Temple IRB Approved

09/26/2018

Title of research: Dosing strategies for de novo once-daily extended release tacrolimus (LCPT) in kidney transplant recipients

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Why am I being invited to take part in this research?

We invite you to take part in a research study because you are 18 years of age or older and a kidney transplant recipient at Temple University Hospital . Tacrolimus is a drug that helps to decrease the strength of your body's immune system to stop your body from rejecting the new kidney you are receiving. You will receive tacrolimus whether or not you agree to be in this study. The purpose of this research is to determine the appropriate dosing of an extended release form of tacrolimus.

What should I know about this research?

- Someone will explain this research to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.
- Information regarding this study is available on Clinicaltrials.gov
- This study is supported by Veloxis Pharmaceuticals, Inc

Who can I talk to about this research?

If you have questions, concerns, or complaints, or think the research has hurt you, contact the research team: 3401 N Broad Street, Philadelphia, PA 19140; *(215)-280-8041* and email

This research has been reviewed and approved b an Institutional Review Board. You may talk to them at (215) 707-3390 or e-mail them at for any of the following:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

Why is this research being done?

We are studying patients who are getting a new kidney. This is because we want to see if extended release tacrolimus will help us to reach target levels of the drug when it is started sooner after surgery. Another part of this research study will involve looking at your gene type for the protein that metabolizes Tacrolimus to see whether or not your type metabolized Tacrolimus more or less quickly. Extended release Tacrolimus may or may not result in reaching the correct level of Tacrolimus faster after transplant surgery especially in patients with the gene type CYP 3A5. To protect your privacy, any genetic testing will be done after we have removed your name and other identifiers and it will not be included in your medical record.

How long will I be in this research?

Your participation in this research will end after your thirty day visit, completed approximately one month after kidney transplant.

What happens if I agree to be in this research?

If you agree to participate in this research you will:

- agree to give Temple University hospital study investigators and research staff permission to view your medical record to get information for research purposes—such as drug doses and blood test results
- complete a one-time short health questionnaire
- provide a one-time saliva sample for genetic testing

If you volunteer to be in this study you are required to give a saliva sample for genetic testing, do a questionnaire about tremors, and receive a different form of tacrolimus (extended-release tacrolimus) at a different point in your care. The difference between the standard of care that you would get if you weren't in this study compared to the care that you would get if you were in the research study are listed here:

Standard of Care/Usual Care (If you weren't in the study)

- All kidney transplant patients (who are not in this research study) at Temple University Hospital will get multiple medications right after kidney transplant surgery to suppress the immune system and prevent kidney rejection. One of the drugs that is given is immediate release/short acting Tacrolimus. The exact day after surgery that Tacrolimus is started is usually decided by your doctor. Once you are discharged and leave the hospital all patients are seen in clinic three times each week. One of the reasons you are seen so often is to monitor the levels of the medications you are taking to prevent kidney rejection. One of the side effects of Tacrolimus is tremors (shaking). In patients who experience tremors, we may already switch to the extended release/long acting form of Tacrolimus which may be less likely to cause this side effect. The other reason that we use extended

release/long acting Tacrolimus in usual care is for patients who have trouble remembering to take their pills. Extended release/long acting Tacrolimus only has to be taken once a day, while immediate release/short acting Tacrolimus has to be taken more often.

Research (How does your care change in study)

- If you decide to participate in this study you will still receive multiple medications to prevent kidney rejection and you will still need to be seen 3 times per week in the clinic to monitor your health and medication levels. **There are four main differences in your care if you agree to participate.**
- **First, you will be given extended release/long acting Tacrolimus instead of immediate release/short acting Tacrolimus**
- **Second, you will start Tacrolimus extended release/long acting immediately after surgery instead of waiting until your doctor starts Tacrolimus extended release/long acting.**
- **Third, you will agree to let us collect a required saliva sample for genetic testing to see how your body metabolizes Tacrolimus**
- **Fourth, you will fill out a survey about tremors 30 days after you have started the Tacrolimus.**

Usual care versus research care are shown in the Table below (Table A).

Table A Tests and Visits Performed with Usual Care and with Research Care

	Usual Care	Research Care	Procedure Performed for Research Only
Blood Tests on Day of Surgery (Creatinine, Potassium, Glomerular Filtration Rate, Glucose and HbA1C)	✓	✓	**No**
Tacrolimus levels (daily in hospital once drug started)	✓	✓	**No**
Tacrolimus levels after hospital discharge (3 times weekly for the first month, usually Mon, Wed, Friday)	✓	✓	**No**
Additional blood Tests after hospital discharge (3 times weekly for the first month, usually Mon, Wed, Friday) Creatinine, Potassium, Glomerular Filtration Rate, Glucose and HbA1C	✓	✓	**No**
Tremor Questionnaire (Day 30)		✓	**Yes**

Saliva sample for genetic testing		✓	**Yes**

The investigators and research staff will also collect health information that relates to the study from the medical record. This health information will be information about kidney function, potassium level, blood glucose, Hemoglobin A1C, and the levels of the study drug in your body all taken from the blood tests listed in Table A above. Only authorized researchers will have your personal health information and be able to link this with your saliva samples or to you or your name. All personal health information will be confidential. In the event that incidental findings are discovered in your medical record you will be notified within 24 hours by the Principal Investigator (Adam Diamond) by phone. Results of genetic testing will not be shared with you. If any incidental findings are discovered, which is not likely, you will be called by phone with these genetic testing results regardless of whether you have opted in or not within 24hrs by the Principal Investigator.

The timeline for this study is that the research staff and investigators will collect health information from your medical record, beginning on the day of your kidney transplant and ending at the 30 day visit. As a result you will approximately be in the study for 30 days. After the 30 day visit data collection will stop. The saliva sample and questionnaire will be collected before your 30 day visit.

Is there any way being in this research could be bad for me?

- **Extended release/long acting Tacrolimus instead of immediate release/short acting Tacrolimus –** We do not expect many differences in the standard side effects of Tacrolimus by using the extended release form. There is a chance that your tacrolimus levels will reach goal more or less quickly with extended release tacrolimus. Therefore there is a chance that your could be more or less likely to be at risk for kidney rejection. Your doctors will be monitoring your tacrolimus levels closely as part of usual care and will increase or decrease your tacrolimus dose as needed. The usual side effects of tacrolimus include: Headache**,** diarrhea**, s**welling in the legs**, t**remors, high blood pressure**,** high cholesterol, high blood sugars, high potassium, altered kidney function, and increased risk of infections, and an increased risk of two types of cancer (skin and lymphoma). As part of usual care, your doctors will be monitoring you for these side effects.

- **Second, you will start Tacrolimus extended release/long acting immediately after surgery instead of waiting until your doctor starts Tacrolimus extended release/long acting –** we do not expect an increased risk from this change in care other than what is already described above.
- **Third, you will agree to let us collect a saliva sample for genetic testing to see how your body metabolizes Tacrolimus -** Your genetic results will not be linked to patient identifiers (your personal information).

- **Fourth, you will fill out a survey about tremors 30 days after you have started the Tacrolimus –** there are no risks from this study procedure but it will take about 10 minutes of your time.
  Risks to Participants- **The use of the study drug tacrolimus extended-release (Envarsus) include:**

- Headache
- Diarrhea
- Swelling in the legs
- Tremors
- High blood pressure
- High cholesterol
- High blood sugars
- High potassium
- Increased serum creatinine
- Upper respiratory tract infection
- Urinary tract infection
- Common cold
- Viral infections
- Fungal infections
- Increased risk of lymphoma
- Increased risk of skin cancer

Risks associated with the use of all tacrolimus products (including the study drug and other forms of tacrolimus):

- Headache
- Diarrhea
- Swelling in the legs
- Tremors
- High blood pressure

- High cholesterol
- High blood sugars
- High potassium
- Increased serum creatinine
- Upper respiratory tract infection
- Urinary tract infection
- Common cold
- Viral infections
- Fungal infections
- Increased risk of lymphoma
- Increased risk of skin cancer

The risk for acute organ rejection is present in all patients after kidney transplant on any immune suppressing therapies. Tacrolimus extended-release doses will be adjusted to achieve blood concentrations consistent with standard of care to minimize risk for organ rejection.

The greatest additional risk provided to participants enrolled in this study is keeping your personal information private and confidential. This is because data will be collected for research purposes from Epic and Alpha medical record and because of the saliva samples for genetic testing. The Temple University and the study investigators will protect all patient records and personal information to the extent permitted by law. Patient identifiers will be kept private and physical forms will be filed in a locked cabinet and electronically stored in a password protected and encrypted manner. Personal health information will be kept confidential.

If you are injured as a result of taking part in this research, *immediately* notify the research team and they will arrange for you to receive medical care. Temple University, and Temple University Health System and its subsidiaries, will not provide monetary compensation or free medical care to you in the event of a research-related injury. You or your insurance company will be billed for your medical care. If you have a research-related injury, please contact Adam Diamond at (215)-280-8041 during regular hours and after hours, weekends, and holidays.

You may also have to pay for the cost of the study medication, which is the tacrolimus extended-release form. Depending on your insurance, the copay of the study medication (tacrolimus extended-release form) may be higher than tacrolimus immediate-release form. In most cases the copay would be a similar cost for the study medication (tacrolimus extended-release form).

Will being in this research help me in any way?

As a volunteer for this research there may or may not be any direct benefit to you. There is a possibility that your target tacrolimus levels will be reached more quickly by starting Tacrolimus extended release/long acting sooner and by using the extended release form. There is a possibility that you may experience less side effects of tremors with the extended release form. However, it is also possible that you will experience no benefit from being in this study. We hope that the information learned from this research will help other patients, in the future, who also need a kidney transplant.

What happens to the information collected for this research?

We are dedicated to protecting your privacy and the confidentiality of your personal health information. To do this, your name and anything else identifying you will be removed from all health information and the saliva sample collected and they will be assigned a random number. Any forms with information that can identify you will be stored in a locked drawer and locked researcher room that can only be seen by research staff.

Results of genetic testing will not be put into your medical record, and will only be used for research purposes. The protected health information will not be reused or disclosed to any other person or entity outside of the research team, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the protected health information would be permitted.

Any results or health information collected for this research will be used indefinitely, or until we are contacted by the patient to indicate that they no longer permit to the use of their information. We may publish the results of this research. However, your name and other identifying information will be confidential and not included in any published papers.

To the extent allowed by law, we limit the viewing of your personal information to people who have to review it. We cannot promise complete secrecy. The IRB, Veloxis Pharmaceuticals, Inc, Temple University, Temple University Health System, Inc. and its affiliates, and other representatives of these organizations may inspect and copy your information.

Your signature documents your permission to take part in this research.

Signature of subject	Date
Printed name of subject	
Signature of person obtaining consent	Date

Printed name of person obtaining consent