CSP #2008 - Pentoxifylline in Diabetic Kidney Disease

NCT03625648

7/27/2026

Participant Name: _____ Date: _____

Title of Study: Pentoxifylline in Diabetic Kidney Disease (PTXRx)

Principal Investigator: INSERT NAME HERE VA Facility: INSERT FACILITY HERE

Principal Investigators for Multisite Study: David Leehey, MD; Rajiv Agarwal, MD, MS

INTRODUCTION

You are being invited to take part in a research study that is being funded by the Department of Veterans Affairs. Before you decide to take part, it is important for you to know why the research is being done and what it will involve. This includes any potential risks to you, as well as any potential benefits you might receive.

Read the information below closely and discuss it with family and friends if you wish. Ask one of the study staff if there is anything that is not clear, or if you would like more details. Take your time to decide. If you do decide to take part in this study, your signature on this consent form will show that you received all of the information below, and that you were able to discuss any questions and concerns you had with a member of the study team.

BACKGROUND AND PURPOSE

Diabetic kidney disease (DKD) is the most frequent cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD) in the U.S. and in U.S. Veterans. CKD is a decrease in the ability of the kidneys to filter out toxic substances. ESRD means the decline in kidney function is severe enough to require dialysis or kidney transplant. Control of blood pressure (BP) and blood sugar has led to some improved results in recent years. However, many patients continue to progress to ESRD, requiring costly dialysis or transplantation and resulting in high death rate. Thus, additional treatments are needed for DKD.

Pentoxifylline (PTX) is a drug approved by the Food and Drug Administration in 1984 for use to treat a disease or disorder that affects blood flow called “peripheral vascular disease”. Newer information suggests that when PTX is used in addition to standard care (blood pressure and blood sugar control, avoiding certain medications, etc.) in patients with DKD, may be protective to the kidneys. However, this information is not definite, and a large-scale clinical trial is needed to determine whether this drug can reduce the occurrence of ESRD and death in patients with DKD.

The goal of this study is to see whether PTX, when added to standard care, leads to a reduction in ESRD and death in type 2 diabetic patients with DKD when compared to standard care plus placebo (a look-alike pill that has no active drug in it). ESRD, that is continuous need for dialysis, receiving a kidney transplant, and death are the identified primary endpoints in this study. Endpoints in this or any other study are events or outcomes that clearly determine if the added treatment is of any benefit.

This study will involve 5,000 participants from 40 VA sites across the country. Here at (*name of VA facility*) we plan to enroll up to 250 participants.

DURATION OF THE RESEARCH

There is a four (4) year enrollment period for this study. Once enrolled, participants will receive their randomized study drug and will be followed for a minimum of five (5) years. Therefore, if you are enrolled early, your participation in the study, that is receiving study drug and follow up, could be up to nine (9) years.

STUDY PROCEDURES

If you qualify and decide to take part in this study, this is what will occur:

- You may have up to 38 scheduled study visits over a 9-year period (or less depending what year you enroll).

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- Your schedule for follow-up visits will be every 90-days; time and dates will be determined between you and the study coordinator.
- We will aim to schedule your study visits on a day when you have an existing appointment at (name of facility). **If this is not possible, then a phone visit may be scheduled.**

YOUR RESPONSIBILITIES DURING THIS STUDY:

- Take the study drug as instructed,
- Keep your study appointments,
- Tell the investigator or research staff if you believe you might be pregnant or are thinking of becoming pregnant,
- Keep the study drug in a safe place for your use only and away from children,
- Complete your questionnaires as requested,
- Ask questions as you think of them,
- Tell the investigator or research staff if you change your mind about staying in the study,
- While participating in this research study, **do not to take part in any other research project without approval from the investigators**.
    - This is to protect you from possible injury from things such as extra blood drawing or potential drug interactions.
    - Taking part in other research studies without first discussing it with the investigators of this study may invalidate the results of this research, as well as that of the other studies.

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SUMMARY OF VISITS

BASELINE VISIT (V1)

During the first in-person visit we will review this consent document with you and answer all your questions. We will also review a VA HIPAA Authorization form with you. The VA HIPAA Authorization form tells you what information we will be collecting about you during this study as well as with whom we will share that information. If you agree to participate and sign the consent and HIPAA, you will receive a copy of both forms.

Once you have agreed to participate in the study, we will check your blood pressure and you will have the blood samples taken. If you already had these blood tests taken on the day of this visit, they will not be repeated.

Otherwise, the following blood samples will be taken for:

- Creatinine/eGFR. Creatinine is a waste product produced by muscles. Creatinine is removed from the body by the kidneys, which filter almost all of it from the blood and release it into the urine. This test measures the amount of creatinine in the blood. An eGFR is a blood test that measures the amount of creatinine in the blood and uses the result in a formula to calculate a number that reflects how well the kidneys are functioning,
- Hemoglobin A1c (HbA1c) blood test will be done. The HbA1c evaluates the average amount of glucose in the blood over the last 2 to 3 months
- A blood test will be done to determine your Calcium, Phosphorus, Magnesium, and Albumin levels. Approximately 1 tablespoon of blood will be taken for these tests.
- A urine sample will also be collected for measurement of urine albumin/creatinine ratio (UACR). The UACR is another measure of the kidney function measuring the amount of creatinine in the urine.
- Women of childbearing potential, that are not menopausal, will also receive a urine pregnancy test. Pregnant women cannot participate in the study.

Your medical history will be reviewed including any current medications you may be taking. This includes prescriptions as well as any over the counter drugs (OTC).

You will be asked to complete the *Kidney Disease Quality of Life* (KDQoL) survey. If you do not want to or feel uncomfortable answering a question, you may skip that question.

RANDOMIZATION INTO THE TRIAL

If you are found to be eligible to participate, you will be randomized to the study drug, that is either PTX 400 mg tablet or the matching placebo tablet. Randomization is a method based on chance alone by which study participants are assigned to a treatment group. There is a 1:1 ratio for assignment. If medically necessary, there is someone who can break the blind and give the information to your care providers in an emergency.

You will have a 50/50 chance of receiving either PTX 400mg or a matching placebo tablet. Which one you will receive will be determined by a computer program, not by choice of the study doctor or yourself. Neither you nor the study doctor will know which treatment you get until after the study is over, which is called “blinding.” If medically necessary, there is someone who can break the blind and give the information to your care providers in an emergency.

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This randomization can occur at the first study visit if all essential information has been obtained, if not you will be notified by the study doctor about the randomization and study drug shipment.

Once you are randomized to your assigned study drug (either PTX 400 mg or Placebo tablet), your initial 90-day supply of study drug will be shipped to your home address. All study drug is mailed from, and must be returned to, the Cooperative Studies Program Clinical Research Pharmacy Coordinating Center (CSPCRPCC) in Albuquerque, New Mexico, via direct mail.

A 90-day supply of the study medication will be mailed to you every 3 months until the end of study participation. The study medication will initially be taken one tablet once daily in the morning with food. Study medication should be taken with food to reduce the risk of stomach discomfort like an upset stomach, nausea, vomiting or indigestion.

VISIT 2 (V2) WEEK 5

- The second visit is an in-person, face-to-face visit and should be done about 5 weeks after your Visit 1 date. **This visit can be conducted over the phone if an in-person visit is not possible.**
- At this visit your study doctor will determine how well you are managing your study drug and if you are having any problems taking the study drug. At this time your dosage could be changed to one tablet, twice a day with food.

ROUTINE STUDY ACTIVITIES

- **Starting at Visit 3, on all ODD NUMBERED study visits (VISITS 3,5,7,9, etc.) the following will be performed:**
- We will ask you about taking your study medication, if you have had any problems or side effects.
- We will ask you if there has been any change in any of your regular medication prescriptions or OTC drugs.
- We will ask you if there has been any change in your health, if you have been sick, injured, or admitted to the hospital.
- We will ask you if you have started dialysis or if you have had a kidney transplant.
- If you are female and of childbearing potential, we will ask if you might be pregnant. And if you are using methods to avoid pregnancy.
- Tell the investigator or research staff if you changed your mind about staying in the study.
- We will schedule the next 90-day follow-up visit.

As part of this study, we will monitor your health to ensure the study is safe. We will check your medical records from your non-VA healthcare providers. We can do this through a VA system that communicates directly with your non-VA health care provider(s), like your community doctor's office. The system pulls in your medical records directly from your non-VA provider, and we can only read them; we cannot make any changes.

VISIT 4; 6 MONTHS AFTER V1 DATE

We will do all Routine Study Activities, and collect the below lab results:

- UACR **-** if you have not had one within 14 days then you will need to have one completed.
- Creatinine/eGFR - if you have not had one within 90 days, then you will need to have one completed.

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VISITS 8, 12, 16, 20, 24, 28, 32, AND 36 (EVERY 6 MONTHS)

We will do all Routine Study Activities plus the following:

- Creatinine/eGFR - if you have not had one within 90 days, then you will need to have one completed.

VISITS 6, 10, 14, 18, 22, 26, 30, 34 (ANNUAL 12-MONTH VISITS):

We will do all Routine Study Activities plus the following:

- Creatinine/eGFR - if you have not had one within 90 days, then you will need to have one completed.
- KDQoL Survey – approximately three (3) weeks prior to this visit we will mail the KDQoL Survey to you for you to complete. We will review the survey questions with you over the phone to collect your answers. If you do not want to or feel uncomfortable answering a question, you may skip that question.

END OF TRIAL VISIT:

This visit will be done in person. We will do all Routine Activities plus the following:

- Creatinine/eGFR - if you have not had one within 90 days then you will need to have one completed.
- KDQoL Survey - If you do not want to or feel uncomfortable answering a question, you may skip that question.

POSSIBLE RISKS OR DISCOMFORTS

RISKS OF TAKING THE STUDY DRUG

The study drug you receive might be Pentoxifylline. Pentoxifylline has been approved in the United States since 1984. It's main treatment of peripheral vascular disease, has decades of documented safety information with minimal side effects.

ANY MEDICATION HAS POSSIBLE SIDE EFFECTS

- Though PTX is usually very well-tolerated, side effects that have been reported in more than 1% of patients include: upset stomach, nausea, vomiting, dizziness, and headache. These are more common when the study drug is first started and usually lessen or disappear over time.
- *To reduce the risk of these side effects,* take the study drug with food. Any increase in dose will be done in slow steps, as tolerated. If side effects are not manageable, your dose may be decreased.
- A few rare events have been reported spontaneously worldwide since marketing in 1972. Uncommon and rare side effects include chest pain, palpitations, hypersensitivity, itchiness, rash, and bleeding.

ADDITIONAL RISKS ASSOCIATED WITH PENTOXIFYLLINE

Pentoxifylline can interact with other medications that you may be currently taking. Make sure your health care provider and your study team know about all the medications you are taking before you start taking the study medication.

Drawing of blood. May result in a bruise that goes away in one week and rarely is associated with a fainting reaction.

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- **Risks of the usual care.** The care you receive for your medical conditions are not risks of the research. Those risks are not included in this consent form. You should talk with your health care providers if you have any questions about the risks of usual care.
- **Intolerance to study treatment.** Study medications should be taken with food to reduce the risk for developing GI disturbances (upset stomach, nausea, vomiting or diarrhea). Most of the GI disturbances are mild and will disappear after the first month.

POTENTIAL BENEFITS

We cannot promise that you will get any benefits from taking part in this research study.

REPRODUCTIVE AND SEXUAL ACTIVITY INFORMATION:

For women participants of childbearing potential: If you are pregnant, become pregnant your participation in the study will have to end. Before you start the study drug and while you are taking part in the study you must use an effective form of birth control. You must also agree to continue to use an effective form of birth control for one additional menstrual cycle following the final study visit. Effective birth control includes:

- Oral, implanted or injectable hormonal contraceptives,
- intrauterine devices (IUDs), and/or
- barrier methods (e.g., condoms, diaphragm, and cervical cap) with spermicide.

If you become pregnant during the study or within 1 month of stopping the study drug, you must immediately tell the study staff. It will be necessary for you to stop taking the study drug immediately and transitioned to "limited participation status." Once you have completed the pregnancy and you are no longer breast feeding, you may be able to return to active participation in the study.

ALTERNATIVES TO PARTICIPATING IN THIS RESEARCH

You may choose not to participate in this study. If this is your decision, there are other choices such as standard care of treatment. You may discuss these options with your doctor. ***No matter your choice, your VA benefits will NOT be affected.***

CONFIDENTIALITY

Taking part in this study will involve collecting confidential information about you. This information will be protected in the following ways:

- Handling and storage of study data will adhere to current VA policies. Study data will not contain information that can directly identify you (such as name, address, etc.); however, it will not be a completely de-identified database since age and study visit dates will be collected.
- The Cooperative Study Program Coordinating Center (CSPCC) at the Hines VA Hospital requires that a copy of the signed consent form be on file at the Hines CSPCC. The consent form is required by CSP policy for the coordinating center to independently certify that all study participants have been consented. Consent forms are stored separately from study data.
- All paper-based records, including KDQoL surveys will be kept in locked file cabinets at the participating sites and Hines CSPCC. Retention and disposal of these documents will follow the published National Archives and Records Administration (NARA) guidelines.

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- The servers housing the study databases will be located at a secure VA facility and housed behind the VA firewall on VA-owned and VA maintained servers. The system will be monitored to ensure that all applicable VA regulations and directives are strictly followed.
- Access to the study data is restricted by the Hines CSPCC to properly credentialed research staff who has completed required VA security trainings. Only CSP-approved individuals will have access to the personal health information (PHI) of study participants.
- To determine your satisfaction with the study medication instructions you may be contacted by representatives from The Joint Commission (TJC) to complete a brief survey. The surveys would be mailed to you from CSPCRPCC. Your responses could be shared with TJC.
- Information about you will be combined with information from other people taking part in the study. We will write about the combined data we have gathered. Any talks or papers about this study will not identify you.

The information collected for this study will be kept confidential. We will include information about your study participation in your medical record. There are times when we might have to show your records to other people. For example, someone from the Office of Human Research Protections, the Government Accountability Office, the Food and Drug Administration (FDA), the Office of the Inspector General, the VA Office of Research Oversight, the VA Central IRB, and our local Research and Development Committee, and other monitors may look at or copy portions of records that identify you.

We have obtained a Certificate of Confidentiality from the Federal Government. This helps protect your privacy by allowing us to refuse to release your name or other information outside of the research study, even by a court order. The Certificate of Confidentiality will not be used to prevent disclosures to local authorities of child abuse or neglect, or harm to self or others. The Certificate does not prevent you or a member of your family from releasing data about yourself or your involvement in this study.

We will include information about your study participation in your medical record.

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 website at any time.

COSTS TO PARTICIPANTS AND PAYMENT

Neither you nor your insurance will be charged for any treatments or procedures that are part of this study. If you usually pay copayments for VA care and medications, you will still pay these co-payments for VA care and medications that are not part of this study.

PAYMENT OFFERED FOR PARTICIPATION:

You will receive a payment for your time and any inconvenience you may have while participating in this study. The payment for your first visit will be $40.00 and then $10.00 for each follow up visit whether they are in person or over the telephone. Your total amount will vary depending as to when you enroll in the study. There will be no payment for unscheduled contact or phone calls without associated visit activities. If you transition to "limited participation status" (*see the "Changing your Participation" section for more information*), regardless as to the reason, you will **not** be eligible to receive payments upon your change in status.

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Payment will be issued according to local medical center policy and procedures and will be explained to you at your initial visit. [LSI/SC to add payment schedule (quarterly vs yearly) and mode of payment (check mailed/ check picked up/ cash at Agent Cashier)]

Internal Revenue Service Form 1099 will be issued to you annually, regardless of amount you have been paid. Your full social security number will be used to complete the IRS 1099 form.

MEDICAL TREATMENT AND COMPENSATION FOR INJURY

Every reasonable safety measure will be used to protect your well-being. If you are injured because of taking part in this study, the VA will provide necessary medical treatment at no cost to you unless the injury was due to your not following the study procedures.

If you should have a medical concern or get hurt or sick because of taking part in this study, call:

Provider Name	Office Hours Number	Pager Number (After-Hours)

Emergency and ongoing medical treatment will be provided as needed.

You do not give up any of your legal rights and you do not release the VA from any liability by signing this form.
PARTICIPATION IS VOLUNTARY

It is up to you to decide if you want to take part in this study. If you decide to take part, you may still withdraw at any time. If you do not wish to be in this study or leave the study early, you will not lose any benefits to which you are entitled. If you do not take part, you can still receive all usual care that is available to you. Your decision not to take part will not affect the relationship you have with your doctor or other staff, and it will not affect the usual care that you receive as a patient.

CHANGING YOUR PARTICIPATION

If you do not wish to take part in the study, you can stop your participation at any time. At that point you will be considered to have limited participation with limited data collection.

We will stop your study drug shipments, your 90-day follow up telephone calls will end, you will not have any face-to-face visits, and we will ask you to mail all remaining study drug and packaging back to the CSPCRPCC.

We will continue to review your medical records to see how you are doing for either the term of the study or the time when you reach one of the study's primary endpoints. If you decide to stop participating in this study, and you withdraw your consent, we will no longer continue to review your medical records to see how you are doing, and we will not collect any information from your medical records.

RIGHT OF STUDY DOCTOR TO STOP YOUR PARTICIPATION

Besides being diagnosed with ESRD, your study doctor may stop your participation if you are not able to take the study drug, or if you are unable to fulfill your responsibilities with the study. If this were to happen, we will review your medical records in 30 days from the time you stopped the study for overall safety. We will then review your medical record every 90 days for the term of the study or the time when you reach one of the

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study's primary endpoints. ***Your usual medical care will not be affected regardless as to why you stopped participating in the study.***

PERSONS TO CONTACT ABOUT THIS STUDY

If you have questions about your rights as a study participant, or you want to make sure this is a valid VA study, you may contact the VA Central Institutional Review Board (IRB). This is the Board that is responsible for overseeing the safety of human participants in this study. You may call the VA Central IRB toll free at 1-877-254-3130 if you have questions, complaints or concerns about the study or if you would like to obtain information or offer input.

SIGNIFICANT NEW FINDINGS

Sometimes during a research study, new information becomes available about the study medication, PTX, that might change a person's decision to stay in the study. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw from the study, your research doctor will arrange for your medical care to continue. If you decide to continue in the study, you might be asked to sign an updated informed consent form. Your research doctor could also decide it may be in your best interests to withdraw you from the study. If so, he or she will explain the reasons and arrange for your usual medical care to continue.

FUTURE USE OF DATA AND RE-CONTACT

Sometimes important information is obtained after the treatment phase of the study is done. By signing this consent, you give permission to the study team to continue to follow your health status after you have finished the study. The study team will use central databases such as, but not limited to, VA medical records, VA National Patient Care Database, and Centers for Medicare & Medicaid Services. Data related to your health status may include your vital status (still living or deceased) and cancer related diagnoses. After you have completed the study, the study team will access your medical records only as it relates to the study.

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Principal Investigators for Multisite Study: David Leehey, MD; Rajiv Agarwal, MD, MS

AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY

Dr./Mr./Ms._____ has explained the research study to you. You have been told of the risks or discomforts and possible benefits of the study. You have been told of other choices of treatment available to you. You have been given the chance to ask questions and obtain answers.

By signing this document below, you voluntarily consent to participate in this study. You also confirm that you have read this consent, or it has been read to you. You will receive a copy of this consent after you sign it.

I agree to participate in this research study as has been explained in this document.

_____	_____	_____
Participant's Name	Participant's Signature	Date

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