree to participate in this study. I have received (or will receive) a signed copy of this form for my records and future reference.

_____

Subject Name (Printed by Subject)

_____ _____

Signature of Subject Date

Person Obtaining Consent

I have read this form to the subject and/or the subject has read this form. I will provide the subject with a signed copy of this consent form. An explanation of the research was given and questions from the subject were solicited and answered to the subject's satisfaction. In my judgment, the subject has demonstrated comprehension of the information. I have given the subject adequate opportunity to read the consent before signing.

_____

Name and Title (Print)

_____ _____

Signature of Person Obtaining Consent Date