FULL PROTOCOL TITLE
A Pilot Study of Terazosin for Parkinson's Disease

SHORT PROTOCOL TITLE
TZ-PD

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INFORMED CONSENT DOCUMENT

Project Title: A Pilot Study of Terazosin for Parkinson's Disease

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This consent form describes the research study to help you decide if you want to participate. This form provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights as a research subject.

If you have any questions about or do not understand something in this form, you should ask the research team for more information.

You should discuss your participation with anyone you choose such as family or friends.

Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We are inviting you to participate in this research study because you are above the age of 40 and have been diagnosed with Parkinson's Disease.

The purpose of this research study is to study the safety and tolerability of Terazosin when taken at 5mg. You will slowly ramp up to taking 5mg, you will not begin taking the drug at 5mg. Researchers at the University of Iowa Hospitals and Clinics are interested in developing new ways to slow the progression of Parkinson's Disease. Terazosin is used to treat high blood pressure or an enlarged prostate, but recent data shows that some of its effects could slow down the progression of Parkinson's Disease symptoms. Terazosin is not FDA approved for use in treating Parkinson's Disease, and its use in this research is investigational. As part of this research study, we are interested in seeing how Terazosin effects energy deficits caused by your Parkinson's disease. We will do this by evaluating the level of a chemical used for energy in your body called ATP. This chemical will be measured in your blood and brain, before and after you start taking Terazosin.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 30 people will take part in this study conducted by investigators at the University of Iowa.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for 3 months and will include 4 in person visits, and 4 telephone call visits. The 1st in person visit will range from 7-8 hours. There will be an in-person follow-up appointment approximately 9 days after the initial visit that will last 2-3 hours. Additionally, there will be in person follow-up appointments 6 weeks and 12 weeks after the first visit that will range from 3-5 hours. There will be four phone call check-ins that will last 20-30 minutes and will record any side effects from the study drug.

WHAT WILL HAPPEN DURING THIS STUDY?

This is a multi-visit study including 8 separate visits; 4 in-person and 4 telephone visits. The in-person visits will involve several or all the following procedures: blood draw, magnetic resonance imaging (MRI), and testing for cognitive, mood, and motor function. You will be randomly assigned to receive one of the 2 study treatments, either Terazosin, or a pill that looks like the drug, but has no active ingredients, called a placebo. This means that whichever study treatment you receive will be determined purely by chance, like flipping a coin. You will have a 50/50 chance of receiving any one of the study treatments. Neither you nor the research team will know which study treatment you are receiving, but we will be able to get this information quickly if we need it to ensure your safety. If you are taking any medication for the treatment of high blood pressure, you should discuss your involvement in this research with your physician. For each in-person study visit, we ask that you come in an OFF state. Meaning, if you are taking carbidopa/levodopa as part of your Parkinson's treatment, you will not have taken this medication for at least 8 hours before your study visit. After the motor exam is complete, or approximately 2 hours into each study visit, you will be able to take your carbidopa/levodopa.

Cognitive Testing

Cognitive testing is a way to learn how you think and perform on a variety of different tasks. These tests evaluate such things as your memory, reasoning, attention, and vocabulary skills. These tests will take about 30 to 60 minutes. During the tests, you may skip any questions that you prefer not to answer. Cognitive testing is for research purposes only. You will not be provided the results from these tests.

Physical and Neurologic Testing

You will be asked to have your height, weight, and vital signs measured. A trained professional will administer a basic neurological examination called the United Parkinson's Disease Rating Scale. Examination will consist of things such as tapping fingers, walking heel-to-toe, balancing on one leg and tapping on joints to measure reflexes. You will be asked to complete a timed up and go assessment, where you will stand up, walk 3 meters, walk back, and sit down. You will also complete a finger tapping exercise using an accelerometer, a tool used to measure acceleration. You will be asked to complete health history questionnaires about any current medical issues and treatment you may be receiving. Additionally, you will be asked to complete a health history questionnaire about medical issues within your family. In all, physical and neurologic testing will require approximately 30 to 60 minutes. Results from these exams are only for research, not for your health care, and will not be provided to you.

Blood Draw

You are being asked to give four 20mL blood samples for this study. This is about 4 teaspoons each time. Because these analyses are being done for research purposes, the results are experimental data. What we learn about you from this sample will not be put in your health record, and your test results will not be shared with you or with your doctor. No one apart from the research team (such as a relative, boss, or insurance company) will be given your results.

Magnetic Resonance Imaging

An MRI scanner takes pictures of the inside of your brain by sending out a magnetic field and radio waves. Because the MRI scanner contains a very strong magnet, you may not be able to have the MRI if

you have certain kinds of metal in your body (like a heart pacemaker, a metal plate, and certain types of heart valves or brain aneurysm clips). You will be asked questions about this before you have the MRI. The MRI scanner is a large machine that contains a hollow tube. You will be asked to lie on your back on a special table that slides into the tube. The sides of the tube will be close to your body and the scanner makes a loud hammering noise while you are inside. You will be able to talk to people in the room through a speaker system. We will monitor you closely while you are inside the scanner. The MRI scan will take approximately 45 to 60 minutes. The MRI is for research purposes only. A radiologist will not read the MRI, therefore structural brain abnormalities such as tumors or vascular abnormalities will not be detected.

Study Treatment Schedule

To minimize risk of side effects from the drug, both study treatments will follow a strict titration schedule to ramp up to the intended study dose. The titration schedule for both study treatments is as follows:

- Week 1 (including first visit): 1mg once daily
- Week 2: 2mg once daily
- Week 3: 3mg once daily
- Week 4: 4mg once daily
- Weeks 5-12: 5mg once daily

If during the titration schedule (outside of the scheduled visits and phone calls) you feel you are having adverse side effects, call your research team contact. If it is a medical emergency, seek medical attention immediately and then report the incident to your research team contact.

Due to the duration of the study visits and the importance of completing the assessments at a consistent time of day during the course of the study, each in-person study visit will begin at 8am at the University of Iowa – Hospitals and Clinics.

Screening Visit (after consent is signed)

- You will complete the Beck Depression Inventory, Beck Anxiety Inventory, Columbia-Suicide Severity Rating Scale, and MRI Screening Sheet to further determine your eligibility
- If you screen eligible after completing the assessments, you will work with the Research Assistant to schedule your first visit

1st Visit: Week 1 (in-person) – 7-8 hours

- Review inclusion/exclusion criteria and complete and videotape UPDRS III, timed up and go, finger tapping, and audio record the speech assessment
- A medical doctor will assess you
- Neurological nurse will collect vitals, height & weight, pregnancy test (if of childbearing age), UPDRS I-II, IV, draw blood (20mL, which is approximately 4 teaspoons), and collect a list of your current medications
- You will receive a 45-60 minute MRI scan and immediately after you will receive the first dose of study drug (either Terazosin or placebo) and dispensed 3 months of study drug
- A research team member will conduct all assessments and complete all necessary questionnaires with you

- 3 hours after the dose you will receive a second blood draw and a 45-60 minute MRI scan

2nd Visit: Week 2 (in-person) – 2-3 hours

- Members of the research team will complete and videotape UPDRS I-IV, timed up and go, finger tapping, and audio record the speech assessment
- Neurological nurse will collect vitals, height & weight, and update medication list, if necessary
- A research team member will collect your demographics, your medical history, and your family medical history
- A research team member will conduct all assessments and complete all necessary questionnaires with you

3rd Visit: Week 3 (phone) – 20-30 minutes

- A research team member will call you to record any side effects you may be experiencing

4th Visit: Week 4 (phone) – 20-30 minutes

- A research team member will call you to record any side effects you may be experiencing

5th Visit: Week 5 (phone) – 20-30 minutes

- A research team member will call you to record any side effects you may be experiencing

6th Visit: Week 6 (in-person) – 3-4 hours

- Members of the research team will complete and videotape UPDRS I-IV, timed up and go, finger tapping, and audio record the speech assessment
- A medical doctor will assess you
- Neurological nurse will collect vitals, height & weight, pregnancy test (if of childbearing age), UPDRS I-II, IV, draw blood (20mL, which is approximately 4 teaspoons), and update medication list, if necessary
- A research team member will review your demographics and make updates to any changes in your medical history
- A research team member will conduct all assessments and review/update all necessary questionnaires with you

7th Visit: Week 9 (phone) – 20-30 minutes

- A research team member will call you to record any side effects you may be experiencing.

8th Visit: Week 12 (in-person) – 4-5 hours

- Members of the research team will complete and videotape UPDRS I-IV, timed up and go, finger tapping, and audio record the speech assessment
- A medical doctor will assess you
- Neurological nurse will collect vitals, height & weight, pregnancy test (if of childbearing age), UPDRS I-II, IV, draw blood (20mL, which is approximately 4 teaspoons), update medication list, if necessary

- You will receive a 45-60 minute MRI scan
- A research team member will review your demographics and make updates to any changes in your medical history
- A research team member will conduct all assessments and review/update all necessary questionnaires with you and you will return study equipment, and medication

TISSUE/BLOOD/DATA STORAGE FOR FUTURE USE

As part of this study we are obtaining blood samples from you. We would like to study your samples in the future, after this study is over. The tests we might want to use to study your samples may not even exist at this time. Therefore, we are asking for your permission to store your samples so that we can study them in the future. These future studies may provide additional information that will be helpful in understanding Parkinson's Disease but it is unlikely that what we learn from these studies will have a direct benefit to you. It is possible that your samples might be used to develop products tests, or discoveries that could be patented and licensed. In some instances, these may have potential commercial value and may be developed to generate profit by the Investigators, University of Iowa, commercial companies, organizations funding this research, or others that may not be working directly with this research team. However, donors of blood samples or data will not retain any property rights to the materials. Therefore, there are no plans to provide financial compensation to you should this occur. We will not perform any genetic testing on your blood samples nor will there be DNA sequencing

If you agree now to future use of your samples but decide in the future that you would like to have it removed from future research, you should contact **Nandakumar Narayanan, MD, PhD at (319) 353-5698.** However, if some research with your **s**amples has already been completed, the information from that research may still be used.

____ Yes, I give permission to store my blood samples for future use.

____ No, I do not give permissions to store my blood samples for future use.

The results from the information (data, blood, MRI) we collect in this research study are not the same quality as what you would receive as part of your routine health care. The testing results will not be reviewed by a physician who normally reads such results. Due to this, you will not be informed of any unexpected findings. The results of your testing will not be placed in your medical record with your primary care physician or otherwise. If you believe you are having symptoms that may require care, you should contact your primary care physician.

KEEPING CONTACT INFORMATION

In the future, we may be conducting follow-up studies similar to this one and may invite you back to participate. To locate you in the future, we will need to keep your contact information on file. Keeping your contact information is optional. If you decide not to have your contact information kept on file, it will not affect your participation in the rest of this research study.

Please indicate your decision by placing your initials in from one of the following statements:

_____ Yes, I agree to have my contact information kept on file for possible future

invitation to participate in research studies.

_____ No, I do not want my contact information kept on file.

VIDEO RECORDINGS

One aspect of this study involves making video recordings of you. Research professionals will utilize these video recordings to study new technologies that can more accurately score the motor portion of this assessment. For this reason, we are asking for you to allow us to take a video recording of you while completing parts of the UPDRS. Each video recording will be identified using a specific ID number. Information such as your name, date of birth, and contact information can be obtained with this ID number but only approved members of the research team have access to this information. No identifiers such as your name, date of birth or other directly identifiable information will be stored with the video recordings. Recordings will be stored in our local, secure computer system in addition to an external hard drive, and only technicians directly involved in processing this data will have access to the data files. No data will be reviewed clinically, and results are not interpreted or provided to participants.

AUDIO RECORDINGS

One aspect of this study involved making audio recording of you. Research professionals will utilize these audio recordings to analyze changes in speech during the duration of this study. For this reason, we are asking for you to allow us to take an audio recording of you while reading sentences. Each audio recording will be identified using a specific ID number. Information such as your name, date of birth, and contact information can be obtained with this ID number but only approved members of the research team have access to this information. No identifiers such as your name, date of birth or other directly identifiable information will be stored with the audio recordings. Recordings will be stored in our local, secure computer system in addition to an external hard drive, and only technicians directly involved in processing this data will have access to the data files. No data will be reviewed clinically, and results are not interpreted or provided to participants.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Terazosin

Common risks associated with taking Terazosin are: dizziness.
Less common risks associated with taking Terazosin are: Chest pain, fainting, fast or irregular heartbeat, pounding heartbeat, shortness of breath, swelling of feet or lower legs
Rare risks associated with taking Terazosin are: weight gain

Pregnancy in women of childbearing potential

If you are a woman of childbearing potential, you should be careful to avoid pregnancy while

participating in this study and use effective contraception. If you are pregnant or plan to become pregnant, you should not participate in this research study. If you think you may have become pregnant during this study, please call your study doctor right away. At each of your in-person visits, you will have a pregnancy test.

Neuropsychological, Behavioral, Physical and Neurological Assessments

The cognitive, behavioral, and neurologic tests pose a minor risk of fatigue and/or frustration. Some of the behavioral questionnaires may include questions that could make some people uncomfortable, particularly measures that record personal mental or physical health and substance use history.

Magnetic Resonance Imaging (MRI)

You may be uncomfortable inside the MRI scanner if you do not like to be in closed spaces ("claustrophobia"). During the procedure, you will be able to talk with the MRI staff through a speaker system. You can tell them to stop the scan at any time. The MRI scanner produces a loud hammering noise, which has produced hearing loss in a very small number of patients. You will be given earplugs to reduce this risk and/or noise blocking headphones.

Blood Sample Collection

The blood drawing procedure may cause some discomfort, and there is the possibility of bruising or infection at the site from which the blood is taken.

Data confidentiality

There is a risk of loss of confidentiality of data. Measures in place to minimize this risk are indicated on the 'What About Confidentiality' section later in the document.

WHAT ARE THE BENEFITS OF THIS STUDY?

We don't know if you will benefit from being in this study. However, we hope, that in the future, other people might benefit from this study.

WHAT OTHER TREATMENT OPTIONS ARE THERE?

Currently there are no known medications that are used to slow the progression of Parkinson's disease; however, there are medications used to treat the symptoms of Parkinson's Disease. The most well know is carbidopa/levodopa. Before you decide whether to be in this study, your doctor will discuss the other options that are available to you.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

All study visits, procedures, and test will be provided at no cost to you. You/your health insurance will remain responsible for your regular medical care expenses that are not part of this study.

WILL I BE PAID FOR PARTICIPATING?

You will be paid $50 for each in-person visit that you complete, for a total of $200 if you complete all 4 visits. You may need to provide your address if a check will be sent to you. You will not receive any payment for the phone call check-ins. You will also receive parking passes the day of your in-person visits to cover the cost of parking in the hospital ramp. Travel compensation will be provided based on the following criteria:

0-25 miles: $20 26-49 miles: $30 50+ miles: $40.

WHO IS FUNDING THIS STUDY?

The University and the research team are receiving no payments from other agencies, organizations, or companies to conduct this research study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

If you are injured or become ill from taking part in this study, medical treatment is available at the University of Iowa Hospitals and Clinics.

The University of Iowa does not plan to provide free medical care or payment for treatment of any illness or injury resulting from this study unless it is the direct result of proven negligence by a University employee.

If you experience a research-related illness or injury, you and/or your medical or hospital insurance carrier will be responsible for the cost of treatment.

WHAT ABOUT CONFIDENTIALITY?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- federal government regulatory agencies,
- auditing departments of the University of Iowa, and
- the University of Iowa Institutional Review Board (a committee that reviews and approves research studies)

To help protect your confidentiality, we will we will keep all data from the cognitive-behavioral battery, demographic profile, medical and family history in locked files. After a series of error checks, the data are stored on a PC in a research assistant's office, which is always locked when not occupied. Access to computer data is strictly limited only to the principal investigator and her research assistant(s) on a protected share drive. Brain imaging data collected on all participants are transferred from the Image Processing Laboratory for subsequent analysis. All data will be identified and stored by ID number only to ensure both confidentiality and blindness. Your blood sample will be labelled by ID and transported by research staff to a lab in Pappajohn Biomedical Institute at the University of Iowa. Your sample will remain there for analysis and storage. Any analysis results will be sent to research staff for data entry. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

The University of Iowa Hospitals and Clinics generally requires that we document your participation in research occurring in a University of Iowa Health Care facility. This documentation will be in either your medical record or a database maintained on behalf of the institution reflecting that you are participating in this study. The information included will provide contact information for the research team as well as information about the risks associated with this study. We will keep this Informed Consent Document in our research files; it will not be placed in your medical record chart.

A version of the informed consent document will be available on the website, Regulations.gov (Docket ID: HHS-OPHS-2018-0021), as required by U.S. Law. The informed consent document will not include information that can identify you. You can search this website at any time.

WILL MY HEALTH INFORMATION BE USED DURING THIS STUDY?

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires University of Iowa Health Care to obtain your permission for the research team to access or create "protected health information" about you for purposes of this research study. Protected health information is information that personally identifies you and relates to your past, present, or future physical or mental health condition or care. We will access or create health information about you, as described in this document, for purposes of this research study. Once University of Iowa Health Care has disclosed your protected health information to us, it may no longer be protected by the Federal HIPAA privacy regulations, but we will continue to protect your confidentiality as described under "Confidentiality."

We may share your health information related to this study with other parties including federal government regulatory agencies such as the FDA, and the University of Iowa Institutional Review Boards and support staff.

You cannot participate in this study unless you permit us to use your protected health information. If you choose *not* to allow us to use your protected health information, we will discuss any non-research alternatives available to you. Your decision will not affect your right to medical care that is not research-related. Your signature on this Consent Document authorizes University of Iowa Health Care to give us permission to use or create health information about you.

Although you may not be allowed to see study information until after this study is over, you may be given access to your health care records by contacting your health care provider. Your permission for us to access or create protected health information about you for purposes of this study has no expiration date. You may withdraw your permission for us to use your health information for this research study by sending a written notice to **Nandakumar Narayanan, MD, PhD, 1336 PBDB, 200 Hawkins Drive, Iowa City, IA 52242.** However, we may still use your health information that was collected before withdrawing your permission. Also, if we have sent your health information to a third party, such as the study sponsor, or we have removed your identifying information, it may not be possible to prevent its future use. You will receive a copy of this signed document.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you

decide to be in this study, you may stop participating at any time. If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

Will I Receive New Information About the Study while Participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can Someone Else End my Participation in this Study?

Under certain circumstances, the researchers might decide to end your participation in this research study earlier than planned. This might happen because in our judgment it would not be safe for you to continue, because your condition has become worse, because you are or became pregnant, because funding for the research study has ended, because the sponsor has decided to stop the research, etc.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, or experience a research-related injury please contact: **Nandakumar Narayanan, MD, PhD at (319) 353-5698.** If you have any immediate questions that need to be addressed outside of normal business hours, please call the **24/7 phone number at 319-356-1616** and inform the operator you are a research subject and ask for the Neurology Resident on call.

If you have questions, concerns, or complaints about your rights as a research subject or about research related injury, please contact the Human Subjects Office, 105 Hardin Library for the Health Sciences, 600 Newton Rd, The University of Iowa, Iowa City, IA 52242-1098, (319) 335-6564, or e-mail irb@uiowa.edu. General information about being a research subject can be found by clicking "Info for Public" on the Human Subjects Office web site, http://hso.research.uiowa.edu/. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Subjects Office at the number above.

This Informed Consent Document is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by signing this Informed Consent Document. Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Subject's Name (printed): _____

_____ _____

(Signature of Subject) (Date)

Statement of Person Who Obtained Consent

I have discussed the above points with the subject or, where appropriate, with the subject's legally authorized representative. It is my opinion that the subject understands the risks, benefits, and procedures involved with participation in this research study.

_____ _____

(Signature of Person who Obtained Consent) (Date)